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Recommendations for Toxicological Investigation of Drug Impaired Driving*

ABSTRACT: Investigation of a suspected alcohol or drug impaired driving (DUID) case ideally contains several key elements, including a trained officer documenting observations of driving and subject behavior, and collection of a biological specimen for comprehensive toxicology testing. There is currently no common standard of practice among forensic toxicology laboratories in the United States as to which drugs should be tested for, and at what analytical cutoff. Having some uniformity of practice among laboratories would ensure that drugs most frequently associated with driving impairment were consistently evaluated, that appropriate methods were used to screen and confirm the presence of drugs, and that more accurate data were collected on the extent of drug use among drivers. A survey of United States laboratories actively involved in providing analytical support to the Drug Evaluation and Classification Program identified marijuana, benzodiazepines, cocaine, prescription and illicit opiates, muscle relaxants, amphetamines, CNS depressants, and sleep aids used as hypnotics, as being the most frequently encountered drugs in these cases. This manuscript presents recommendations as to what specific members of these drug classes should at a minimum be tested for in the investigation of suspected DUID cases. Additionally we include recommendations for analytical cutoffs for screening and confirmation of drugs in blood and urine. Adopting these guidelines would ensure that the most common drugs would be detected, that laboratories could compare epidemiological findings between jurisdictions, and that aggregate national statistics on alcohol and drug use in drivers involved in fatal injury collisions were representative of the true rates of drug use in the driving population.

KEYWORDS: forensic science, drug, impaired, impaired performance, automobile driving, driving under the influence of drugs

Toxicologists in the United States have been discussing the need for better standardization in the scope and analytical cutoffs used in drug testing performed in drug impaired driving investigations. In May 2004, a group representing toxicologists, Drug Recognition Experts (DREs) and prosecuting attorneys active in the area of driving under the influence of drugs (DUID) was convened under the auspices of the National Safety Council's Committee on Alcohol and Other Drugs (COAD), and its subcommittee on Drugs: Pharmacology and Toxicology. The panel was charged with identifying problems with the current system of prosecuting impaired driving cases, from the point of detection through adjudication. The discussions were wide ranging, however the lack of consistency of practice among laboratories was one of the major limitations identified. Tasks were assigned to the major stakeholder groups attending. The Joint Drugs and Driving Committee of the Society of Forensic Toxicologists (SOFT) and the American Academy of Forensic Sciences (AAFS) and the COAD were assigned responsibility for surveying practices among laboratories performing toxicology in support of state DRE programs and more generally for toxicological investigations of drug impaired driving cases (1).

Laboratories engaged in performing toxicological testing in support of DRE programs were identified and surveyed with respect to their analytical practices. At a follow up meeting in October 2005, survey results were presented and there was discussion of development of recommendations for laboratories performing this testing to follow in order to ensure the greatest chance of detecting drugs most likely to be encountered in blood and urine in impaired driving cases. Subsequently the authors of this manuscript (LJF, SK, and BKL) developed the following recommendations for a minimum menu of drugs which should be tested for based on drugs most frequently encountered in DUID investigations (2–5), together with recommended cutoff targets for screening and confirmation in blood and urine, based on the availability of immunoassay screening technology and standard instrumentation available to most laboratories working in this field.

Survey of Current Practice

Current practice in toxicology laboratories supporting DRE programs was determined by a survey of all participating labs that could be identified. The survey included questions on scope and analytical cutoffs of services provided, as well as statistics on the frequency of drugs identified in DUID casework. The survey conducted in 2004–2005 was the third survey of this type with prior surveys having been conducted in 1996 and 1999. Completed surveys were received from 42 laboratories in 24 states. This survey response represented 71% of identified laboratories and 66% of the states with active DRE Programs at the time of the survey. Respondents represented city, county, state, and privately funded laboratories serving wide ranging populations (100,000 to >5,000,000). The survey results disclosed significant variability between laboratories in terms of scope and analytical cutoffs used in testing performed in DUID cases.

One-hundred percent of survey respondents used an immunoassay to perform presumptive drug screening on blood or urine specimens. Forty-one percent of the responding laboratories added

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one or more additional techniques to increase the scope of drug screening performed. Methods included thin layer chromatography; high performance liquid chromatography (HPLC); gas chromatography with a variety of detectors: nitrogen-phosphorus detector (GC-NPD), flame ionization detector (GC-FID), electron-capture detector (GC-ECD); gas chromatography/mass spectrometry (GCMS); or liquid chromatography/mass spectrometry (LCMS). Cutoff concentrations for presumptive drug screening (Tables 1 and 2) varied by as much as two orders of magnitude, which is more likely to reflect a laboratory policy rather than actual differences in analytical performance of the immunoassay, as most assays and instruments offer similar sensitivity. Similar variability was observed for thresholds used for confirmatory drug analyses. One-hundred percent of the laboratories performed confirmatory drug analysis by GCMS. Twenty-two percent of the responding laboratories additionally used LCMS, HPLC, GC-FID, or GC-NPD in confirmatory drug analyses in blood or urine.

An evaluation of the data also showed that in 28% of the laboratories reporting analytical services for both blood and urine, there was no difference between urine and blood screening and confirmation levels. It is inappropriate to use the same cutoffs in blood and urine because drug and metabolite concentrations in blood can be substantially different from those in urine following either therapeutic use or abuse. The survey also identified differences in screening and confirmation cutoffs within the same jurisdiction. For example, urine screening cutoffs ranged from 20 to 1000 ng/mL and confirmation cutoffs from 13 to 300 ng/mL for methamphetamine between laboratories in one state. Consequently, the same sample might test either positive or negative depending on which laboratory it was sent to, which is clearly not a good public policy. Although some differences are expected due to the variety of analytical techniques and resources available, the results clearly indicate the need for more uniformity.

Specimen Selection

Differences of opinion exist among toxicologists regarding whether blood or urine is the most appropriate specimen in a DUID case. Blood drug concentrations can be interpreted by comparison with other populations, and in some circumstances, ratios of parent drug to metabolite in blood can differentiate acute from recent or chronic use. Blood is however more difficult to collect, requiring a phlebotomist or medical staff, which can delay collection. Urine, while easily collected, can test positive for drugs long after the impairing effects have dissipated, and there is no verified correlation between urine drug concentrations and effects. In the majority of jurisdictions, the type of specimen collected is a function of the local statute and investigative practices of the law enforcement

TABLE 1—*Survey data—urine screen and confirmation levels.*

	Screen			Confirmation		
Drug/Drug class	No. of labs responding	Cutoff range (ng/mL)	Mode (ng/mL)	No. of labs responding	Cutoff range (ng/mL)	Mode (ng/mL)
Amphetamines (Methamphetamine)	37	20–1100	1000	33	10–1100	50
Barbiturates (Secobarbital)	33	5–1000	200	29	5–1000	100
Benzodiazepines (Oxazepam)	32	10–300	200	28	5–150	50
Cannabinoids (11-nor-delta-9-carboxy-tetrahydrocannabinol)	37	7–55	50	34	2–50	5
Cocaine metabolite	38	50–500	300	33	15–500	20
Methadone	18	20–2200	300	28	10–300	50
Opiates (Morphine)	38	20–2200	300	34	10–500	20
Phencyclidine (PCP)	31	5–200	25	29	5–50	25
Propoxyphene	16	20–2200	300	26	10–300	100
LSD	5	0.5–25	0.05	4	0.1–10	None
Meprobamate	16	5–5000	1000	26	5–5000	500

TABLE 2—*Survey data—blood screen and confirmation levels.*

	Screen			Confirmation		
Drug/Drug class	No. of labs responding	Cutoff range (ng/mL)	Mode (ng/mL)	No. of labs responding	Cutoff range (ng/mL)	Mode (ng/mL)
Amphetamines (Methamphetamine)	31	20–1000	50	29	20–1000	50
Barbiturates (Secobarbital)	29	2–1000	100	27	2–1000	100
Benzodiazepines (Oxazepam)	25	1–300	100	25	1–300	100
Cannabinoids (11-nor-delta-9-carboxy-tetrahydrocannabinol)	30	2–50	20	28	2–50	20
Cocaine metabolite	30	20–300	50	30	20–300	50
Methadone	17	20–200	50	24	20–200	50
Opiates (Morphine)	32	10–200	50	30	10–200	50
Phencylcidine (PCP)	28	2.5–100	10	25	2.5–100	10
Propoxyphene	18	10–250	50	24	10–250	50
LSD	6	0.5–10	None	5	0.5–10	None
Meprobamate	17	2–5000	1000	26	2–5000	1000

agency, and laboratories must work with the specimens provided. Consequently, the recommendations for scope and analytical cutoffs of testing provide guidance for testing of both specimen types. Increasingly there is interest in use of oral fluid as a specimen for DUI investigations; however, insufficient information exists at this time upon which to base recommendations.

Recommendations for Scope of Analytical Testing

Scope of testing in these recommendations was determined from previous publications that have identified drugs or drug classes that are impairing (2) and from statistical data gathered from laboratories engaged in DRE casework who participated in the survey and subsequent discussions. The most frequently encountered drugs were quite consistent between jurisdictions, although there were regional differences in their relative abundance (Table 3).

Based on these data and our experience in analysis of these types of cases, we propose a list of drugs (Table 4) that laboratories receiving specimens for testing in DUID cases should be able to routinely detect. Because there is substantial regional variability in patterns of recreational drug use, additional drugs specific to a laboratory's demographic area may need to be included. The substances identified in Table 4 do not represent an exhaustive or comprehensive list of analytes or impairing substances. As with all other forensic toxicology investigations, it may be important to broaden the scope or repertoire of testing in accordance with specific facts of the case.

For drug screening, which is typically done by immunoassay, laboratories are limited by the target analytes and sensitivities available from manufacturers. Immunoassays are not commercially available for all drugs of interest, such as gamma-hydroxybutyrate. Additionally, highly targeted immunoassays that are available (such as carisoprodol, zolpidem) are not necessarily practical or cost-effective due to the need to test for such a large number of potentially impairing substances, particularly in the case of central nervous system depressants. Assays designed to screen for a particular class of drug such as benzodiazepines or opiates may lack sufficient cross-reactivity to other members of that drug class to be

TABLE 3—*Survey data—most frequently encountered drugs. Labs (n = 40) were requested to list the 10 drugs most often identified. The drugs and their frequency of mention are listed in the table.*

Drug	Frequency
Cannabis	39
Benzodiazepines*	37
Cocaine	37
Hydrocodone	30
Morphine/Codeine	28
Methamphetamine	26
Carisoprodol/Meprobamate	26
Oxycodone	16
Methadone	12
Antidepressants†	11
Zolpidem	10
Phencylcidine (PCP)	8
Butalbital/Barbiturates‡	7
Diphenhydramine	6
3,4-Methylenedioxymethamphetamine	5
Propoxyphene	5
Ephedrine/Pseudoephedrine	2
Cyclobenzaprine	1
Dextromethorphan	1
Gamma-hydroxybutyrate	1
Ketamine	1
Phenothiazines	1
Tramadol	1

*Diazepam = 28, Alprazolam = 27, Oxazepam/Nordiazepam = 7, Clonazepam = 4, Lorazepam = 3, Temazepam = 1, and benzodiazepines with no specific information = 2.

†Venlafaxine = 2, Amitriptyline = 1, Fluoxetine = 1, Citalopram = 1, and antidepressants with no specific information = 6.

‡Butalbital = 5, Barbiturates with no specific information = 2.

TABLE 4—*Recommended scope and analytical cutoffs of toxicological analysis in DUID investigations.*

	Blood (ng/mL)		Urine (ng/mL)	
Target analyte	Screen	Confirmation	Screen	Confirmation
DRE category—Cannabis				
THC	–*	2	–*	2
Carboxy-THC	10	5	20†	5
11-OH-THC	–*	2	–*	2
DRE category—CNS stimulants				
Methamphetamine	20	20	200	50
Amphetamine	20	20	200	50
MDMA	20	20	200	50
MDA	20	20	200	50
Cocaine	–*	10	–*	20
Benzoylecgonine	50	50	300	50
Cocaethylene	–*	10	–*	20
DRE category—CNS depressants				
Alprazolam	–‡	10	–‡	50 total†
Chlordiazepoxide	–‡	50	–‡	50 total†
Clonazepam	–‡	10	–‡	50 total†
7-aminoclonazepam	–‡	10	–‡	50 total†
Diazepam	–‡	20	–‡	50 total†
Nordiazepam	50	20	100	50 total†
Lorazepam	–‡	10	–‡	50 total†
Oxazepam	50	50	100	50 total†
Temazepam	–‡	50	–‡	50 total†
Trazodone	–§	25	–§	50
Amitriptyline	–§	25	–§	50
Nortriptyline	–§	25	–§	50
Diphenhydramine	–§	25	–§	50
Carisoprodol	–§	500	–§	500
Meprobamate	–§	500	–§	500
Zolpidem	–§	20	–§	20
Butalbital	–*	100	–*	100
Phenobarbital	–*	100	–*	100
Secobarbital	100	100	200	100
Phenytoin	–§	500	–§	5000
Carbamazepine	–§	500	–§	5000
Topiramate	–§	1000	–§	1000
Gamma-hydroxybutyrate	–§	5000	–§	10000
DRE category—narcotic analgesics				
Codeine	–‖	10	–‖	50
6-acetylmorphine	–‖	10	–‖	10
Hydrocodone	–‖	10	–‖	50
Hydromorphone	–‖	10	–‖	50
Methadone	50	10	300	50
Morphine	20 free¶	10	200	50 total†
Oxycodone	–‖	10	–‖	50
Propoxyphene	50	50	300	50
Tramadol	–§	20	–§	20
DRE category—dissociative drugs				
Dextromethorphan	–§	20	–§	50
Phencyclidine	10	10	25	10

THC, Delta-9-tetrahydrocannabinol; Carboxy-THC, 11-nor-9-carboxy-delta-9-tetrahydrocannabinol; 11-OH-THC, 11-hydroxy-delta-9-tetrahydrocannabinol; MDMA, 3,4-Methylenedioxymethamphetamine; CNS, central nervous system.

*Immunoassay screening not targeted to this analyte.

†Combination of free and conjugated analyte.

‡Immunoassay screening targeted to nordiazepam, oxazepam or both; not an effective tool for screening all drugs in this class.

§Not routinely screened for by immunoassay.

‖Immunoassay screening targeted to morphine; not an effective tool for screening all drugs in this class.

¶Free drug, not conjugated.

able to produce a presumptive positive result. A comprehensive approach to screening in DUID cases would require some additional chromatographic screening in order to rule out drugs with low immunoassay cross-reactivity and those for which no immunoassay currently exists. As a general principle in forensic toxicology, presumptive results from drug screening procedures should be confirmed by a complementary specific technique such as mass spectrometry.

Recommendations for Analytical Cutoffs of Testing

Recommendations for appropriate cutoffs for screening and confirmation in both blood and urine are provided for some of the most important analytes in DUID investigations (Table 4). These thresholds were established to reflect the performance of both commercially available screening technology and confirmatory techniques, both of which are routinely used in forensic toxicology laboratories. These recommended cutoffs are based on analytical methodology and good laboratory practice rather than pharmacology or the probability of impairment. It should be noted that in many instances the laboratory may use an immunoassay cutoff concentration that is lower than the manufacturer's recommended cutoff, particularly if the assay is marketed towards workplace drug testing. This is an accepted practice as long as laboratories properly validate these methods and establish in-house cutoff concentrations using appropriate matrix in accordance with laboratory accreditation requirements. Table 4 does not contain recommendations for the DRE categories of Hallucinogens and Inhalants. The hallucinogens LSD, peyote, and psilocybin and commonly abused inhalants such as butane, ether, freon, nitrous oxide, toluene, and xylene will significantly impair the user's ability to operate a motor vehicle safely. There are currently limited techniques for routine screening of blood and urine for these compounds. Current practice in laboratories is a targeted analysis when case information suggests involvement or referral to a reference laboratory.

Analytical Considerations

Target Analysis versus Panel of Testing

We propose that testing for a comprehensive panel of analytes such as those in Table 4, is preferred in DUID investigations over an approach which targets only the drug or drugs suspected or listed by the investigating officer. Although more expensive and time consuming, this approach is preferred for several reasons including the fact that polydrug use is common among DUID suspects, and multiple drugs are often present in addition to those causing the most overt symptoms. Additionally, some symptoms are common to more than one class of drugs, and drug symptoms can vary depending on the phase of drug use. Also, in our experience suspects often will admit to use of one "less serious" drug but not others. Having comprehensive analytical results is important when providing the link between the observations of the subject's driving behavior and drug use. In addition, if a DRE officer is involved in the investigation, analyzing for all DRE categories is important for standardization of data being gathered on a national level by the International Association of Chiefs of Police (IACP).

Case Management and Communication

The laboratory and its staff are the technical experts on the appropriate approach to drug testing, and should have the discretion to order further tests based on preliminary results or other relevant indicators from the investigative report. If a laboratory is not able to offer analytical support for a particular drug or drug category, the laboratory has a responsibility either to identify another laboratory that can provide the necessary analytical support, or to notify the requesting agency that the test has not been performed. It should be clearly communicated to the client what drugs are tested for and which are not. It is not reasonable for the laboratory to assume that a law enforcement officer or prosecutor would know the cross-reactivity of a screening assay used, or the scope of drugs included in a GCMS or LCMS confirmation method. This can be accomplished in the report itself or in other documentation provided by the laboratory to its clients.

Analytical Approach

Laboratories need to fully understand and document the cross-reactivity of immunoassays used. It was not clear from the survey if all laboratories had established that the assays do not have equal cross-reactivity to all drugs within a given class. For example, opiate, amphetamine, and benzodiazepine assays can have markedly different sensitivities to chemically related members within each class. It is good laboratory practice to analyze additional known standards to establish the cross-reactivity for each drug which the laboratory reports. Importantly, all immunoassay screen positive results should be confirmed by mass spectrometry (GCMS or LCMS).

Confirmatory Methods

It is good laboratory practice for laboratories to validate their methods, establish a linear range, and limits of detection and quantitation. Operational laboratory guidelines have been established by SOFT and AAFS (6). We recommend that forensic laboratories follow these guidelines.

Conclusions

A traffic stop for impaired driving, whether caused by alcohol or other drugs, removes that driver from the road, and prevents the risk of injury or death to that driver, and other road users. Additionally it initiates a process, which when it works, can change the behavior of that individual and reduce the risk for future re-offense.

The DRE program, established by National Highway Traffic Safety Administration in 1988 and managed by the IACP is a structured program for law enforcement officers to assess a suspected drug impaired driver. The officer systematically collects and documents the symptoms of drug use and impairment. In cases where a DRE is not available or the suspect has been injured and can not be evaluated, it is critical that law enforcement at the scene use all tools available to them including training provided to all law enforcement officers on symptoms of drug use, crash reconstruction, and witness statements to document impairment, if any. Toxicological analysis of a biological specimen is the final step in this process and provides a nexus for the officer's observations. These recommendations do not list all analytes capable of impairing a driver's ability to operate a motor vehicle safely and we encourage laboratories to expand the scope of analysis as necessary for their region or for a particular case. This minimum list of drugs and the laboratory quality assurance practices recommended in this manuscript, if implemented by laboratories in drug impaired driving investigations, will increase the detection of drugs most likely to be encountered in DUID cases and promote more consistent practice

within the field. Laboratories involved in DUID testing should evaluate their current capabilities, strive to achieve these recommendations and clearly communicate their capabilities and limitations to their clients. In this way, the toxicologist helps to create a nexus between the officer's observations of the subject's driving behavior and drug use. Hence, DUID investigations must be consistently, scientifically and objectively evaluated.

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