

# The Effects of Adulterants and Selected Ingested Compounds on Drugs-of-Abuse Testing in Urine

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## Abstract

*Household chemicals such as bleach, table salt, laundry detergent, toilet bowl cleaner, vinegar, lemon juice, and eyedrops are used for adulterating urine specimens. Most of these adulterants except eyedrops can be detected by routine specimen integrity tests (creatinine, pH, temperature, and specific gravity); however, certain adulterants such as Klear, Whizzies, Urine Luck, and Stealth cannot. These adulterants can successfully mask drug testing if the concentrations of certain abused drugs are moderate. Several spot tests have been described to detect the presence of such adulterants in urine. Urine dipsticks are commercially available for detecting the presence of such adulterants, along with performance of tests for creatinine, pH, and specific gravity. Certain hair shampoo and saliva-cleaning mouthwashes are available to escape detection in hair or saliva samples, but the effectiveness of such products in masking drugs-of-abuse testing has not been demonstrated. Ingestion of poppy seed cake may result in positive screening test results for opiates, and hemp oil exposure can cause positive results for marijuana. These would be identified as true-positive results in drugs-of-abuse testing even though they do not represent the actual drug of abuse.*

Persons abusing drugs attempt to adulterate urine specimens to escape detection in drug testing. In this review, the effects of diluted urine, household chemicals, and Internet-based urinary adulterants such as potassium nitrite, pyridinium chlorochromate, and glutaraldehyde on urine drug testing will be discussed. Moreover, techniques available in clinical laboratories to identify such adulterated specimens, including spot tests and dipsticks, are also addressed. The effect of ingesting poppy seed cakes, hemp oil, and coca tea on analysis of drugs of abuse is addressed.

Drug abuse is a critical problem not only in the United States but also throughout the world. Commonly abused drugs are cocaine, cannabinoids, amphetamine, phencyclidine (PCP), and benzodiazepines. Designer drugs such as 3,4-methylenedioxyamphetamine and 3,4-methylenedioxy-methamphetamine (Ecstasy) are commonly used in rave parties, along with Rohypnol (flunitrazepam) and  $\gamma$ -hydroxybutyric acid.

On September 15, 1986, President Reagan issued Executive Order No. 12564 directing federal agencies to achieve a drug-free work environment. The Department of Health and Human Services (formerly the responsibility of the National Institute on Drug Abuse) developed guidelines and protocols for drugs-of-abuse testing. The Mandatory Guidelines for Federal Workplace Drug Testing Programs were first published in the *Federal Register* on April 11, 1988,<sup>1</sup> and were since revised on June 9, 1994,<sup>2</sup> and September 30, 1997.<sup>3</sup> Another notice was issued on April 13, 2004.<sup>4</sup> The overall testing process under mandatory testing consists of proper specimen collection, initiation of the chain of custody, and analysis of the specimen (screening and gas chromatography–mass spectrometry [GC-MS] confirmation,

if needed) by a Substance Abuse and Mental Health Services Administration (SAMHSA)-certified laboratory. The screening by immunoassay should be performed using a US Food and Drug Administration–approved method. The confirmation should be performed by a second technique, preferably by GC-MS). Federal guidelines for cutoff levels of 5 abused drugs in screening and confirmation phases of the drug testing program are summarized in **Table 1**.

It is estimated that approximately 20 million employees are screened each year in the United States for illicit drugs. Marijuana is the most frequently abused drug. Drug testing programs in the United States can be classified as mandatory or nonmandatory. In the mandatory category (eg, the Department of Transportation program), a regulated employer is required by federal regulation to test the employees. In the nonmandatory category, employers choose to test for reasons other than federal requirements. Private employers who are not mandated to test under federal authority have instituted employee drug testing to create a drug-free workplace. These programs also formalized the role of a specialist physician termed medical review officer (MRO). The MRO is an integral part of a drug testing program who can determine the cause of positive results in drug testing (eg, interference or other prescription drugs) and counsel the employee. It is required that a laboratory submit a drug testing result to the MRO within 5 working days of receiving the specimen, and the result must be certified by the certifying scientist.

Federal guidelines define an adulterated specimen as a urine specimen containing a substance that is not a normal constituent or containing an endogenous substance at a concentration that is not a normal physiologic concentration. In the military where the urine sample collection process is supervised, the chances of receiving adulterated specimens are reduced, but in preemployment screening where direct supervision of specimen collection is not practiced, a person may attempt to escape detection by adulterating specimens to avoid unwanted consequences of failing a drug test. Several precautions are taken by

personnel at the collection site to avoid adulteration of submitted specimens, such as asking the donor to remove outer garments (coat or jacket) that may contain concealed adulterating substances. The collector needs to ensure that all personal belongings such as purse or briefcase stay with the collector, but the donor may retain his or her wallet. The collector also directs the donor to empty his or her pockets and display the items to ensure that no item is present that could be used to adulterate the specimen.

## Commercially Available Products to Escape Detection

Common household chemicals such as laundry bleach, table salt, toilet bowl cleaner, hand soap, and vinegar have been used for many years as adulterants of urine specimens in an attempt to avoid a positive drug test result. There is also a popular belief that drinking goldenseal tea helps escape detection. Varieties of products have become commercially available and can be ordered through Internet sites and toll-free numbers. Home test kits are also available commercially to test for certain drugs. Synthetic urine is available from Internet sites as a sure method to beat a drug test in settings where collection of a urine specimen is not supervised. Quick Fix Synthetic Urine is a bottle of premixed urine with all the characteristics of natural urine (correct pH, specific gravity, and creatinine level). The product can be heated in a microwave oven for up to 10 seconds to achieve a temperature between 90°F and 100°F. It can also be taped next to a heating pad to maintain the normal temperature of urine for up to 6 hours in a pocket.

Commercially available products to beat drug tests can be classified under 2 broad categories. The first category includes specific fluids or tablets, along with substantial water intake, to flush out drugs and metabolites. Many of these products can produce diluted urine, and the concentrations of drugs or

**Table 1**  
Federal Guideline for Cutoff Levels for Screening and Confirmation in Urine of Five Abused Drugs

Drug	Screening Level (ng/mL)	Confirmation Level (ng/mL)
Marijuana metabolites ( $\Delta^9$ -tetrahydrocannabinol-9-carboxylic acid)	50	15
Cocaine metabolite (benzoylecgonine)	300	150
Opiate metabolites	300 or 2,000	300 or 2,000
Morphine	—	300 or 2,000
Codeine	—*	300 or 2,000
6-Acetyl morphine <sup>†</sup>	—*	10
Phencyclidine	25	25
Amphetamine	1,000	500
Methamphetamine <sup>‡</sup>	—	500

\* A combination of codeine and morphine may be detected by opiate immunoassays. These assays do not differentiate between codeine and morphine.

<sup>†</sup> Tested only when the morphine concentration is  $\geq 2,000$  ng/mL by the initial screening tests.

<sup>‡</sup> Specimen must also contain amphetamine at a concentration  $\geq 200$  ng/mL.

metabolites can be significantly reduced. Common products are Absolute Detox XXL Drink, Absolute Carbo Drinks, Ready Clean Drug Detox Drink, Fast Flush Capsules, and Ready Clean Gel Capsules. The second category of products includes in vitro urinary adulterants, which are added to urine after specimen collection to pass a drug test. Stealth (contains peroxidase and peroxide), Klear (nitrite), Instant Clean ADD-IT-ive (glutaraldehyde), and Urine Luck (pyridinium chlorochromate [PCC]) are urinary adulterants available through the Internet. Iodine is a strong oxidizing agent and may potentially destroy abused drugs, especially tetrahydrocannabinol (THC), if present in urine.<sup>5</sup> A recent article indicates that papain, a cysteine protease with intrinsic ester hydrolysis ability, can significantly reduce the concentration of 11-norcarboxy- $\Delta^9$ -tetrahydrocannabinol (THC-COOH), a metabolite of marijuana, if added to the urine specimen in vitro. This product is relatively inexpensive and commercially available. Papain, however, did not significantly decrease concentrations of other drugs analyzed (by enzyme multiplied immunoassay and fluorescence polarization immunoassay [FPIA]), except nordiazepam.<sup>6</sup>

### Diluted Urine: An Attempt to Escape Detection by Decreasing the Concentrations of Drugs of Abuse

A negative result for the presence of abused drugs in a urine specimen does not mean that no drug was present. It is possible that the amount of drug was below the cutoff value for detection in the laboratory assay. Diluting urine is a simple way to make an otherwise positive drug test result negative. Federal guidelines recommend placing a toilet bluing agent in the toilet tank, if possible, so that the reservoir of water in the toilet bowl always remains blue. There should be no other source of water in the enclosure where urination takes place.

Consumption of a large amount of fluid before drug testing is a way to avoid a positive test result.<sup>7</sup> A creatinine concentration below 20 mg/dL or a specific gravity below 1.003 should be considered an indication of diluted urine. Creatinine analysis in urine is a very effective method to detect diluted urine. Needleman and Porvaznik<sup>8</sup> considered a creatinine value of less than 10 mg/dL as suggestive of replacement of a urine specimen largely by water. Beck et al<sup>9</sup> reported that 11% of all urine specimens submitted to their laboratory for drugs-of-abuse testing were diluted.

The SAMHSA program does not allow analysis of diluted urine specimens at lower screening and confirmation cutoffs. However, the Correctional Services of Canada (CSC), for diluted urine specimens, incorporates lower screening and confirmation cutoffs for drugs and metabolites (amphetamine: screening cutoff, 100 ng/mL; confirmation cutoff, 100 ng/mL;

benzoylecgonine: screening and confirmation cutoffs, 15 ng/mL; opiates, screening and confirmation cutoffs, 120 ng/mL; PCP: screening and confirmation cutoffs, 5 ng/mL; and cannabinoids, screening cutoff, 20 ng/mL; confirmation cutoff, 3 ng/mL). Fraser and Zamecnik<sup>10</sup> reported that 7,912 urine specimens collected and analyzed between 2000 and 2002 by the CSC were diluted, and of those specimens, 26% had positive screening results using SAMHSA cutoff values. When lower values for cutoff and confirmation were adopted, 1,100 specimens tested positive for 1 or more illicit drugs. The positive rate of diluted specimens was 18.2% in CSC institutes and 22.3% in parolee specimens. The drug most often confirmed as positive in diluted specimens was marijuana. Codeine and/or morphine were also commonly confirmed in these urine specimens and ranked second after marijuana in prevalence.<sup>10</sup> Soldin et al<sup>11</sup> reported that there was more than a 100% increase in cocaine-positive specimens when the cutoff was lowered to 80 ng/mL from 300 ng/mL in a pediatric population because neonates cannot concentrate urine to the same extent as adults.

Luzzi et al<sup>12</sup> studied the analytic performance criteria of 3 immunoassay systems (EMIT, Beckman EIA, and Abbott FPIA [Abbott Laboratories, Abbott Park, IL]) for detecting abused drugs with concentrations less than established cutoff values. They concluded that drugs can be screened at concentrations much lower than the cutoffs established by SAMHSA. For example, the authors proposed a THC-COOH cutoff value of 35 ng/mL using EMIT and 14 ng/mL for the Beckman EIA and the FPIA, for which SAMHSA guidelines stated a cutoff value of 50 ng/mL. The proposed cutoff values were based on the studies of precision of the assays at proposed lower detection limits at which the coefficient of variation was less than 20%. This lowering of the cutoff values increased the number of positive specimens in the screening tests to 15.6%. A 7.8% increase was also observed in the confirmation stage of drugs-of-abuse testing.<sup>12</sup>

New SAMHSA regulations indicate that a specific gravity less than 1.0010 (new refractometers can detect such low concentrations, to 4 decimal places accurately) or more than 1.020 and a creatinine concentration less than 5 mg/dL are inconsistent with normal human urine.<sup>13</sup> Edgell et al<sup>14</sup> performed a controlled hydration study with 56 volunteers to determine whether it is possible to produce such diluted urine. Subjects were given 2,370 mL of fluid, and urine specimens were collected at the end of each hour for a 6-hour test period. No urine specimen satisfied the paired substitution criteria (specific gravity  $\leq 1.001$  or  $> 1.020$  and creatinine  $\leq 5.0$  mg/dL) for diluted urine (although 55% of subjects produced at least 1 diluted urine specimen during the first 3 hours of hydration with a creatinine concentration  $< 20$  mg/dL and a specific gravity  $< 1.003$ ). This finding supports the criteria set by SAMHSA for classifying a specimen as substituted.<sup>14</sup>

Barbanel et al<sup>15</sup> studied specific gravity and/or creatinine concentrations in 803,130 random urine specimens submitted to the laboratory. Creatinine and specific gravity measurements were performed on 13,467 of these specimens, and none of them met the lower limit for specific gravity (<1.001) and creatinine concentration (<5 mg/dL). The samples that met 1 of the 2 criteria were from neonates or patients who were severely ill and unlike anyone in the workforce undergoing testing for abused drugs. Samples from 11 patients met the criteria for substituted urine (creatinine concentration, <5 mg/dL; specific gravity, >1.020), but all of the patients were seriously or terminally ill.<sup>15</sup> Cook et al<sup>16</sup> demonstrated that an osmolality cutoff of less than 50 mOsm/kg (50 mmol/kg) can be indicative of substituted urine.

### Flushing, Detoxification Agents, Diuretics, and Herbal Tea to Escape Detection

Flushing and detoxification are frequently advertised as effective means of passing drug tests. Cone et al<sup>17</sup> evaluated the effect of excess fluid ingestion on false-negative marijuana and cocaine urine test results. They studied the ability of Naturally Clean Herbal Tea, goldenseal tea, and hydrochlorothiazide to cause false-negative results. Volunteers drank 1 gallon of water (4 doses in a 4-hour period) or herbal tea or hydrochlorothiazide 22 hours after smoking marijuana cigarettes or intranasal administration of cocaine. The creatinine levels dropped below the cutoff 2 hours after intake of excessive fluid. Marijuana and cocaine metabolite levels (as measured by EMIT and TDx) decreased significantly, and results frequently switched from positive to negative after subjects consumed 2 quarts of fluid. Even excess water consumption effectively diluted a urine specimen to cause false-negative results. Consumption of herbal tea produced diluted urine faster than consumption of water alone.<sup>17</sup> Consumption of goldenseal tea produces dark urine and can be identified by visual inspection.<sup>18</sup> A more sophisticated approach to identify marker compounds of goldenseal tea in a specimen suspected of contamination is the use of high-performance liquid chromatography.<sup>19</sup>

Diuretics are used in sports for 2 purposes: to flush out previously taken banned substances by forced diuresis and to achieve quick weight loss to qualify for a group in a lower weight class. Ingestion of salicylate-containing drugs and sodium bicarbonate is also done to avoid positive results in drug testing.<sup>6</sup> The Medical Commission of the International Olympic Committee bans the use of diuretics. There is no commercially available immunoassay for detecting diuretics such as hydrochlorothiazide in urine, and a sophisticated technique such as liquid chromatography combined with tandem

mass spectrometry is necessary to confirm the presence of diuretics in doping analysis.<sup>20</sup>

### Common Household Chemicals as Urinary Adulterants

People try to beat drug testing by adding adulterants to urine specimens. Several adulterants can cause false-negative results in drug testing by immunoassays. Common adulterants for masking drug testing are as follows: (1) table salt, (2) household vinegar, (3) liquid laundry bleach, (4) concentrated lemon juice, (5) goldenseal tea (produces dark urine), and (6) eyedrops.

Although FPIA is less subject to interference from adulterants than the EMIT assay, some interference has also been reported with FPIA. Sodium chloride caused negative interference with all drugs tested by EMIT and a slight decrease in measured concentrations of benzodiazepines by FPIA. Sodium bicarbonate caused false-positive results with an EMIT opiate assay and with PCP testing by FPIA. Hydrogen peroxide caused false-positive benzodiazepine results by FPIA.<sup>21</sup> Uebel and Wium<sup>22</sup> studied the effects of household chemicals (sodium hypochlorite, Dettol [chloroxylenol], glutaraldehyde, Pearl hand soap, ethanol, isopropanol, and peroxide) on cannabis and methaqualone test results using EMIT assays. Most of the agents tested interfered with the test results, and the greatest effect was observed with glutaraldehyde and Pearl hand soap for methaqualone (false-negative). Dettol and Pearl hand soap also caused false-negative results in cannabis tests. Addition of isopropanol, ethanol, and peroxide invalidated a methaqualone test result.<sup>22</sup>

Schwarzhoff and Cody<sup>23</sup> studied the effect of 16 adulterating agents (ammonia-based cleaner, L-ascorbic acid, eyedrops, drain opener, goldenseal tea, lemon juice, lime solvent, liquid bleach, liquid hand soap, methanol, sodium chloride, tribasic potassium phosphate, toilet bowl cleaner, white vinegar, ionic detergent, and whole blood anticoagulated with EDTA) on analysis of urine by FPIA for abused drugs. They tested these adulterating agents at a 10% by volume concentration of urine with the exception of goldenseal tea because of its insolubility. For goldenseal tea, 1 capsule was suspended in 60 mL of urine. Of 6 drugs tested (cocaine metabolites, amphetamines, opiates, PCP, cannabinoid, and barbiturates), the cannabinoid test was most susceptible to adulteration. Approximately half of the agents tested (ascorbic acid, vinegar, bleach, lime solvent, eyedrops, and goldenseal tea) caused false-negative results. Cannabinoid and opiate assays were susceptible to bleach, and actual degradation of THC was confirmed by GC-MS. The PCP and benzoylecgonine (the metabolite of cocaine) analyses were affected by alkaline agents.<sup>23</sup> Baiker et al<sup>24</sup> reported that hypochlorite (a common

ingredient of household bleach) adulteration of urine caused a decreased concentration of THC as measured by GC-MS. A false-negative result was also observed with the FPIA screen and the Roche Abuscreen (Roche Diagnostics, Indianapolis, IN).<sup>24</sup> Another report described adulteration of urine specimens with denture cleaning tablets.<sup>25</sup>

The ability of eyedrops to cause false-negative drug test results in the screening phase of the analysis is troublesome because the presence of components of eyedrops in adulterated urine cannot be detected by routine specimen integrity testing or routine urine analysis. Pearson et al<sup>26</sup> studied in detail the effect of eyedrops on drugs-of-abuse testing and the mechanism by which components of eyedrops produce false-negative drug testing results. Eyedrops are effective in causing false negative results in the analysis of the THC metabolite, THC-COOH. GC-MS analysis showed that there was no modification in the structure of the THC metabolite by the components of eyedrops. At low concentrations of eyedrops, the false-negative cannabinoid result was due to the benzalkonium chloride ingredient of eyedrops. Eyedrops decreased the THC assay results in EMIT/drugs-of-abuse assays and Abuscreen, although eyedrops had no effect on the glucose-6-phosphate dehydrogenase drug conjugate used in the EMIT assay. Results of the ultrafiltration studies with eyedrops suggest that the THC metabolite partitions between the aqueous solvent and the hydrophobic interior of benzalkonium chloride micelles, thus reducing the availability of THC metabolite in antibody-based assays.<sup>26</sup> Eyedrops and analgesic heat rub ointment can also cause false-negative drug test results with sweat testing.<sup>27</sup> Components of eyedrops in urine may be detected by using high-performance liquid chromatography combined with UV detection at 262 nm, a method originally developed for analysis of ophthalmic formulations.<sup>28</sup>

## Specimen Integrity Tests

The collection site and the laboratory have a number of mechanisms to detect potentially invalid specimens. The temperature of the urine, for example, should be 90.5°F to 98.9°F. The specific gravity should be between 1.005 and 1.030, and the pH should be between 4.0 and 10.0. The creatinine concentration should be 20 to 400 mg/dL. A specimen is considered diluted if the creatinine is less than 20 mg/dL and the specific gravity is less than 1.003. The laboratory should perform creatinine and pH analysis of all specimens submitted for drugs-of-abuse testing. Additional tests are also recommended to detect the presence of other adulterants.

Determination of specific gravity is mandatory for any specimen with a creatinine concentration of less than 20 mg/dL. Substituted urine specimens have creatinine concentrations less than 5 mg/dL and a specific gravity of less than

1.001 or more than 1.020. The urine is adulterated if the pH is less than 3 or more than 11.<sup>6</sup> Adulteration with sodium chloride at a concentration necessary to produce a false-negative result always produces a specific gravity of more than 1.035. Use of household chemicals such as bleach, acid, soap, detergent, and vinegar alters the pH of urine to a value outside the physiologic range that can be easily detected by specimen integrity tests. Specimens adulterated with liquid soap are usually cloudy. The presence of eyedrops in adulterated urine cannot be detected by routine specimen integrity testing. Moreover, newer urine adulterants such as Urine Luck, UrinAid, Klear, and Whizzies can also cause false-negative result in drug tests. The presence of these compounds in urine may escape detection by routine specimen integrity tests.

## Adulteration Product Urine Luck

Wu et al<sup>29</sup> reported that the active ingredient of Urine Luck is 200 mmol/L of PCC. They reported a decrease in the response rate for all EMIT II drug screens and for the Abuscreen morphine and THC assays. In contrast, Abuscreen amphetamine assays produced a higher response, and no effect was observed on the results of benzoylecgonine and PCP. This adulteration of urine did not alter GC-MS confirmation test results for methamphetamine, benzoylecgonine, and PCP. However, apparent concentrations of opiates and THC as determined by GC-MS were reduced.<sup>29</sup> Paul et al<sup>30</sup> also studied the effect of Urine Luck on testing for drugs of abuse. When THC-COOH-containing urine specimens were treated with 2 mmol/L of PCC, 58% to 100% of the THC-COOH was lost. The loss increased with decreasing pH and increasing time of incubation (0-3 days). There was no effect on the concentration of free codeine or free morphine if the pH of the urine was in the range of 5 to 7, but at a lower pH, significant loss of free morphine was observed. Amphetamine, methamphetamine, benzoylecgonine, and PCP remained unaffected by PCC at a urine pH of 3 to 7.<sup>30</sup>

## Spot Tests for Detecting Urine Luck (PCC) in Urine

Wu et al<sup>29</sup> also described the protocol for detection of PCC in urine using spot tests. The indicator solution contains 10 g/L of 1,5-diphenylcarbazine (DPC) in methanol. The indicator detects the presence of the chromium ion and is colorless when prepared. Two drops of indicator solution is added to 1.0 mL of urine. If the sample becomes reddish purple, the test result is positive.<sup>29</sup>

Paul et al<sup>30</sup> also used DPC for detection of PCC in urine. When this reagent was added, the sample immediately became red-violet if PCC was present. The chromium-DPC complex showed a characteristic absorption peak at 544 nm and a shoulder peak at 575 nm. The ratio of absorption can be

used to detect the presence of PCC as chromium in urine, and the concentration of chromium can be estimated by measuring absorption at 544 nm, with a linear association between concentrations of 0.5 and 20  $\mu\text{g/mL}$ .<sup>30</sup> Addition of a few drops of PCC-adulterated urine to approximately 0.5 mL of potassium iodide solution followed by addition of a few drops of 2N hydrochloric acid leads to liberation of iodine from potassium iodide, and this can also be used as a spot test to detect PCC. Addition of 4 or 5 drops of 3% hydrogen peroxide to approximately 200  $\mu\text{L}$  of urine adulterated with PCC (approximately 6-7 drops from a transfer pipette) caused rapid formation of a dark brown color (due to reduction of heptavalent chromium by hydrogen peroxide), and a dark brown precipitate appeared on standing. In contrast, unadulterated urine turned colorless after addition of hydrogen peroxide.<sup>31</sup>

Ferslew et al<sup>32</sup> described a capillary ion electrophoresis technique for detecting chromate ion and nitrite ion in urine specimens suspected of adulteration. The DPC colorimetric test for chromate, which can be easily automated, can serve as a screening test. Capillary electrophoretic analysis can be used to confirm the presence of chromate in adulterated specimens, if necessary. A good correlation was observed between chromate concentrations in urine using the colorimetric test and the capillary electrophoretic analysis.<sup>33</sup> Paul<sup>34</sup> described 6 spectroscopic methods for the detection of oxidants, including chromate. The presence of oxidants (as adulterants in urine) was established by initial oxidation of ferrous to ferric ion and then detection of ferric ion by chromogenic oxidation or complex formation. Paul<sup>34</sup> used *N,N*-dimethylamino-1,4-phenylenediamine, 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid), and 2-amino-*p*-cresol for chromogenic oxidation. The reagents for the chromogenic complex formation were xylenol orange, 8-hydroxy-7-iodo-5-quinolinesulfonic acid, and 4,5-dihydroxy-1,3-benzene-disulfonic acid.<sup>34</sup>

## Adulteration of Urine With Nitrite-Containing Agents

The product Klear comes in 2 microtubes containing 500 mg of white crystalline material. This product readily dissolves in urine without affecting color or temperature. Klear may cause a false-negative GC-MS confirmation result for marijuana. ElSohly et al<sup>35</sup> first reported this product as potassium nitrite and provided evidence that nitrite leads to decomposition of ions of 9-THC and its internal standard. They reported that using a bisulfite step at the beginning of sample preparation could eliminate such interference.<sup>35</sup>

Tsai et al<sup>36</sup> further studied the effects of nitrite on immunoassay screening for other drugs, including cocaine metabolites, morphine, THC metabolites (THC-COOH), amphetamine, and PCP. Nitrite at a concentration of 1.0 mol/L

had no effect on the Abuscreen assay. At a higher nitrite concentration, the amphetamine assay became more sensitive, and the THC metabolite assay became less sensitive. The GC-MS analyses of benzoylecgonine, morphine, amphetamine, and PCP were not affected, whereas recovery of the THC metabolite was significantly reduced. Again, this interference could be eliminated by bisulfite treatment.<sup>36</sup>

Duration of nitrite exposure and the urine matrix also affect the THC-COOH assay. In an *in vitro* study, 40 clinical urine specimens confirmed as positive for THC-COOH were supplemented with 1.15 or 0.30 mol/L of nitrite. The results indicated that the pH of the urine and the original drug concentrations have major roles in dictating the effectiveness of nitrite in causing false-negative THC metabolite test results. With an acidic pH, significant decreases in the immunoassay screening results can be observed in all urine specimens within 4 hours of adulteration with nitrite regardless of the original concentration of THC-COOH (range of concentration, 33-488 ng/mL as determined by GC-MS). All specimens were negative for THC-COOH after 1 day. In contrast, the immunoassay results of urine specimens with a basic or neutral pH were less affected by nitrite exposure. Approximately two thirds of the samples with pH values greater than 7.0 had positive immunoassay results, even 3 days after supplementing with nitrite.<sup>37</sup>

Nitrite in urine may arise *in vivo* and is found in urine in a low concentration. Patients receiving medications such as nitroglycerine, isosorbide dinitrate, nitroprusside, and ranitidine may have increased nitrite levels in their blood. However, concentrations of nitrite were less than 36  $\mu\text{g/mL}$  in specimens cultured positive for microorganisms, and nitrite concentrations were less than 6  $\mu\text{g/mL}$  in patients receiving medications that are metabolized to nitrite. On the other hand, nitrite concentrations were 1,910 to 12,200  $\mu\text{g/mL}$  in urine specimens adulterated with nitrite.<sup>38</sup> Whizzies is another urine adulterant available from the Internet. This adulterant also contains potassium nitrite.

## Spot Tests for Nitrite

Addition of a few drops of a nitrite-adulterated urine specimen to 0.5 mL of 1% potassium permanganate solution followed by addition of a few drops of 2N hydrochloric acid turns a pink permanganate solution colorless with effervescence. The presence of very high glucose in urine (>1,000 mg/dL) and ketone bodies may cause a false-positive result. However, it takes approximately 2 to 3 minutes for the solution to turn colorless. On the other hand, if nitrite is present, the solution turns colorless immediately. Another spot test to detect nitrite uses a 1% potassium iodide solution. Addition of a few drops of nitrite-adulterated urine to 0.5 mL of potassium iodide solution followed by addition of a few drops of 2N hydrochloric acid results in immediate release of iodine from

the colorless potassium iodide solution. Shaking of this solution with n-butanol results in the transfer of iodine to the organic phase. If no nitrite is present, the potassium iodide solution remains colorless. There is no interference from a high glucose level or ketone bodies if present in the urine.<sup>31</sup>

Nitrite can also be detected by diazotizing sulfanilamide and coupling the product with *N*-(1-naphthyl)ethylenediamine. The presence of nitrite in urine can also be confirmed by analysis using high-performance liquid chromatography using an IonPac AS 14 analytic column with an anion self-generating suppressor and conductivity detector. By using a single point calibration, the assay was linear up to a nitrite concentration of 12,000 µg/mL. The detection limit was 30 µg/mL.<sup>39</sup> Kinkennon et al<sup>40</sup> described a capillary electrophoresis method for detection of nitrite in urine specimens suspected of adulteration. The method involves separation of nitrite by capillary electrophoresis and direct UV detection at 214 nm. Separation was achieved by using a bare fused silica capillary column and a 25-mmol/L phosphate buffer at pH 7.5. The method was linear for a nitrite concentration of 80 to 1,500 µg/mL, with a limit of detection of 20 µg/mL. However, CrO<sub>4</sub><sup>2-</sup> and S<sub>2</sub>O<sub>8</sub><sup>2-</sup>, as well as high concentrations of Cl<sup>-</sup>, interfered with the chromatography results.<sup>40</sup>

### Stealth as a Urinary Adulterant

Stealth is an adulterant advertised as an effective way to escape detection in a urine drug test. Stealth consists of 2 vials, one containing a powder (peroxidase) and another containing a liquid (hydrogen peroxide). Both products are added to the urine specimen. Stealth is capable of producing false-negative results using the Roche ONLINE and CEDIA (Microgenics, Fremont, CA) immunoassay methods when marijuana metabolites, lysergic acid diethylamide, and opiates (morphine) are present in the urine at 125% to 150% of cutoff values. Adulteration of an authentic positive sample provided by a marijuana user caused the sample to screen as negative with these immunoassay reagents.<sup>41</sup> A low concentration of morphine (2,500 ng/mL) could be effectively masked by Stealth, but a higher concentration (6,000 ng/mL) tested positive by immunoassay (Roche ONLINE and Microgenics CEDIA). GC-MS confirmation can be affected if Stealth is present in the urine. Cody et al<sup>42</sup> reported that GC-MS analysis of Stealth-adulterated urine using standard procedures proved unsuccessful in several cases, and in 4 of 12 cases, neither the drug nor the internal standard was recovered.

Valtier and Cody<sup>43</sup> described a rapid color test to detect the presence of Stealth in urine. The addition of 10 µL of urine to 50 µL of tetramethylbenzidine working solution followed by addition of 500 µL of a 0.1-mol/L phosphate buffer

solution caused a dramatic color change of the specimen to dark brown. Peroxidase activity could also be monitored by using a spectrophotometer. A routine specimen integrity check using pH, creatinine, specific gravity, and temperature did not detect the presence of Stealth in urine.<sup>43</sup> My experience shows that if a few drops of a urine specimen adulterated with Stealth are added to potassium dichromate followed by a few drops of 2N hydrochloric acid, the specimen becomes deep blue immediately, but the color usually fades with time.

### Glutaraldehyde as an Adulterant of Urine

Glutaraldehyde has also been used as an adulterant to alter urine drug test results.<sup>44</sup> This product is available under the trade name UrinAid. The manufacturer sells this product for \$20 to \$30 per kit. Each kit contains 4 to 5 mL of glutaraldehyde solution, which is added to 50 to 60 mL of urine. Glutaraldehyde solutions are available in hospitals and clinics as a cleaning or sterilizing agent. A 10% solution of glutaraldehyde is available from pharmacies as over-the-counter medication for treatment of warts. Glutaraldehyde at a concentration of 0.75% by volume can lead to false-negative screening results for a cannabinoid test using the EMIT II drugs-of-abuse screen. Amphetamine, methadone, benzodiazepine, opiate, and cocaine metabolite tests can be affected at glutaraldehyde concentrations between 1% and 2% with EMIT immunoassays. At a concentration of 2% by volume, the assay of cocaine metabolites is significantly affected (apparent loss of 90% sensitivity). A loss of 80% sensitivity was also observed with the benzodiazepine assay.

Wu et al<sup>45</sup> reported that glutaraldehyde also interfered with the CEDIA for screening of abused drugs. Goldberger and Caplan<sup>46</sup> reported that glutaraldehyde caused false-negative results with EMIT but also caused false-positive PCP results with the FPIA (Abbott Laboratories) and Kinetic Interaction of Microparticles in a Solution Immunoassay (KIMS, Roche Diagnostics).

Although the presence of glutaraldehyde as an adulterant in urine can be detected by GC-MS, Wu et al<sup>47</sup> described a simple fluorometric method for the detection of glutaraldehyde in urine. When 0.5 mL of urine was heated with 1.0 mL of a 7.7-mmol/L concentration of potassium dihydrogen phosphate (pH 3.0) saturated with diethylthiobarbituric acid for 1 hour at 96°C to 98°C in a heating block, a yellow-green fluorophore developed if glutaraldehyde was present. Shaking the specimen with n-butanol resulted in the transfer of this adduct to the organic layer, which can be viewed under long wavelength UV light. Glutaraldehyde in urine can also be estimated by using a fluorimeter.<sup>47</sup>

## Mechanism of Action of Adulterants

Adulterants such as bleach cause false-positive results in THC radioimmunoassays but false-negative results with FPIA and the EMIT assay. These erroneous results are due to the direct effect of bleach on the reagents in the immunoassays.<sup>18,48</sup> Adulterants that are strong oxidizing agents such as Klear (potassium nitrite), Urine Luck (PCC), and Stealth (peroxidase and hydrogen peroxide) cause false-negative results in the immunoassays used for screening drugs by directly destroying THC metabolites (THC-COOH). In the GC-MS confirmation stage, these adulterants interfere with confirmation of THC-COOH because of the destruction of THC-COOH and the internal standard, as well as interference during the extraction phase. To overcome this problem, the use of reducing agents such as sodium hydrosulfite or sulfamic acid before extraction has been recommended.<sup>35</sup> However, such steps can allow detection of the remaining THC-COOH but cannot recover the lost concentration of the marijuana metabolite.

Most oxidizing agents used as adulterants are more effective if the pH of urine is acidic. To prevent destruction of drugs by oxidizing agents, addition of carbonate as a buffering agent before or after the urine is voided has been recommended.<sup>49</sup> Other oxidizing agents such as potassium permanganate, hydrogen peroxide–ferrous ammonium sulfate, periodic acid, potassium persulfate, and sodium oxychloride can also destroy THC-COOH within 48 hours. The effect of oxidizing agents on THC-COOH primarily depends on the reduction potential, pH, temperature, time of reaction, and urine constituents. Horseradish-peroxidase with hydrogen peroxide and a combination of hydrogen peroxide with Japanese radish, black mustard seed, and red radish are effective in destroying THC-COOH. Interestingly, hydrogen peroxide alone was not effective in destroying any drug.<sup>50</sup>

Adulterants can also interfere with the extraction process. Stealth is known to interfere with extraction of codeine and

morphine for GC-MS confirmation.<sup>41</sup> My experience indicates that PCC is effective for decreasing the semiquantitative response rate for THC and opiates using Abuscreen (FPIA). The incubation time had an important role in decreasing the response rate. Nitrite is very effective in reducing the response rate of THC, but the PCP assay was also affected.

## Federal Guidelines for Additional Testing to Detect Adulterants

SAMHSA guidelines require additional tests for urine specimens with abnormal physical characteristics or that show characteristics of an adulterated specimen during initial screening or confirmatory tests (eg, nonrecovery of internal standard and unusual response). A pH less than 3 or more than 11 and a nitrite concentration greater than 500 µg/mL indicate the presence of adulterants. A nitrite colorimetric test or a general oxidant colorimetric test can be performed to identify nitrite. These criteria are summarized in **Table 2**.

Similarly, the presence of chromium can be confirmed by a chromium colorimetric test or a general test for the presence of oxidant. A confirmatory test can be performed using multiwavelength spectrophotometry, ion chromatography, atomic absorption spectrophotometry, capillary electrophoresis, or inductively coupled plasma mass spectrometry.

The presence of halogen (chloride, fluoride, or bleach) should be confirmed by a halogen colorimetric test or a general test for the presence of oxidants. Confirmatory tests may use multiwavelength spectrophotometry, ion chromatography, atomic absorption spectrophotometry, capillary electrophoresis, or inductively coupled plasma mass spectrometry.

The presence of glutaraldehyde should be detected by a general aldehyde test or the characteristic immunoassay response in 1 or more drug immunoassay tests for initial screening. The presence of PCC should be confirmed by using

**Table 2**  
Identification of Adulterated and Substituted Specimens Following Substance Abuse and Mental Health Services Administration Guidelines

Parameter	Diluted Specimen	Adulterated Specimen	Substituted Urine
Creatinine (mg/dL)	<20	—	>5
pH	—	<3 or >11	—
Specific gravity	<1.003	—	<1.0010 or >1.020
Nitrite (µg/mL)*	—	≥500	—
Chromium (µg/mL)*	—	≥50	—
Pyridinium chlorochromate*	—	≥50 µg/mL chromium (VI) equivalent or 200 µg/mL nitrite equivalent	—
Glutaraldehyde*	—	Present	—
Halogen (chloride, fluoride, bleach)*	—	Halogen colorimetric test: ≥200 µg/mL nitrite equivalent or ≥50 µg/mL chromium equivalent	—
Surfactant*	—	Colorimetric test with >100 µg/mL dodecylbenzene sulfonate equivalent	—

\* No guideline has been established for concentrations of these adulterants in diluted urine, if present.

a general test for the presence of oxidant and a GC-MS confirmatory test.

The presence of a surfactant should be verified by using a surfactant colorimetric test with a greater than or equal to 100 µg/mL dodecylbenzene sulfonate equivalent cutoff. Jones and Esposito<sup>51</sup> described a modified methylene blue procedure for the detection and quantitation of surfactants in urine. Based on the analysis of negative samples, an anionic surfactant level of 100 µg/mL or greater could be considered adulterated, but most likely, adulterated specimens will have levels greater than 800 µg/mL.<sup>51</sup>

### On-Site Adulteration Detection Devices (Dipsticks) for Urine Specimens

Standard urinalysis test strips such as Multistix (Bayer Diagnostics, Tarrytown, NY) and Combur-Test (Roche Diagnostics) are sometimes used to detect the presence of adulterants in urine. However, among various pads in the test strip, only pads for detection of nitrite, pH, and specific gravity have some value. The specific gravity test does not differentiate between a specific gravity of 1.000 and 1.005 and, therefore, is very difficult to apply to identify substituted or diluted urine. The nitrite pad also detects a clinically significant range.

On-site adulterant detection devices have become commercially available. These dipstick devices offer an advantage over spot tests because an adulteration check can also be performed at the collection site. Peace and Tarnai<sup>52</sup> evaluated the performance of 3 on-site devices: Intect 7, MASK Ultrascreen, and AdultaCheck 4. Intect 7 simultaneously tests for creatinine, nitrite, glutaraldehyde, pH, specific gravity, PCC, and bleach. Ultrascreen tests for creatinine, nitrite, pH, specific gravity, and oxidants. AdultaCheck 4 tests for creatinine, nitrite, glutaraldehyde, and pH. Peace and Tarnai<sup>52</sup> adulterated urine specimens with Stealth, Urine Luck, Instant Clean ADD-IT-ive, and Klear at optimum use concentrations and concluded that Intect 7 was most sensitive and correctly identified adulterants. AdultaCheck 4 did not detect Stealth, Urine Luck, or Instant Clean ADD-IT-ive. Ultra Screen detected a broader range of adulterants than AdultaCheck 4. However, in practice, it only detected these adulterants at levels well above their optimum usage, making it less effective than Intect 7.<sup>52</sup>

However, King<sup>53</sup> reported that AdultaCheck 4 is an excellent way to detect contamination in urine specimens. AdultaCheck 6 and Intect 7 test strips can determine a range of creatinine values, although the precise concentration of creatinine cannot be determined. Similarly, neither test strip can determine the precise pH of a urine specimen but can only show the range. However, AdultaCheck 6 and Intect 7 test strips are capable of successfully identifying urine specimens with abnormally low creatinine levels and/or pH.<sup>54</sup>

### Adulteration of Hair and Saliva Specimens for Drug Testing

Hair and saliva are considered alternative specimens to urine for drugs-of-abuse testing. Drugs can become trapped in the segment of hair as it develops in a hair follicle. As the hair segment emerges from the follicle and becomes keratinized, it carries the drug trapped in the hair. This trapping of drugs permits analysis a few months after the actual abuse and has a much longer window of detection than urine or saliva testing. However, several factors may influence amount of drug trapped in the hair.

Rollins et al<sup>55</sup> studied the effect of hair color on the amount of codeine trapped in hair follicles by using volunteers and codeine as a model compound. They observed a strong correlation between hair concentration of codeine and melanin concentrations. After 5 days of codeine exposure, 100% of samples from subjects with black hair showed codeine concentrations higher than the suggested federal guideline of 200 pg/mg, 50% of subjects with brown hair demonstrated codeine levels above the cutoff, and subjects with blonde or red hair showed values less than 200 pg/mg.<sup>55</sup>

The presence of THC-COOH in oral fluid is a better indicator of recent use of marijuana than detection of the metabolite in urine. However, concentrations of drugs in oral fluid are low, and small amounts of saliva collected present analytic challenges for saliva testing.<sup>56</sup> The main advantage of saliva and hair testing is that the donor has little chance to adulterate the specimen. Saliva testing is already in use in the transportation and insurance industries, and there is increasing interest in saliva testing in the workplace and for roadside testing for driving under the influence of drugs. It also seems that given the advances of technology and reproducibility of test results, oral fluid test results will be able to survive legal challenges.<sup>57</sup>

Several products are available for sale through the Internet with claims that by washing the hair with these products, a person can pass a drug test. Clear Choice Hair Follicle Shampoo claims to remove all residues and toxins within 10 minutes of use. One application is sufficient for shoulder length hair, and the effect can last for 8 hours. Root Clean hair cleansing system shampoo is also commercially available. However, no systematic study has been reported of the effects of using these products to pass a drug test.

Although the chances of adulteration of saliva specimens are very low to nonexistent, the Saliva Multi-Drug Screen Test 5 (THC, cocaine, opiate, methamphetamine, and benzodiazepine) is commercially available so that a person can self-test for the presence of these drugs at home in a saliva specimen before providing a specimen for actual testing. Oratect multiple drug screen oral fluid testing is a saliva-based test for several drugs (cutoffs: amphetamines, 50 ng/mL; benzodiazepine, 20 ng/mL; cocaine, 100 ng/mL; marijuana, 50 ng/mL; opiates,

20 ng/mL; and PCP, 4 ng/mL). A mouthwash is available commercially (<http://www.ipassedmydrugtest.com>) claiming that rinsing the mouth twice with this product can help a person pass saliva-based drug testing, which is a popular method of testing by insurance companies. Another product from the same company claims to clean hair of any drugs or toxins if the specially formulated shampoo is used. However, the effectiveness of such products in escaping detection by drug tests has not been established by scientific research.

Wong et al<sup>58</sup> studied in detail the effects of commercially available adulterants and foodstuffs on oral fluid drug testing. An on-site oral fluid drug screen (Oratect) showed no effect of American Continental or ethnic food (Asian and Hispanic) on the drug screen result when the adulterant or food was consumed 30 minutes before analysis. Similarly, common beverages, including orange and apple juice, did not cause false-positive results in drugs-of-abuse screening. Cosmetics, toothpaste, mouthwash, and cigarettes also did not show any effect. Wong et al<sup>58</sup> also evaluated the commercially available oral fluid adulterants (Clear Choice, Fizzy Flush, and Spit n Kleen Mouthwash) for their ability to cause a false-negative drug test result and reported that these products are not capable of destroying drugs of abuse in saliva specimens.

## True-Positive Results in Drugs-of-Abuse Screening

### Ingestion of Poppy Seed Cakes

Poppy seed contains opiates, and consuming poppy seed cakes or muffins can produce a positive screening result and, eventually, GC-MS confirmation of morphine and possibly codeine in urine. The concentrations of morphine and codeine were 2,797 ng/mL and 214 ng/mL, respectively, in a healthy volunteer who ingested 3 poppy seed bagels. Opiate was present in the urine 25 hours after ingestion.<sup>59</sup> No opiate was present 45 hours after ingestion. To circumvent this problem, the Department of Health and Human Services increased the screening cutoff of opiate immunoassays from 300 ng/mL to 2,000 ng/mL.

In 1 study, 4 volunteers ate 3 poppy seed bagels each. Neither morphine nor codeine was detected in oral fluids. However, the levels of morphine ranged from 312 to 602 ng/mL in urine. When 3 volunteers ate 1 poppy seed bagel and then an unlimited amount of poppy seeds in 1 hour (volunteer 1, 14.82 g; volunteer 2, 9.82 g; and volunteer 3, 20.82 g), the oral fluid tested positive up to 1 hour after ingestion at a 40-ng/mL cutoff (highest morphine level, 205 ng/mL). Urine specimens were positive for 8 hours.<sup>60</sup> In Germany, a blood level of free morphine should be less than 10 ng/mL in drivers. Moeller et al<sup>61</sup> studied blood and urine morphine levels after subjects consumed poppy seed products. All 5 volunteers

showed positive opiate urine drug test results (up to 2,079 ng/mL by a semiquantitative Abbott assay; urine morphine level, 147-1,300 ng/mL by GC-MS). No blood specimen tested positive for free morphine but yielded morphine levels up to 24 ng/mL following hydrolysis.<sup>61</sup>

Recently, Hill et al<sup>62</sup> studied the effect of ingesting a large amount of poppy seeds on the urinary concentrations of morphine in volunteers. The poppy seed study was performed using Australian poppy seeds because they contain the largest amount of morphine of any poppy seeds available on the US market. The morphine content of Australian poppy seeds ranges from 90 to 200 µg of morphine per gram of poppy seed, whereas Dutch and Turkish poppy seeds contain only 4 to 5 µg of morphine per gram of poppy seed. Ten subjects (6 male and 4 female) ingested 2 servings of poppy seed pastry per week (generally on Monday and Tuesday; 8.1 mg average morphine per serving) for 3 weeks (total morphine consumed, 49 mg). Hair specimens were obtained before and after the study. Urine specimens were obtained for a 24-hour period following poppy seed ingestion and 3 to 5 hours after subsequent ingestion of the poppy seed pastry. The maximum values of urinary morphine ranged from 2,929 to 13,857 ng/mL (as determined by mass spectrometry). Moreover, urinary morphine levels remained higher than the 2,000 ng/mL cutoff for as long as 10 hours. Of 10 subjects, 7 reported drowsiness for 1 hour after eating the poppy seed pastry. The effect lasted 2 to 4 hours. Despite high urinary morphine levels, all subjects had hair levels of morphine less than the standard cutoff (0.04-0.48 ng/10 mg of hair; cutoff, 2 ng/10 mg of hair).<sup>62</sup>

### Health Inca Tea and Mate de Coca Tea

Drinking Health Inca Tea may cause a positive test result for the cocaine metabolite benzoylecgonine. Although US Customs regulations require that no cocaine be present in any herbal tea, literature references indicate that some Health Inca Tea sold in the United States contains cocaine. Jackson et al<sup>60</sup> reported a urinary concentration of benzoylecgonine after ingestion of a cup of Health Inca Tea by volunteers. Benzoylecgonine was present even 26 hours after ingestion. The maximum urinary benzoylecgonine concentration of 1.4 to 2.8 mg/L was observed 4 to 11 hours after ingestion of Health Inca Tea.<sup>63</sup>

Mate de Coca is a commercially available tea made from coca leaves (*Erythroxylon coca*). Turner et al<sup>64</sup> prepared tea by allowing 1 Mate de Coca tea bag to be immersed in 250 mL of boiling water for 25 minutes. The bag was removed and squeezed into the tea to drain additional water. A 5-mL sample was taken for analysis, and volunteers drank the rest. Urine samples were obtained at 2, 5, 8, 15, 21, 24, 43, and 68 hours after drinking tea. All urine samples tested positive for benzoylecgonine, the metabolite of cocaine, by immunoassay. The amount of cocaine in tea was estimated to be 2.5 mg.<sup>64</sup>

## Passive Inhalation of Marijuana

Exceeding the cutoff limit for marijuana tests is difficult to achieve through passive inhalation. The Department of Transportation indicated that MROs should not recognize passive drug exposure as a legitimate medical explanation for a positive test result.<sup>13,65</sup> THC released in air is most likely to exist incorporated as an aerosol particle with a concentration following mixing that becomes highly diluted.

One study indicated that passive inhalation of marijuana may lead to positive screening and confirmation test results in oral fluid up to 30 minutes after exposure.<sup>66</sup> Niedbala et al<sup>67</sup> later studied the effects of passive inhalation of marijuana on urine and oral fluid testing results using high marijuana-containing cigarettes. In study 1, 4 smokers smoked THC mixed with tobacco (39.5 mg of THC) in an unventilated 8-passenger van, and 4 volunteers were passive smokers. In study 2, 4 volunteers smoked marijuana only (83.2 mg of THC). Oral fluid specimens were obtained using the Intercept Oral Specimen Collection Device (OraSure Technology, Bethlehem, PA). Participants were allowed to go outside the van 60 minutes after exposure. Oral fluid specimens were obtained at baseline (30 minutes before exposure); 0, 15, and 45 minutes inside the van; and 1, 1.25, 1.5, 1.75, 2, 2.5, 3.5, 4, 6, and 8 hours outside the van. Oral fluid specimen collection continued up to 72 hours after exposure. Urine specimens were also obtained. Oral fluid was tested for THC metabolites by using the Cannabinoids Intercept Micro-Plate enzyme immunoassay with a cutoff of 3 ng/mL (for the confirmation assay, 2.0 ng/mL). For urine specimens, a 50-ng/mL cutoff was used. All urine specimens tested negative (cutoff, 50 ng/mL) for all passive smokers (GC-MS showed THC metabolite concentrations in the range of 5.8 to 14.7 ng/mL 6 to 8 hours after exposure). In study 1, in which oral fluid specimens were collected in the van, some subjects showed a positive response owing to contamination of the oral fluid collection device with THC smoke, but in study 2, when all oral fluid specimens were obtained outside the van, no positive specimens were observed. On the other hand, all smokers showed significant THC in oral fluid and urine as expected. The mean urinary concentration was 75 ng/mL 4 hours after smoking.<sup>67</sup>

## Ingestion of Products Containing Hemp Oil

A positive cannabinoid workplace drug test following ingestion of a commercially available hemp oil preparation has been reported. The first specimen with a negative test result was 53 hours after ingestion.<sup>68</sup> Alt and Reinhardt<sup>69</sup> reported the presence of THC metabolites 80 hours after the ingestion of 40 to 90 mL of hemp seed oil by volunteers. THC was also detected in blood samples as early as 1 hour after ingestion. Alt and Reinhardt<sup>69</sup> also reported the presence

of THC in hemp food products such as hemp bar, hemp flour, and hemp liquor.

On the other hand, Hemp Ale, an alcoholic beverage formulated, brewed, and bottled by Frederick Brewing (Frederick, MD) does not contain any THC. The manufacturer states that the amount of hemp seed added during the brewing process varies less than 1% between batches. The hemp seeds go through 2 wash cycles before brewing so that vegetative material that potentially may contain THC is removed. Gibson et al<sup>70</sup> reported the absence of THC in Hemp Ale and concluded that ingestion of a moderate amount of the drink is not sufficient to produce a positive cannabis drug screen result. Although some studies showed that consumption of hemp oil can produce a positive THC, Leson et al<sup>71</sup> reported that consumption of 125 mL of hemp oil (0.6 mg of THC) produced a THC metabolite level of only 5.2 ng/mL. Gustafson et al<sup>72</sup> used 7 volunteers in their study (double-blind, placebo-controlled) who received 0, 0.39, 0.47, 7.5, and 14.8 mg/d of THC. No specimens were positive for the low doses (0.39 and 0.47 mg). Only the high doses (7.5 and 14.8 mg) produced a positive THC test result (50- and 100-ng/mL cutoffs, respectively). However, only 23.2% to 45.8% of specimens showed positive results.<sup>72</sup>

## Conclusions

Adulterants impose a new challenge in the testing for abused drugs. Routine specimen integrity testing involving pH, creatinine, specific gravity, and temperature is inadequate for detecting the presence of more recently introduced adulterants such as Urine Luck, Klear, and Stealth. These agents can cause false-negative results in immunoassay screening steps and may also affect the GC-MS confirmation step if the abused drugs are present in modest concentrations (100%-150% of cutoff concentrations). Therefore, the true presence of a drug can be missed if these agents are used for adulteration. Fortunately, spot tests have been introduced, and several dipstick tests (eg, AdultaCheck 4, AdultaCheck 6, and Intect 7) are available for validation of specimen integrity. Studies are also needed of the effectiveness of hair shampoo for causing false-negative results in a hair drug test and mouthwash products for invalidating saliva testing for abused drugs. Ingestion of poppy seed cake and hemp oil leads to true-positive results with opiate and THC assays, and laboratory professionals should also be familiar with this information.

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