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Ms. Cooper,

This report provides my comments and recommendations for those issues reviewed during our two conference call with judges and staff from the Louisiana drug courts on September 14 and October 11, 2010.

The following issues were addressed, with my comments:

- **Use of video monitoring of urine specimen collections**

  Use of remote video monitoring for observation of urine specimen collections and its effectiveness against adulteration and substitution was discussed. It was recognized that such remote monitoring of urine specimen collection eliminates safety issues associated with collectors being sequestered in a closed collection restroom with criminal justice system donors. It appears that adequately structured video monitoring of urine specimen donation could be as effective as direct *in situ* observation in deterring and identifying attempts at specimen adulteration and manipulation. However, a concern was raised regarding the privacy issues whereby a donor would have no guarantee as to who was observing their provision of a urine specimen. Given that the U.S. Supreme Court’s rulings in urine drug testing cases have recognized that urination has significant privacy implications, I recommended that relevant case law be examined to determine if such remote video monitoring of urine specimen provision is acceptable under these criminal justice situations.
• Addressing urine specimen dilution

Clearly, urine specimen dilution through excess fluid ingestion prior to urine specimen donation is one of drug users’ greatest resources to attempt to thwart effective detection of drug use. In recognition of this issue, the federal workplace drug testing program (under the aegis of the Substance Abuse and Mental Health Services Administration, SAMHSA) now includes mandatory specimen validity testing on every urine specimen. Whether urine specimen dilution and its role in avoiding positive test results is a significant issue within a given drug testing program should be determined in order to inform appropriate policy responses (evidence based practice). I recommended that, at a minimum, a pilot program be instituted whereby all urine specimens collected over a period of time be objectively assessed for dilution (e.g. urine creatinine) coupled with an assessment of whether there is any evidence of drug presence, even if below conventional cutoff concentrations (instrumented immunoassay screening can allow for such an assessment by comparing the numeric test results for the donor with those for the cutoff calibrator and the drug-free control). If it is found that dilute specimens also have evidence of drug present, and that absent the dilution would have tested positive, then that evidence can be used to justify formulation of a policy to detect and respond to urine specimen dilution.

I also note that federal workplace urine drug testing guidelines require that a specimen fail both creatinine and specific gravity criteria to be considered “dilute”, “substituted” or “invalid”. I consider either creatinine or specific gravity to be a suitable marker of a highly dilute specimen. The U.S. Federal Courts’ drug testing program has established criteria that recognize either creatinine or specific gravity as a suitable marker of a dilute specimen. Originally, the Nuclear Regulatory Commission’s urine drug testing program similarly considered either marker suitable for identifying a urine specimen as dilute. I also note that the federal workplace urine drug testing program has no effective sanction against a donor for providing a “dilute” specimen other than an MRO’s (Medical Review Officer) authority to require another specimen to be collected, but under direct observation (note that urine specimen collection in federal workplace drug testing programs is generally not collected under direct observation). Unfortunately, direct observation provides no protection whatsoever against a donor providing another highly dilute specimen. The only effective sanction which occurs in the federal workplace urine drug testing program for provision of a highly dilute urine specimen is when a urine specimen has been found to have creatinine and specific gravity values so dilute that the specimen could not have come from the normal human kidney and is thus considered a “substituted” specimen. I recommend that criminal justice urine drug testing programs not follow such a conservative approach to urine specimen dilution unless required by statute to do so. Accordingly, criminal justice urine drug testing programs need to draft policy language that puts the donor on notice that a highly dilute urine specimen is unacceptable and may be considered a failure to comply with the court-ordered drug testing conditions. I am prepared to provide further detailed policy guidance on this issue.

In my opinion, provision of a urine specimen reflecting an unacceptable level of dilution should be considered a failure to comply with the court-ordered conditions of successful participation in the urine drug testing program. Such highly dilute specimens should not be called “positive”, a term which should be reserved for a finding of the presence of drugs, and should be distinguished from a “positive“ drug test result. Positive drug tests should be recognized as part of the chronic relapsing
disorder of addiction. On the other hand, intentionally attempting to thwart effective drug testing should be viewed as an intentional dishonesty to the court. Again, I am prepared to provide further guidance on this issue.

- **Ethyl glucuronide (EtG) cutoff**

EtG has received renewed attention as a long-lived (up to a few days) biomarker of ethanol ingestion. Although formed as only a very minor metabolite after ethanol ingestion, given the multi-gram amounts of ethanol consumed in drinking, sufficient amounts of EtG are formed after drinking that it can be detected in urine for several days, depending upon the sensitivity and reporting cutoff of the detection method used. However, given the possibility of “innocent” or unknowing exposure to ethanol (through use of hand sanitizers, mouthwash, communion wine, or food prepared with ethanol) and the sensitivity of EtG analyses to detect exposure to even small amounts of ethanol, a sufficiently high cutoff must be used to ensure that knowing use of ethanol can be clearly distinguished from such unknowing innocent exposures. Given the several peer-reviewed published studies addressing such low level and potentially innocent exposures to ethanol, I recommend a urine EtG cut-off of at least 500 ng/mL or even 1,000 ng/mL to convincingly demonstrate knowing use of ethanol as opposed to passive innocent exposure. I also note that case law addressing the admissibility, evidentiary weight and interpretation of EtG test results is limited, but with some recent cases finding that the cutoffs employed were too low and allowed for the possibility of the observed test results to be due to innocent exposure. Significantly, the federal Substance Abuse and Mental Health Services Administration (SAMHSA), responsible for federal workplace drug testing guidelines, had published an Advisory in September 2006 expressing their serious concerns about EtG testing and the use of EtG alone to demonstrate use of ethanol. Unfortunately, SAMHSA did not specifically indicate that their concerns stemmed simply from the use of too-low cutoffs. Thus, their Advisory stands as a somewhat damning statement about the use of EtG in general. Accordingly, it is important to use a sufficiently high EtG cutoff (i.e. 500 or 1,000 ng/mL) to avoid claims of innocent exposure to ethanol. Furthermore, proponents intending to use EtG test results to demonstrate use of ethanol, need to be prepared to address challenges to the admissibility of and evidentiary weight given to EtG test results, and need to be prepared to bear their burden of proof through provision competent expert testimony. One final point about EtG is that it is an analyte subject to the effects of urine specimen dilution. Accordingly, objective measures of urine dilution (i.e. creatinine or specific gravity) need to be taken into account when interpreting urine EtG test results.

Laboratories are also offering analyses for ethyl sulfate (EtS) as complimentary and confirmatory to EtG analyses. Like EtG, EtS is also formed as a minor metabolite of ethanol. One basis for also analyzing for EtS is that there is the possibility of the formation as well as the degradation of EtG in infected urine specimens, while EtS appears to be less susceptible to such *in vitro* transformations. However, I am not convinced that such concerns are sufficient to merit routine testing for both EtG and EtS. I believe that with properly handled urine specimens (e.g. prompt testing after collection, and/or refrigerated storage pending testing) either EtG or EtS would serve as a suitable marker of ethanol consumption.
• Confirmation test cut-offs

Although modern instrumented immunoassays have extremely high positive predictive value, especially for cocaine, cannabinoids and opiates, some programs may still choose to confirm initial screening test results through secondary confirmation testing using highly sensitive and specific mass spectrometric methods (i.e. GC/MS, LC/MS/MS). I recommend that any such confirmation testing, when performed, be performed at the laboratory’s Limit of Detection (LOD) or Limit of Quantitation (LOQ), rather than using higher federal workplace drug testing confirmation cutoffs. This is to ensure that otherwise correct identification of drug use at the immunoassay screening stage not be improperly impugned simply because of a failure to confirm at workplace confirmation cutoffs. There is scientific, regulatory and legal support for such a LOQ or LOD confirmation testing policy. Even the federal workplace drug testing guidelines (SAMHSA) recognize the utility of repeat testing not at a specific cutoff but simply to demonstrate the presence of drug. There is also case law within the federal courts recognizing that a “negative” report for a confirmation test but which clearly demonstrates the presence of drug still demonstrates drug use sufficient for federal probation revocation. Such a decision at the federal district court level was upheld by a federal court of appeals.

I should also note that the federal workplace drug testing program cutoffs for cocaine metabolite and amphetamine and methamphetamine have recently been lowered, as of 10/1/10. For cocaine metabolite, the screening cutoff has been lowered from 300 ng/mL to 150 ng/mL and the cocaine metabolite confirmation cutoff lowered from 150 ng/mL to 100 ng/mL. For amphetamines, the screening cutoff has been lowered from 1,000 ng/mL to 500 ng/mL and the confirmation cutoff for amphetamine and methamphetamine lowered from 500 ng/mL to 250 ng/mL. I recommend that these lower screening cutoffs be followed (the immunoassay test kit manufacturers have responded in providing immunoassays using these lower cutoffs). But, as noted above, I recommend that any subsequent confirmation testing be performed at the laboratory’s LOD or LOQ.

• Interpretation of extended positive cannabinoid test results

It has been demonstrated that, when using current urine cannabinoid immunoassays with a cutoff of 50 ng/mL, cessation of chronic use of cannabinoids can be followed by a prolonged period of positive test results (i.e. 2–3 weeks, rarely longer) after cessation of use. Note that occasional users of cannabis (i.e. use once or twice each week) are likely to stay positive for only 1–2 days after use, rarely longer. There is now a sufficient body of published peer-reviewed scientific literature to allow for the interpretation of sequential cannabinoids drug test results after acute and chronic use. The urine cannabinoid concentrations (ideally normalized for dilution), the time frames between tests, any usage claims made by the donor, and other relevant client-specific factors are all important to consider in interpreting such sequential positive test results and whether they are consistent with prolonged elimination after cessation of chronic use or rather demonstrate ongoing and renewed use.
It should be noted that such clear interpretations may not always be possible and may require additional specimens to be collected. I am prepared to further address the details surrounding such interpretative issues.

• **Use of visually-read non-instrumented urine drug test devices**

I understand visually-read non-instrumented urine drug testing devices are only occasionally utilized in the Louisiana drug court programs. Nonetheless, I recommend that there be objective criteria established for device performance requirements for bid submissions. There are now many of these visually-read non-instrumented urine drug testing devices available, in varying configurations, and with varying performance capabilities. At a minimum, I recommend that any such devices being considered be FDA-cleared (through the 510(k) substantial equivalence process). In addition, there should be peer-reviewed published literature on studies by a third party documenting the performance characteristics of the device (e.g. performance with spiked as well as clinical specimens, with drug concentrations slightly below and slightly above the specified cutoff concentrations), as well as cross-reactivity data. Unfortunately, few current devices have such scientific literature support. I note that such detailed device performance information may be contained within the FDA submission documents. I also recommend that the test device manufacturers provide devices for your staff to make an actual assessment of user-friendliness and acceptance (ease of use, readability, specimen volume requirements, etc.).

Although some of these visually-read non-instrumented devices have demonstrated good performance, their is a relative lack of case law precedents addressing the use and probative value of positive test results from such visually-read non-instrumented devices without further confirmation testing. Thus, at the moment it appears that positive test results from such devices may need to be confirmed if sanctions are to be applied.

• **Testing for new drugs**

There are several “new” drugs being used and abused which are presenting challenges for their effective detection. The new drugs of synthetic cannabinomimetics (Spice, K2, et al.), cathinones, “bath salts”, benzylpiperazines, and others, create special challenges for conventional urine drug testing programs. For many of these new drugs, there is little known about human metabolism and elimination and so knowing what molecular entity(ies) to test for in a urine specimen remains challenging. Even more problematic is that there are many of these different types of new drugs emerging, both within a given chemical class as well as across chemical classes, and thereby presenting a challenge to those diagnostic companies developing immunoassay tests to determine which tests to add to urinalysis drug test menus. It takes extensive research and time (at least 1–2 years) to develop such immunoassay kits and then get them through the FDA approval/clearance process. Until individual specific drugs or well-defined drug classes become a significant problem, leading to widespread demand for drug testing for these new drugs, it is difficult for immunoassay
diagnostic companies to justify the time and expense to develop these assays for every new drug that comes along. And these new drugs are emerging at a rapid pace with the designer drug chemists always ready with a new analog to stay ahead of regulatory authorities. Accordingly, immunoassay kits allowing rapid and facile testing for many of these new drugs are not yet available. That leaves laboratory-based chromatographic methods (GC/MS, LC/MS, etc) to be developed to detect these emerging drugs. Analytical procedures using these chromatographic techniques are easier to develop than for immunoassays. However, they also suffer from our lack of human clinical data on what analytes should be tested, and then having those analytes available as standards from which chromatographic and mass spectral criteria can be developed. For a few of the synthetic cannabinomimetics, some metabolite data is available and accordingly a few laboratories have offered tests for some for these drugs/metabolites.

I hope I have addressed the primary issues discussed in our conference calls. As the Louisiana drug courts’ policies and procedures are further developed I am prepared to review these documents and provide further guidance as necessary. Please feel free to contact me with any questions or if I can provide further details.

Dr. Leo Kadehjian