

# Toxicology News

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## GHB and Precursors (Part II): Management and Analysis

By Sarah Kerrigan

**G**amma-hydroxybutyrate (GHB) and its metabolic precursors, 1,4-butanediol (BDL) and gamma-butyrolactone (GBL), have gained notoriety in the media of late. They have been implicated in celebrity overdoses and GHB has been dubbed the “date-rape drug.”

In the March issue, part one of this article focused on the demographics of GHB use; analogs, precursors, and legal alternatives; and pharmacology and effects.

### Clinical management of GHB intoxication

Management of acute GHB intoxication focuses on alleviating symptoms and providing support. Airway management, mechanical ventilation, prevention of aspiration, and measures to counter bradycardia are commonly required. Extubation following 2–6 hours of mechanical ventilation is common.

Due to the rapid absorption of GHB, gastric lavage or activated charcoal may be ineffective and indicated only if co-ingestion of other substances is suspected. There are no widely accepted antidotes to GHB, although physostigmine, a cholinesterase inhibitor, has shown some promise as a reversal agent. The opiate and gamma-aminobutyric acid (GABA) antagonists, Narcan and Flumazenil, are ineffective.

Spontaneous recovery from GHB overdose is common, usually within a few hours. A period of combative, agitated, or confused behavior should be anticipated immediately following recovery. Patients often have no recollection of having taken GHB due to the anterograde amnesia associated with the drug.

### Drug-facilitated sexual assault

There have been reports of “out of body” experiences from persons who use GHB. While some drug users try to sustain this state by continually ad-

ministering small doses of the drug, the property has attracted a more sinister use of the drug: chemical submission. GHB’s central nervous system depressant effects, rapid onset, memory effects, and fast metabolism make it particularly effective for the purpose of drug-facilitated sexual assault. Liquid GHB, which is readily concealed in water bottles or similar non-suspicious vessels, can immobilize a person or render one comatose within a relatively short period of time. It is claimed that GHB increases libido; however, it is more likely that the perceptions of enhanced sexual arousal and performance result from the decreased social inhibitions associated with the drug.

A recent study concluded that although nearly two-thirds of urine specimens obtained from sexual assault victims contained alcohol or drugs, less than 3% of these were attributable to GHB or Rohypnol. Another study of 1179 alleged cases of sexual assault in 49 states indicated that GHB was present in approximately 4% of victims’ urine samples. The highest rate of GHB use was in California (8%), compared with 0–6% for all other states. However, GHB-facilitated sexual assault may often go undetected: Screening tests for GHB are limited and many laboratories do not routinely test for it. GHB has a very short half-life and is largely undetected in urine after 12 hours. Delays in collection of biological evidence and unwillingness of the victim to report the crime compound the problem.

### Toxicological analysis

Because of the efficient transformation of GHB’s precursors BDL and GBL in vivo, toxicological analyses are commonly targeted towards

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## GHB

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GHB. In antemortem samples, metabolic precursors like BDL and GBL are frequently undetected. However, in postmortem samples following GBL or BDL overdose, these precursors may be detectable. GBL is not detected in blood or urine following administration of GHB, indicating that lactonization of GHB does not occur *in vivo*.

*In vitro* conversion of GHB to GBL has been readily used for toxicological analyses. GBL is more amenable to conventional methods of extraction and gas chromatography compared with GHB, which is considerably more polar and less volatile. Acidification of the specimen results in lactonization, after which a solvent such as methylene chloride or chloroform can be used to extract the GBL. These processes typically result in conversion and recovery of about 70% of the GHB as GBL. However, care must be taken during evaporation of the lactone to prevent sample loss.

Despite its low molecular weight (86 Da), GBL has been analyzed directly using GC/MS. However, the characteristic ions have low mass-to-charge ratios and an additional extract, one that does not undergo acidification, should also be analyzed to determine whether intact GBL is present in the sample.

GHB can be analyzed directly using either liquid-liquid or solid-phase extraction techniques. Due to its small size and polar moieties, extracts tend to be non-specific, containing many other endogenous carboxylates and polar molecules. Derivatization is necessary prior to chromatographic analysis. Silylation of the hydroxyl and carboxylate moieties using common derivatizing agents is widely used.

Analysis of GHB without *in vitro* conversion to the lactone may be advantageous from a methodological and legislative perspective. Derivatization of GHB increases thermal stability, reduces volatility, and increases the molecular weight, enhancing confidence in mass spectral identification.

Care must be taken to prevent inadvertent lactonization of GHB to GBL by exposure to acid or heat. Interference from other structurally similar endogenous substances should also be considered, particularly  $\beta$ -hydroxybutyric acid, which is excreted in large quantities in the urine of diabetics and during ketoacidosis. Urea is another common interfering agent. Silylation of urea and GHB can produce derivatives with similar chromatographic and mass spectral characteristics. These and other interferences can be overcome by using chemical ionization GC/MS.

## Blood and urine concentrations

Low doses of GHB produce euphoria, but higher doses may cause sedation and profound central nervous system depression. Oral or intravenous doses of 10 mg/kg produce amnesia and hypotonia, 20–30 mg/kg can induce sleep, and doses above 50 mg/kg can produce anesthesia. Illicit doses of GHB are reported to be approximately 35 mg/kg, although doses vary considerably among individuals, depending on experience with the drug, tolerance, and intended use.

Oral doses of 25 and 50 mg/kg produced average peak plasma concentrations of 55 and 90 mg/L, respectively. Narcoleptic patients who received oral doses of 50 mg/kg produced peak plasma concentrations in the range 48–125 mg/L. Doses of 25 mg/kg produced dizziness or drowsiness with an average peak plasma concentration of 80 mg/L at 0.5 h. Blood GHB concentrations less than 50 mg/L have been associated with euphoria, uninhibited behavior, lightheadedness, and arousal. Above 50 mg/L, sleepiness, slurred speech, and loss of consciousness have been reported. Seizure-like activity, coma, and death have occurred at concentrations in excess of 250 mg/L. Peak urine concentrations on the order 1100 mg/L were reached within 4 hours of an oral dose of 100 mg/kg. Blood and urine concentrations reported in the literature are summarized in Table 1.

**Table 1. Blood and urine concentrations of GHB**

Concentration (mg/L)	Observations	
Blood	Urine	
33	714	Impaired driving, confusion, disorientation, nystagmus
33	-	Impaired driving
47	308	Drug-facilitated sexual assault, memory loss
<52	-	Wakefulness
52–156	-	Light sleep
73	-	Impaired driving
101 (serum)	141000	Coma
125 (serum)	-	Blood alcohol concentration of 0.13, nausea, dizziness, coma
130	1600	Confusion, ataxia, vomiting
156–260	-	Moderate sleep
157	-	Asleep behind the wheel
221	2200	Nonfatal overdose
>260	-	Heavy sleep
280	6171	Fatality (postmortem)
330 (peripheral)	-	Fatality (postmortem)
648 (heart)	-	Fatality (postmortem)
761 (femoral)	407	Fatality (postmortem)
1473 (heart)	407	Fatality (postmortem)
-	1086	Impaired driving, nystagmus, unconsciousness
-	1975	Impaired driving, confusion, ataxia, nystagmus, sleep

### Effects of GHB on driving

Clinical studies have shown that as little as 10 mg/kg GHB can impair memory and critical flicker fusion frequency. In contrast, other studies have shown that 25 mg/kg GHB did not impair attention, vigilance, alertness, short-term memory, or psychomotor coordination. Nevertheless, GHB has been implicated in several instances of driving under the influence (DUI), with common observations being ataxia, nystagmus, poor coordination, slurred speech, hypotonia, confusion, somnolence, and unconsciousness. A common scenario involves a driver asleep at the wheel in a stationary vehicle at a traffic light or intersection.

Concurrent use of other drugs makes it difficult to isolate the symptoms attributable to GHB. Although the effects of GHB on driving performance have not yet been scientifically investigated, epidemiological data suggests that, at sufficient dose, the sedative and hypnotic effects of the drug impair cognitive and psychomotor function. In 11 DUI cases, blood GHB concentrations were 81–360 mg/L and urine concentrations were 780–2380 mg/L. In another study of eight impaired drivers, blood GHB concentrations were 26–127 mg/L.

### Endogenous GHB

Concentrations of endogenous GHB in the human brain are extremely low compared with the amount needed to produce a pharmacologic response, reported to be at least 100-fold higher. Micromolar concentrations are found in some areas of the mammalian brain, with specific GHB binding sites concentrated in the hippocampus and cortical areas. GHB is also present in non-neuronal tissues. It has been detected in the kidney at concentrations tenfold higher than those found in the brain. Heart and skeletal muscle was also found to contain GHB at concentrations five-fold higher than neuronal tissue. It undergoes metabolic conversion to succinic semialdehyde (SSA) and succinate before entering the tricarboxylic acid cycle. GHB is both derived from and catabolized to SSA by different enzymes, and there is evidence to suggest that mammalian neuronal tissue can reduce SSA to GHB as well as convert GABA to GHB.

Arbitrary cutoff concentrations are frequently used when reporting GHB. There are no mandated guidelines, so institutions that analyze for GHB are responsible for establishing their own thresholds. In antemortem blood and urine samples, cutoffs of 5 or 10 mg/L are widely used, whereas postmortem cutoffs on the order 50 mg/L have been recommended due to artifactual GHB production. In a selection of

about 100 non-GHB-related deaths, heart and femoral blood were found to contain on average 12 mg/L (range, 2–36 mg/L) and 11 mg/L (range, 2–48 mg/L) GHB, respectively. In deaths attributed to GHB, postmortem blood concentrations were 98–596 mg/L. Postmortem urine is less susceptible to artifactual GHB production, containing on average 5 mg/L (range, 0–14 mg/L) GHB. Because of this, urine is the preferred specimen for GHB-related death investigation.

Endogenous concentrations of GHB in antemortem blood and urine are typically less than 5 mg/L. However, storage conditions and preservatives play an important role in the artifactual production of GHB in biological specimens. Absence of sodium fluoride and storage at room temperature may increase GHB concentration. Postmortem blood stored for 40 days at 25 °C in the absence of sodium fluoride showed elevated GHB concentration (9–433 mg/L) compared with preserved blood stored at 4 °C (5–77 mg/L). Yellow-top tubes, which contain trisodium citrate, citric acid, and dextrose, have been shown to artifactually produce GHB in antemortem blood samples.

Some authors have attributed postmortem increases in GHB and GABA to the decreased activity of the Krebs cycle and enzymatic changes that occur following death. Artifactual GHB may be produced from GABA and SSA during anoxic conditions. Oxidation of GHB to succinic semialdehyde is the rate-limiting step in the catabolic pathway of GHB. Conversion of GHB to SSA proceeds at approximately one one-thousandth of the rate at which SSA is converted to succinate by succinic semialdehyde dehydrogenase. Factors that regulate either of the enzymes involved, particularly GHB dehydrogenase, can influence tissue concentrations of endogenous GHB as well as the physiologic response from exogenously administered GHB.

It is expected that inhibition of GHB dehydrogenase in vivo will increase endogenous concentrations of GHB. This has been demonstrated using drugs known to inhibit this enzyme, such as barbiturates, diphenylhydantoin, valproic acid, and salicylates.

Interestingly, it has also been shown that GHB dehydrogenase is inhibited by endogenous substances including ketone bodies,  $\alpha$ -ketoglutarate, branched ketoacids derived from amino acid degradation, and degradation products of phenylalanine. This is perhaps the most compelling explanation for the postmortem and artifactual production of GHB. However, in the presence of certain organic acidemias, antemortem blood and urine samples can also

accumulate extremely high concentrations of endogenous GHB.

### Succinic semialdehyde dehydrogenase deficiency

A rare metabolic anomaly was identified in 1981, in which a deficiency in succinic semialdehyde dehydrogenase caused an accumulation of GHB and SSA. This disorder can cause severe psychomotor retardation, ataxia, and convulsions. There have been several reports of this disorder, which is also referred to as 4-hydroxybutyric aciduria. In response to the defect, physiological fluids accumulate large quantities of GHB that produces numerous neuropharmacological effects. Difficulty associated with speech, psychomotor retardation, hypertonia and hyperkinesia have been reported. In one study, the following abnormalities were observed in 23 patients: motor delay, including fine motor skills, 78%; language delay, 78%; hypotonia, 74%; mental delay, 74%; seizures, 48%; decreased or absent reflexes, 39%; ataxia, 30%; behavioral problems, 30%; hyperkinesia, 30%; and electroencephalographic abnormalities, 26%.

The disease is believed to be the result of defects in the succinic semialdehyde gene. Urinary concentrations of GHB can reach 1000-fold of those found in normal subjects. Clinical improvements in some individuals have been observed after treatment with vigabatrin.

### Conclusion

Gamma-hydroxybutyrate, its analogs, and metabolic precursors pose a formidable challenge to scientific, law enforcement, and legislative bodies. Interpretation of toxicological findings is often complicated by the presence of endogenous GHB and delay in specimen collection as well as storage and preservation issues. The popularity of the drug, its widespread appeal, and the ready availability of unregulated alternatives to GHB ensure its future use as a recreational intoxicant for some time to come.

### Suggested Reading

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## NACB Test Guidelines Seminar

The National Academy of Clinical Biochemistry is sponsoring an Edutrak seminar at the upcoming AACC/CSCC Annual Meeting on “Laboratory Medicine Practice Guidelines: Recommendations for the Use of Laboratory Tests to Support the Impaired and Overdosed Patient in the Emergency Department.”

Chaired by Alan Wu of Hartford Hospital, sessions will include “Recommendations for Drug Test-

ing to Support Emergency Department Toxicology,” “Recommendations on Analytical and Reporting Issues for Drugs of Abuse Testing,” “Recommendations for Breath Alcohol Analysis and Testing of Serum Ethyl Alcohol and Other Volatiles,” and “Recommendations of Laboratory Assays for Substance Abuse and Exposure.”

The draft guidelines can be viewed on line at [www.nacb.org/emergency/Toxicology\\_LMPG.htm](http://www.nacb.org/emergency/Toxicology_LMPG.htm).

The session will be held August 1–2 at McCormick Place in Chicago.

To obtain the Annual Meeting registration brochure, contact the AACC Customer Service Department by phone at (800) 892-1400 or by e-mail at [custserv@aacc.org](mailto:custserv@aacc.org). On-line registration is available at [www.aacc.org/meetings/2001annmeet/default.stm](http://www.aacc.org/meetings/2001annmeet/default.stm).

## International TDM Congress

The 7th International Congress of Therapeutic Drug Monitoring and Clinical Toxicology will be held in Washington, D.C., September 1–6. For information, contact the International Congress of Therapeutic Drug Monitoring and Clinical Toxicology, 4 Catarqui Street, Suite 310, Kingston ON K7K 1Z7 Canada, (613) 531-8166, [congress@eventsmgt.com](mailto:congress@eventsmgt.com) or visit its website at [www.iatdmct.org](http://www.iatdmct.org).

## SOFT Meets in New Orleans

The Society of Forensic Toxicologists’ annual meeting will be September 30 through October 5 in New Orleans.

To view the preliminary program and obtain more information, visit the SOFT website at [www.soft-tox.org](http://www.soft-tox.org).

## California Toxicologists Meet

The California Association of Toxicologists, one of the largest organizations of forensic and clinical toxicologists in the nation, meets quarterly to present current research and to discuss toxicology topics. Anyone interested in toxicology is invited to attend. For further information, contact the meeting host or visit the association’s website at [www.cal-tox.org](http://www.cal-tox.org).

Upcoming meetings and contacts include:

August 4: Jim Meeker, Redwood Toxicology Laboratory, 3573 Westwind Blvd., Santa Rosa, CA 95403, (707) 577-7958.

November 2–3: Rong Jen Hwang, Santa Barbara County Sheriff-Coroner Toxicology Lab, 66 South Antonio Road, Santa Barbara, CA 93110-1720, (805) 861-5383.

## Supreme Court Rules Against Drug Tests Without Consent

The U.S. Supreme Court has ruled that a hospital cannot test maternity patients for illegal drug use without their consent if the purpose is to alert the police to a crime.

The drug-testing program at issue began when staff members at the Charleston public hospital operated by the Medical University of South Carolina became concerned about an increase in the use of cocaine by patients receiving prenatal treatment. The hospital staff, local police, and local officials developed a policy in which hospital staff performed drug tests on pregnant patients suspected of drug use and forwarded positive results to police.

“A state hospital’s performance of a diagnostic test to obtain evidence of a patient’s criminal conduct for law enforcement purposes is an unreasonable search if the patient has not consented to the procedure,” wrote Justice John Paul Stevens in the majority opinion in the case *Ferguson v. Charleston*.

The 6–3 opinion stated that the policy did not qualify for the “special needs” exception in which the court has allowed some searches without warrants if a public good outweighed the intrusion on the individual’s privacy rights.

“While the ultimate goal of the program may well have been to get the women in question into substance abuse treatment and off drugs, the immediate objective of the searches was to generate evidence for law enforcement purposes in order to reach that goal,” Stephens wrote. “Given that purpose and given the extensive involvement of law enforcement officials at every stage of the policy, this case simply does not fit” in the special needs category.

Ten women who had been tested by the hospital brought the suit, claiming civil rights violations by the city and hospital. Because of the lawsuit and a related civil rights investigation by the Clinton administration, the hospital dropped the policy in 1994.

The policy was believed to be unique in the United States, but if it had passed the court’s review, other jurisdictions might have considered implementing similar programs.

The justices who dissented from the opinion were Antonin Scalia, Clarence Thomas, and William Rehnquist.

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## Laboratories Report Workload Figures for January 1998

By Wayne R. Markus

In the AACC-CAP forensic urine drug testing survey (UDC-B) for 1998, a questionnaire was included to record workload for the month of January 1998.

One hundred four laboratories completed the questionnaire.

Some participants indicated that external blind proficiency testing specimens might be included,

which would affect the numbers and percentages of confirmed positives in a small way.

The table below summarizes the data these laboratories reported.

The aberration in the ethanol data, in which more than 100% of confirmations were positive, is probably caused by some participants including positive specimens in the "confirmed positive" column, but failing to include them as screen-positive specimens in the "number to confirmation" column.

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Workload Questionnaire Results from 1998 UDC-B Proficiency Testing Survey

	Number of Specimens Screened	Number to Confirmation	Percent to Confirmation	Confirmed Positive Total	Percent of Confirmations Positive	Percent Confirmed Positive
Cannabinoids	990,688	40,638	4.102%	37,018	91.1%	3.737%
Ethanol	185,543	3825	2.062%	4124	107.8%	2.223%
Benzoylcegonine	1,143,820	24,455	2.138%	21,112	86.3%	1.846%
Opiate Group	1,006,921	23,763	2.360%	14,624	61.5%	1.452%
Codeine		19,063		11,065	58.0%	1.099%
Hydrocodone		9227		2492	27.0%	0.247%
Hydromorphone		10,273		3049	29.7%	0.303%
6-MAM		374		177	47.3%	0.018%
Morphine		19,011		10,931	57.5%	1.086%
Oxycocoe		1130		203	18.0%	0.020%
Barbiturate Group	536,588	8703	1.622%	7408	85.1%	1.381%
Amobarbital		7091		363	5.1%	0.068%
Butalbital		7244		1018	14.1%	0.190%
Pentobarbital		7091		372	5.2%	0.069%
Phenobarbital		7243		859	11.9%	0.160%
Secobarbital		7153		371	5.2%	0.069%
Benzodiazepine Group	549,089	8632	1.572%	6503	75.3%	1.184%
Alprazolam metabolite		5116		866	16.9%	0.158%
Flurazepam metabolite		4799		561	11.7%	0.102%
Lorazepam metabolite		2635		601	22.8%	0.109%
Nordiazepam		3525		2439	69.2%	0.444%
Temazepam		4607		3191	69.3%	0.581%
Oxazepam		6661		5221	78.4%	0.951%
Triazolam		3726		549	14.7%	0.100%
Amphetamine Group	989,634	15,131	1.529%	4750	31.4%	0.480%
Amphetamine		13,663		3185	23.3%	0.322%
Methamphetamine		13,730		3834	27.9%	0.387%
Propoxyphene	435,673	2330	0.535%	1461	62.7%	0.335%
Methadone	445,120	2145	0.482%	2126	99.1%	0.478%
Phencyclidine	967,069	2522	0.261%	548	21.7%	0.057%
Methaqualone	324,842	62	0.019%	14	22.6%	0.004%
LSD	1042	200	19.194%	22	11.0%	2.111%
All Drugs	7,576,029	132,406	1.748%			

## Taiwan Conducts Urine Tests As Part of War on Drugs

By Chiareiy Liu, Wening Tsay, and Jih-Heng Li

The abuse of methamphetamine and heroin became a problem of social concern in Taiwan in 1990. The government declared a "war against drugs" in 1993 with the Department of Justice, the Department of Health, and the Department of Education launching separate and inter-agency programs to curb the supply of and the demand for these drugs. Urine drug testing was introduced as one of several measures designed to achieve these goals.

The approach is similar in many ways to the various testing programs in the United States, and includes testing of arrestees and parolees in the criminal justice system, workplace testing of specific categories of workers and "foreign laborers," and some random testing of high school students. The testing is carried out by a variety of agencies.

### County government health bureau laboratories

In 1991, the health bureaus of the country's 25 county governments were given the responsibility to perform urine drug testing for local police and justice officers in support of their legal proceedings. Because these bureaus were previously concerned with other issues of public health, their initial efforts involved equipping their laboratories with basic drug-testing instrumentation and training personnel in drug-testing protocols. Immunoassay (mostly Abbott Laboratories' TDx) and thin-layer chromatography (TLC) (Ansys Technologies' TOXI-LAB) were adopted as the preliminary and confirmation tests.

Because of the limitations of TLC, the local laboratories were encouraged to forward specimens with uncertain test results to a designated laboratory in the central government's Department of Health for retesting. Test results that were challenged were also retested by this laboratory using gas chromatography/mass spectrometry (GC/MS). Approximately 70,000 urine specimens were routinely tested for amphetamines and opiates each year. The average positive rates were approximately 50% for amphetamines and 10% for morphine (1).

The performance of these laboratories was evaluated through monitoring results of proficiency testing samples provided once a year by the Department of Health. Annual workshops were also organized to provide additional training for laboratory personnel. Studies have compared the test results derived from the use of different methods, instruments, and test approaches (2, 3).

### Certified drug-testing laboratories

To relieve the heavy burden endured by the local health bureaus and in anticipating broader implementation of drug testing as a deterrent, the Department of Health embarked on a laboratory certification program in 1995 (4). This program is modeled after the National Laboratory Certification Program of the United States and greatly benefited from its experience, including receiving assistance from several participants of the U.S. program.

As in the U.S. program, immunoassay and GC/MS protocols are used for the preliminary and confirmation tests. Cutoffs of the preliminary tests are 500 ng/mL for amphetamines and 300 ng/mL for morphine. Confirmation cutoffs for amphetamine, methamphetamine, morphine, and codeine are 500 ng/mL, 500 ng/mL, 300 ng/mL, and 300 ng/mL, respectively. (The presence of 200 ng/mL of amphetamine is also required for designating a specimen positive for methamphetamine.)

Fourteen government and private laboratories have been certified under this program to date. To gain certification, laboratories must pass semi-annual inspections and maintain 90% accuracy with no false-positive results in testing 10 proficiency samples every three months.

### Clinical laboratories in hospitals

Approximately 60 hospitals' clinical laboratories constitute the third group of urine drug-testing agencies. Urine drug testing is an integral part of the health examinations required of foreign laborers entering the nation's work force. These tests are conducted upon entry application and every six months thereafter. Again, the Department of Health monitors the performance of these clinical laboratories through the submission of proficiency test samples.

The test methodologies used by these laboratories vary. For example, in 2000, 54 clinical laboratories used instrumentation-based tests, while six used non-instrumented test kits. (In 1999, 13 laboratories used non-instrumented test kits.) In general, only preliminary tests are performed in these laboratories; positive specimens are submitted to the laboratories certified by the Department of Health for GC/MS confirmation.

Currently, there are about 300,000 foreign laborers in Taiwan, mainly from southeast Asian countries. Tests for amphetamines and opiates are mandatory when health examinations are conducted. Tests for marijuana are also required prior to entry and are conducted in the home countries. In 1999, approximately 0.02% of foreign laborer specimens were positive for amphetamines and opiates. In 2000, the positive rates

for amphetamines remained the same, while the positive rates for opiates increased to 0.03% (5). The largest number of foreign laborers come from Thailand, and the positive rates of Thai laborers appear to be higher.

### Test cutoffs

The cutoff values for designating results as positive or negative remain an issue of concern and confusion. In general, the cutoffs adopted for the certification process are used by the certified laboratories. These cutoffs are applied to parolee, workplace, and student specimens as well as those submitted by the police and other officers in the criminal justice system for legal proceedings. In contrast, the Department of Justice Bureau of Investigation's laboratory cutoffs approximate the detection limits of their testing protocols. Currently, there is active discussion among drug-testing providers and users and regulatory agencies on uniform cutoffs for specimens submitted for different purposes.

### Drug abuse trends

Over the past eight years, yearly methamphetamine seizures decreased from over 2,500 kg to less than 1,000 kg. During this same period, seizures of marijuana and MDMA increased significantly (3). The police have also reported increased use of these drugs at rave dance clubs. Use of Rohypnol with criminal intent has also been reported. Surveys are currently being conducted to assess the severity of

abuse of these new drugs in Taiwan.

A few laboratories have reportedly established test methods and accepted urine samples for the analysis of these drugs. The incumbent authority, the National Bureau of Controlled Drugs, is planning a proficiency program to evaluate their accuracy.

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