CLINICAL & FORENSIC

# Toxicology News

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## Dietary Supplements Face Fewer Regulations

*By Alfredo J. Quattrone*

Dietary supplements have increased greatly in popularity in the past six years, even in the face of confusion as to just what benefits these items might offer, as compared to the risks associated with new dietary supplement ingredients. Dietary supplements are defined as foods that contain one or more "dietary ingredient" intended to supplement the diet by oral ingestion.

Dietary supplements may take the form of an extract, constituent, metabolite, or concentrate. They may be made into tablets, capsules, softgels, gelcaps, bars, liquids, sprays, or powders. However, by law, the labeling information on dietary supplements must not represent these items as typical or conventional foods, as the sole item of any meal or diet, or as a drug, because any dietary supplement "product is not intended to diagnose, treat, cure, or prevent any disease" (1).

### Dietary supplements act

Under the Dietary Supplement Health and Education Act (DSHEA) passed by Congress in 1994, components of dietary supplements might consist of "dietary ingredients" and "new dietary ingredients." In order for an ingredient in a supplement to be a "dietary ingredient," it must contain one or more of the following substances: a) a vitamin; b) a mineral; c) an herb or other botanical; d) an amino acid; e) a dietary substance designed to increase the total dietary intake (such as enzymes or tissues from organs or glands); or f) a concentrate, metabolite, constituent, or extract, with other current restrictions. "New dietary ingredients" are those legal components that were not sold in the U.S. in any supplement form prior to Oct. 15, 1994, when the DSHEA was signed into law.

The DSHEA places dietary supplements and their ingredients into a special food category, whereby component "dietary ingredients" and "new dietary ingredients" are largely exempt from the food additive safety amendments of the federal Food, Drug, and Cosmetic Act. However, the law does not allow new and current "dietary ingredients" to be drugs, controlled substances, or any other legally restricted substances. Also, dietary supplements may carry a "structure or functional activity" claim, as long as the claim does not refer to any disease or condition as generally recognized by the U.S. Food and Drug Administration (FDA). The DSHEA also requires that every supplement be labeled as either a general dietary supplement or a more specific supplement (for example, a vitamin, mineral, or specific botanical, such as a "gingko supplement").

### Supplement claims

Dietary supplements may carry structure or function claims as long as the items are marketed without any labeling claims directed at the treatment, diagnosis, prevention, or cure for any specific disease or condition. Following the structure or function claims, supplement labels must also display the FDA disclaimer statement: "This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease."

Misbranding of dietary supplements has often taken the form of non-legitimate structure and/or function claims, as well as a lack of the required disclaimer statement. A legal structure or function claim on a label can take a form such as "supports healthy cardiac function" or "helps maintain healthy knees," but cannot mention any disease or condition

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## Inside...

# CAP Makes Improvements in The Urine Toxicology Survey

*By Tai C. Kwong*

The College of American Pathologists has offered the Urine Toxicology (UT) Survey for many years. In its current form, five human urine or synthetic urine specimens spiked with various drugs and drug metabolites are sent to subscribers three times a year. Subscriber performance is graded and a critique is written for each of the specimens.

The UT Survey is intended for clinical laboratories that perform a urine-based drug screen in the evaluation of a patient suspected of a drug overdose. The list of drugs used as challenges is extensive. Therefore, successful participation requires the ability to perform a broad spectrum drug screen using a chromatographic method. Thus, the survey is beyond the capability of laboratories that use only immunoassays for their drug screens; the UDS Survey is better suited to serve those laboratories. UT subscriber laboratories are also expected to perform confirmation tests on their initial findings whenever possible.

While the UT Survey has been successful and has met its intended goal, the Toxicology Resource Committee (TRC) has received informal comments from subscribers. These included suggestions that the specifications of the survey specimens could be more clinically relevant to simulate real-life specimens seen by clinical labs. Critics suggested that the specimens could be spiked with fewer drugs and metabolites rather than in combinations that are unrealistic and pose purely analytical challenges. Moreover, it was suggested that the critiques could be written to have more educational value and be less of a recitation of the percentage of respondents who have been successful and a breakdown of the analytical methods used.

The TRC took all this feedback into consideration in redesigning the UT Survey for 2001. The three main improvements are that surveys now include a case history with each specimen, more realistic specimens, and a new format for critiques.

### Case history and specimen specification

Specimens are now designed to be clinically relevant challenges. Each specimen is intended to simulate a clinical specimen sent to the clinical laboratory for toxicology analysis. It is accompanied by a brief, but credible, case history. The specimen contains a realistic combination of drugs and/or metabolites at appropriate concentrations. The case history, however, may not necessarily be a clue to the drugs and metabolites contained in that specimen. This is because, as we all know, a patient's history can be unreliable and clinical signs and symptoms can be confusing and may not be attributable solely to the toxic effect of the drugs ingested.

The TRC is fully cognizant of the fact that most clinical laboratories have a "fixed" or "standard" urine drug screen, and it is performed regardless of the patient's history or presenting symptoms. Most clinical laboratories do not have the resources or expertise to target the search for a particular toxin based on history and clinical presentation. Yet, the case history has educational value in offering an opportunity for the laboratory technical staff to relate their drug screen findings to the patient's clinical history and presentation.

The TRC has instituted a minimum target concentration of 250 ng/mL for all analytes except Δ9-THC-carboxylic acid, 6-monoacetyl-morphine, and phencyclidine. Because the matrix of UT Survey specimens is human urine pools, it is inevitable that there may be trace amounts of drugs and metabolites. These contaminants are present at concentrations that have no clinical significance in the context of drug overdose and are usually below the detection limits of the analytical methods used in routine clinical urine drug screens. They have been detected and reported by a few laboratories that are equipped with state-of-the-art mass spectrometers and have a laboratory policy to pursue detection and identification at the limits of detection of their instruments. The minimum target concentration policy has been implemented to avoid inappropriately penalizing these laboratories for reporting false-positive results because they have advanced analytical capabilities.

### New critique format

The new approach to writing the critiques places the emphasis on being informative and educational. Each critique is a concise summary of the pharmacology, clinical toxicology, and analytical toxicology of the drug(s). It is not intended to be a detailed monograph on the topic. The TRC will continue to publish monographs on selected drugs on a periodic basis. The critiques consist of the following sections:

*Pharmacology and therapeutics.* This section includes a brief summary of background information on the drug(s) (For medications, this includes therapeutic uses and dosages, formulations, and the manner in which they are supplied. For drugs of abuse, it covers the epidemiology and pattern of abuse.); a summary of the relevant pharmacokinetics, biotransformation pathways, and major metabolites; and the mechanism of drug action.

*Clinical toxicology.* This section includes discussions of typical clinical signs and symptoms of a drug overdose; toxicokinetic parameters such as absorption, appearance of toxic symptoms, and clinical course of intoxication; the mechanism of toxicity and standard treatment, including the availability of a specific antidote; and the role of the toxicology laboratory in supporting the diagnosis and management of the drug overdose.

*Analytical issues.* The discussion of analytical issues includes the advantages and limitations of the various methodologies available in terms of sensitivity, specificity, turnaround time, and degree of complexity. This discussion takes place in the context of survey and respondent results.

The goal of the TRC is to provide a proficiency survey program that not only helps toxicology laboratories monitor laboratory performance and satisfy regulatory requirements, but that is also educational. Improving this program is a continual process that depends on subscriber feedback. Subscribers are invited to communicate their suggestions, comments, and criticism to members of the TRC.

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# Dietary Supplements

*Continued from page 1*

because only a drug can legally bear a claim to treat, diagnose, cure, or prevent any disease. Indeed, the DSHEA requires that the FDA must be notified of all new labeling claims within 30 days after marketing of the dietary supplement (2).

### Supplement labels

Dietary supplement labels must identify each dietary ingredient contained within each item. Those ingredients not listed within the "Supplement Facts" panel must be listed in an "other ingredients" statement beneath the panel. The phrase "active ingredient" may not be used on any dietary supplement item, because that phrase implies the dietary supplement contains a drug (3–5). In contrast to the requirement that drugs, biologicals, other pharmaceuticals, and medical devices must be proven safe and effective for their intended use prior to marketing, DSHEA contains no provisions for FDA to approve dietary supplements for safety or effectiveness. Also unlike drugs and other medical products, manufacturers and distributors of dietary supplements are not formally required to record, investigate, or forward to FDA any reports concerning injuries or illness that might be related to the use of a dietary supplement. Under the DSHEA, the FDA has the burden of showing that a dietary supplement has caused injury or death, and is therefore unsafe, before it can take action against the manufacturer of such a product.

No accepted definitive or authoritative list of dietary ingredients marketed before Oct. 15, 1994, has been developed. The DSHEA makes it the responsibility of manufacturers and distributors to determine if a dietary ingredient is or is not "new," and to document that such ingredients marketed before Oct. 15, 1994, are indeed safe (6–7).

Manufacturers need not register themselves or their dietary supplements with the FDA before producing or selling the products, unless their products contain "new ingredient(s)." Manufacturers have to file their dietary supplement claims with the FDA 75 days before the start of sales. Also, firms may have to provide the FDA with any reported illness evidence at any time, should there be any reports of harm, injury, or death.

Under the DSHEA, the manufacturing firm is responsible for determining that each dietary supplement that it manufactures or distributes contains no drugs or restricted substances. With few exceptions, substances found in drugs or other pharmaceuticals may not be considered to be "new dietary ingredients." Exceptions might include substances demonstrated to be present in and sold as part of a food prior to Oct. 15, 1994. However, such new ingredients may not be on any restricted use or controlled product list (such as tobacco, alcoholic beverages, or controlled substances).

### Center for Food Safety and Applied Nutrition

Within the FDA, the Center for Food Safety and Applied Nutrition (CFSAN) has legal oversight of all dietary supplements. CFSAN has made significant efforts to monitor for illegal products (such as products that contain unsafe ingredients or manufacturers that make false or misleading claims). CFSAN obtains its information from complaints from health professionals and consumers, adverse events reported to the FDA's MedWatch program, inspections of dietary supplement manufacturers and distributors, review of the Internet and other news sources, and other sources. The FDA has focused its resources on the greatest public health concerns, specifically on dietary supplements that may have caused death, injury, or illness.

Three key issues have had priority for dietary supplement enforcement: a) misbranded (mislabeled) products; b) products fraudulently containing known pharmaceutical agents; and c) products thought to be unsafe because of the presence of toxic, hazardous, or controlled substances (8–9). Enforcement activities have taken place against firms that have marketed dietary supplements containing pharmaceutical ingredients (including chlordiazepoxide, glyburide, phenformin, fenfluramine hydrochloride, testosterone, methyltestosterone, ephedrine, chlorpheniramine, and phenacetin), toxic alkaloids (including aristolochic acid; 0.3% hypericin from St. John's wort; pyrrolizidine alkaloids from comfrey; yohimbine, a monoamine oxidase/MAO inhibitor, from yohimbe; polyphenols, tannins, diterpenoids, and other heptotoxins found in germander; tetrahydropalmatine, which causes sedation, analgesia, and neuromuscular blockade and paralysis, from *Stephania* flora species; ephedrine, pseudoephedrine, and other *Ephedra* alkaloids, which cause hypertension, heart palpitation, neuropathy, myopathy, psychosis, stroke, and memory loss, as derived from mahuang and other *Ephedra* plants), drugs of abuse (such as GHB, GBL, 1,4-BD), anabolic steroids (androstene-3,17-diol), or highly toxic salts (8–10). With the limited resources, FDA monitoring of potentially harmful dietary supplements will continue to be difficult.

### Federal Trade Commission role

So-called infomercials and advertising for dietary supplements are regulated by the Federal Trade Commission (FTC). The FDA has continued to work closely with the FTC regarding the advertising associated with dietary supplements. Advertising and promotional materials received by consumers via the mail are also regulated under different laws and are subject to regulation by the U.S. Postal Inspection Service. Individuals who think they have suffered a serious harmful effect or illness from a product the FDA regulates, including dietary supplements, are encouraged to report problems to the FDA's MedWatch by calling the hotline at 1-800-FDA-1088 or by reporting it on-line at *www.fda.gov/medwatch/report/hcp.htm.*

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10. www.dhs.ca.gov/fdb/HTML/Drug/nejmlet.htm

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## Testing in Opiate Therapy Requires Assay Knowledge

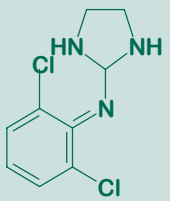
*By Jimmie L. Valentine and Samuel Mathews*

Opioid dependence is a pressing social and medical problem. Chronic opiate users find it extremely difficult to kick the habit without therapeutic intervention. Currently two classes of medications are used for detoxification: non-opiate (clonidine) and opiate (methadone, *l*-acetylmethadol, or buprenorphine).

Clonidine (Figure 1), the alpha – 2 adrenergic agonist, reduces neurotransmissions from the locus ceruleus area of the brain. Many of the autonomic symptoms of opiate withdrawal, such as nausea, vomiting, sweating, and tachycardia, are typically suppressed in this area of the brain by opiates. Thus clonidine can alleviate many of the symptoms associated with opiate withdrawal, but not the opioid craving.

The other therapeutic approach treats the opiate-tolerant individual with a cross-tolerant drug, that is, a drug that satisfies the opioid craving and prevents withdrawal symptoms while permitting the person to function in society. An example is methadone, an analgesic drug that like morphine is an agonist at the mu (μ) analgesic receptor and that acts as a substitute for morphine to prevent opiate-induced withdrawal and craving. Methadone has been used since the1960s to treat opiate withdrawal, principally heroin addiction. Another drug effective for treating opiate dependency is a synthetic congener of methadone, levo-acetylmethadol (*l*-acetylmethadol, also known as levomethadyl acetate or LAM, and sometimes LAAM). An advantage of *l*-acetylmethadol is that its dosing interval is three times a week as opposed to daily for methadone. Further, a lower dose of *l*-acetylmethadol has been found to be clinically equivalent to a higher dose of methadone.

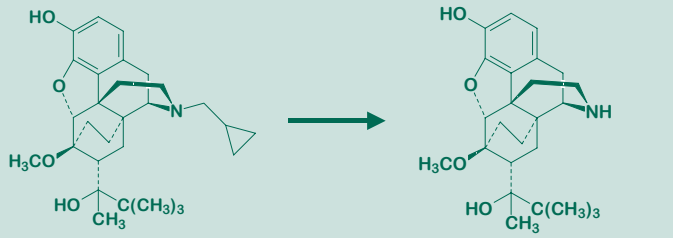
**Figure 1.**




**Clonidine 230.10**

Buprenorphine (Figure 2) is a mixed agonist-antagonist synthetic

**Figure 2. Buprenorphine and metabolite**




**Buprenorphine**
**467.65**

**Nor-Buprenorphine**
**413.55**

opiate that acts as a partial agonist at the μ-receptor and an antagonist at the kappa receptor. This mixed opiate receptor function is believed to impart less central nervous system depression than a pure μ-agonist while satisfying opiate craving. The major urinary metabolite is nor-buprenorphine.

Metabolism of methadone and *l*-acetylmethadol produces a common minor urinary metabolite, methadol (Figure 3). Methadone is the pharmacologically active drug whereas *l*-acetylmethadol can be considered to be a prodrug, the active compounds being the mono- and di-nor metabolites. Methadol is inactive. Methadone forms two additional inactive metabolites, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP) and 2-ethyl-5-methyl-3,3-diphenylpyraline (EMDP).

The power to prescribe either methadone or *l*-acetylmethadol for opiate addiction has been restricted in the United States to treatment programs that obtain a special license and comply with extensive rules and regulations. However, methadone can be prescribed as a Schedule II narcotic for the management of pain or for short-term inpatient management of opiate withdrawal. Outpatient detoxification requires referral to a specially licensed program.

There is a move under way to permit physicians with minimal continuing education training in opiate addiction to treat individuals on an outpatient basis, using drugs like methadone or *l*-acetylmethadol. This movement has grown out of the success of primary-care physicians in treating alcohol problems and prescribing non-opiate drugs like clonidine to treat opiate withdrawal. Further, mixed oral agonist-antagonist drugs like buprenorphine with little potential for diversion or intravenous abuse will soon be available for prescribing. Thus, laboratorians should anticipate that analysis requests for some of these drugs will be forthcoming.

## The role of testing

A mainstay in the special clinic programs, as well as many pain management programs, has been random or regular urine drugs-of-abuse testing. Because the methadone treatment programs have been in existence for so many years, standard urine drug-screening panels that include methadone have been used by many laboratories or even performed on-site at the clinics using point-of-care testing devices. In addition to methadone, these immunoassay-based tests typically screen for amphetamines, barbiturates, benzodiazepines, cannabinoid metabolite, cocaine metabolite, methaqualone, opiates, phencyclidine, and propoxyphene. Depending on the treatment program, an enzyme test for ethanol might also be included in the panels.

In methadone treatment programs, the presence of methadone and absence of opiates was usually taken as a sign of compliance by the provider of the urine specimen. The absence of the other drugs simply assured the program staff that the program participant was not abusing other drugs. Some of the drugs included in the panels were simply vestiges of the days when most of the methadone programs were created. Drugs like methaqualone and barbiturates were popular abused drugs at such times.

If urine drug screening panels such as those described above continue to be used to monitor persons during opiate withdrawal, laboratories or drug-treatment programs must address whether the tests provide the right information. To illustrate we will discuss a post-treatment program that has regularly used urine drug testing for monitoring and give a case presentation of one individual.

## Background

The geographical area served by our laboratories contains two licensed clinics that presently use methadone and *l*-acetylmethadol. One of the clinics serves mostly heroin addicts while the other treats patients dependent on a wider variety of opioids, such as meperidine, hydrocodone, and oxycodone. Abuse of these latter therapeutic drugs often occurs in health professionals who have access to them.

The various medical arts licensing boards (dentistry, medicine, nursing, pharmacy, and veterinary) in our state require random drug testing of individuals who have been shown through administrative hearings or consent agreements to have abused drugs. Following completion of an approved drug rehabilitation program, the licensee is required to attend regular support meetings designed for health professionals and to submit to random drug testing. Each individual in the random testing program is assigned a color (such as red or green) and is required to place a telephone call to a central automated number before 9:00 a.m. each day. A recording gives the

color of the day and if that is the individual's assigned color, they have two hours to report for an observed urine collection. Failure to report within two hours may result in a hearing before the governing board. As part of the chain of custody for such random testing, the individual providing the specimen must declare all drugs taken in the previous seven days. This requirement provides the laboratory with an indication of what drugs to expect in a comprehensive screen and also provides the medical board an indication of the individual's veracity when compared with laboratory results.

In the laboratory evaluation of such urine specimens, an immunoassay and thin-layer chromatography screen is performed followed by a gas chromatography/mass spectrometry (GC/MS) selected ion monitoring or GC/MS full scan confirmation of any positive screening results. The GC/MS full scan analysis also permits identification of any drugs missed in the initial screen. These types of analyses facilitate the identification of a wide range of therapeutic and illicit drugs.

## Case presentation

We evaluated the laboratory results from a male who had participated in the above described urine random drug testing program for approximately one year. On the accompanying chain-of-custody form this individual declared coumadin and acetaminophen as the only drugs taken, both of which were verified in each urine specimen submitted. During this time the immunoassay screens that included methadone were all negative.

A subsequently submitted random urine specimen that was likewise negative for methadone in the immunoassay screen produced four MS full-scan chromatographic peaks that had not been previously observed. Because of varying dietary habits and over-the-counter herbal products, such a spurious appearance of chromatographic peaks was not considered unusual and additional work-up at the initial presentation was not performed. However, on subsequent specimens the consistent appearance of these peaks suggested that regular use of a drug was occurring.

One of the chromatographic peaks gave a mass spectral library quality match of 96 for acetylmethadol. This assignment suggested that the other chromatographic peaks were metabolites of *l*-acetylmethadol. The metabolites of *l*-acetylmethadol had been previously characterized in humans (Figure 3) and using this as a guide, the mass spectra of the other three chromatographic peaks were found to be consistent with nor-*l*-acetylmethadol, di-nor-*l*-acetylmethadol, and methadol (Table 1). This confirmation of the presence of *l*-acetylmethadol and its metabolites meant that this individual either was enrolled in one of the two licensed programs in our area or had obtained the drug illegally. Based on the laboratory results, the particular medical arts board

**Figure 3. Levo-acetylmethadol (LAM) metabolism**

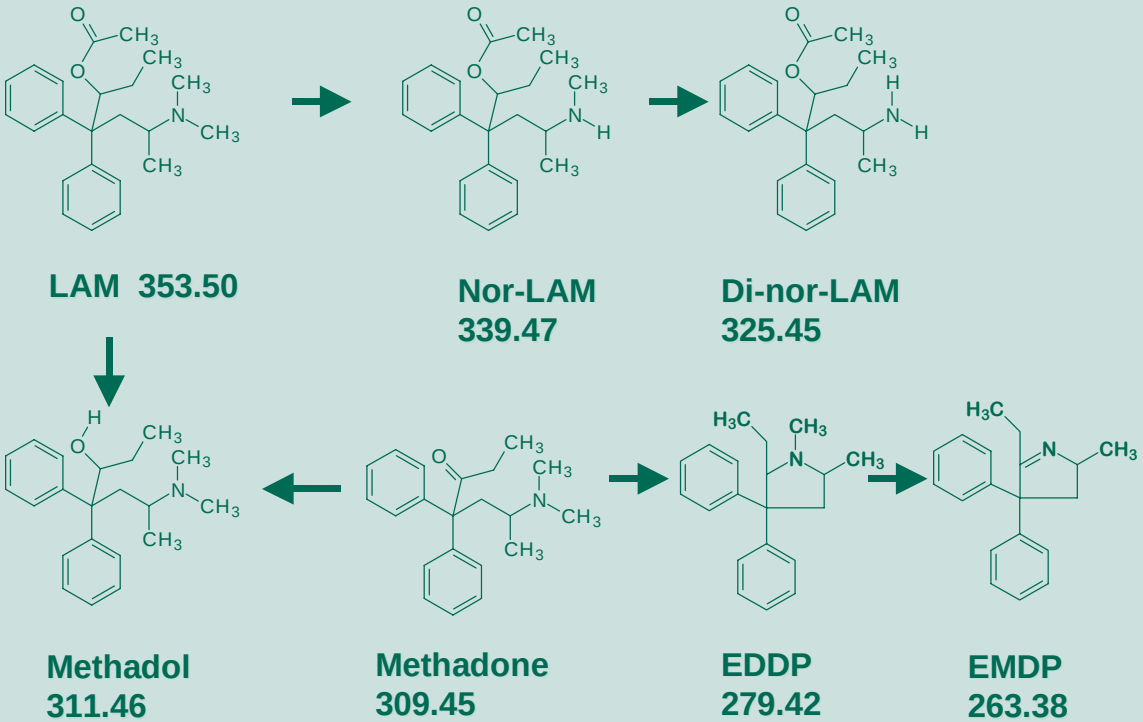


**Table 1. Mass spectral characteristics of *l*-acetylmethadol and its metabolites**

| Compound | Retention time (min) | Ions m/z (abundance) |
|---|---|---|
| *l*-Acetylmethadol | 10.703 | 353(2), 338(3), 225(8), 165(5), 91(5), 72(100), 56(2) |
| Nor-acetylmethadol | 10.55 | 337(14), 332(29), 278(10), 165(10), 133(20), 91(26), 57(38), 56(100) |
| Methadol | 11.82 | 267(47), 208(16), 207(22), 193(13), 178(12), 165(16), 87(100), 86(26), 72(12), 44(41) |
| Di-nor-acetylmethadol | 10.67 | 325(1), 265(3), 222(13), 208(16), 193(21), 178(12), 165(15), 133(18), 120(100), 105(10), 91(17), 77(6), 57(5), 44(97), 43(25) |

confronted the individual and found that he had become a patient at one of the licensed clinics that dispenses *l*-acetylmethadol for treatment of patients with opiate addictions other than heroin. Since his enrollment in the program had not been approved, the board supervising this individual had him appear at an administrative hearing and show cause why his license to practice should not be revoked.

### Discussion and conclusions

Our experience with the above case suggests that laboratories might in the future be called on to provide testing appropriate for the clientele being served by specialized opiate withdrawal programs, particularly if the dispensing of the substitute opiates is liberalized for outpatient treatment by private physicians. In our case presented above, in the immunoassay screen (Microgenics CEDIA), the methadone antibody did not sufficiently cross-react with *l*-acetylmethadol or its metabolites to produce a positive screen. Yet, it is known that some methadone immunoassays from other manufacturers will cross-react (1). Thus, advance knowledge that the person being tested was in an *l*-acetylmethadol treatment program would have permitted selection of a methadone immunoassay screen that had sufficient cross-reactivity with *l*-acetylmethadol and its metabolites.

The same rationale would need to be applied to immunoassay testing of individuals who might have previously abused drugs such as meperidine, oxycodone, hydromorphone, or hydrocodone and were currently in or being followed after attending treatment programs. In the case of meperidine, barbiturate tests from most manufacturers exhibit some cross-reactivity because of the similarity in structure. The situation with cross-reactivity of oxycodone, hydromorphone, or hydrocodone to the morphine antibody used in most opiate immunoassay screens is less certain from manufacturer to manufacturer. Each laboratory must determine the degree of cross-reactivity if adequate screening results are to be achieved for those drug analytes in similar chemical classes.

### Reference

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# OxyContin Abuse Grows

*By Michele Merves and Bruce A. Goldberger*

OxyContin (Purdue Pharma) is a controlled-release formulation of oxycodone, a semi-synthetic opioid agonist. OxyContin is indicated for the management of moderate-to-severe pain when the use of an opioid analgesic is needed for more than several days. It is similar to morphine in analgesic potency.

OxyContin is available in oral doses of 10 mg, 20 mg, 40 mg, and 80 mg of oxycodone, and is usually administered at 12-hour intervals. The dose is typically titrated until the desired analgesic effect is achieved. The *Physician's Desk Reference* states that the 80-mg tablets are for use in opioid-tolerant patients only. Because of its abuse potential, OxyContin is classified as a Schedule II drug by the Drug Enforcement Administration.

When administered appropriately, the controlled-release form of oxycodone provides excellent pain relief that is often not achieved with other analgesics. This has made the drug popular among legitimate users. Recently, however, drug abusers have found a way to use it that produces an intense high.

### Use and abuse

OxyContin tablets are intended to be swallowed whole. However, when the tablets are crushed, the contents can be snorted, dissolved in water and injected, or perhaps smoked. OxyContin is often called the "poor man's heroin" or "hillbilly heroin," and common street names include "Oxy" and "OC." It sells on the street for about $1 per milligram.

Oxycodone is derived from the opium alkaloid thebaine and targets opioid receptors in the central nervous system. By stimulating these receptors, it activates various responses such as analgesia, euphoria, and sedation. Oxycodone is principally abused for its euphoric effects.

The symptoms of OxyContin overdose are similar to those of any opioid overdose and include respiratory and central nervous system depression, constricted pupils, bradycardia, and hypotension. Concurrent administration of other centrally acting drugs potentiates its effects and toxicities. Treatment includes the administration of an opioid antagonist such as naloxone and the support of the cardiovascular and respiratory functions.

Oxycodone is metabolized by N- and O-demethylation forming noroxycodone and oxymorphone, respectively. Glucuronide conjugation follows. These metabolites, in addition to the excess free and conjugated oxycodone, are excreted in the urine. The elimination half-life of OxyContin is slightly longer than that of immediate-release oxycodone—4.5 hours versus 3.2 hours.

## Growth in abuse

OxyContin has received much press recently due to the number of overdoses and deaths associated with its abuse. Physicians, pharmacists, drug treatment centers, law enforcement personnel, and medical examiners have all reported an increase in OxyContin abuse. Confirming this, the Drug Abuse Warning Network (DAWN) has reported a 400% increase in oxycodone-related deaths based on reports from medical examiner offices throughout the U.S. Further, an analysis of recent emergency department admissions by DAWN also indicates a significant increase in oxycodone mentions.

To reduce illegal diversion, many states are considering new regulations regarding OxyContin dispensing. Also, Purdue Pharma has publicized its efforts to develop a reformulated version that it hopes to market within three years. The new formulation will contain an opioid antagonist that will decrease the effects of oxycodone when administered parenterally.

## Suggested Reading

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2. Drug Enforcement Administration website (www.dea.gov).
3. OxyContin Diversion and Abuse, National Drug Intelligence Center, U.S. Department of Justice, January 2001.

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The purpose of *Clinical & Forensic Toxicology News* is to provide practical and timely information on the clinical, forensic, technical, and regulatory issues faced by toxicology laboratories.

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