Department of Health and Human Services
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Prevention
Drug Testing Advisory Board

January 26-27, 2011

The Center for Substance Abuse Prevention (CSAP) Drug Testing Advisory Board (DTAB) meeting was convened at 8:30 a.m. on January 26, 2011 in the SAMHSA Building (Sugarloaf and Seneca Conference Rooms), 1 Choke Cherry Road, Rockville, Maryland 20857.

In accordance with the provisions of Public Law 92-463, the meeting was open to the public on January 26 from 11:00 a.m. to 4:35 p.m. and on January 27 from 8:30 a.m. to 12:15 p.m. EST.

Board members present:

Janine Denis Cook, DFO and Chair
Robert Bonds
Dr. James Bourland
Dr. Larry Bowers
Dr. Lawrence Brown
Phyllis Chandler
Laurel Farrell
Dr. Courtney Harper
Barbara Rowland
Dr. Donna Smith
Jim Swart
Dr. Steve Wong

Others present for the meeting:

CAPT Carol Rest-Mincberg, DWP, CSAP
Hyden Shen, DWP, CSAP
CDR Jennifer Fan, DWP, CSAP
Charles LoDico, DWP, CSAP
Ronald Flegel, DWP, CSAP
Dr. Sean Belouin, DWP, CSAP
Dr. Deborah Galvin, DWP, CSAP
William Sowers, DWP, CSAP
Giselle Hersh, DWP, CSAP
Fran Harding, CSAP
Dr. Rick Broderick, SAMHSA
Ed Jurith, ONDCP
Wayne Chalk, NRC
LTC Dr. Timothy Lyons, DoD
Dr. Yale Caplan, DOT Consultant
Dr. Ed Cone, consultant
Dr. Michael Walsh, The Walsh Group
Denny Crouch, Aegis Labs
Dr. Marilyn Huestis, NIDA
Dr. Frank Esposito, RTI International
Dr. R. H. Barry Sample, Quest Diagnostics
Dr. Joe Autry
Vanessa Berry, DoJ
Rina Hakimian, OGC
Bohdan Baczara, DOT
Cindy Ingrao, DOT
Christopher Mangione, US Courts
Zhihao Hui, FDA
Bob Schoening, Coast Guard
Dr. Donna Bush, FDA
Toian Vaughn, OPBB, SAMHSA
Nevine Gahed, SAMHSA
Dr. John Mitchell, RTI
Jared Cooper, RTI
Erica Harbison, RTI
Susan Crumpton, RTI
Dr. Michael Keene, CDM Group
Cindy Kunz, CDM Group
Kim Cohen, CDM Group
Bill Corl, Omega Labs
Dale Dirks, OraSure
Debra Fraser-Hoes, OraSure
Dean Fritch, OraSure
M. P. George, Alere Toxicology
David Goncalves, DrugPak, LLC
Heather Healy, AFA
Keith Kardos, OraSure
Sarah Buchanan, OraSure
Abigail Potter, ATA
Paul Speidel, Psychemedics
Marsha VandeNei, Schneider Trucking
Helen White, DATIA
David Whiteside, J.B. Hunt
Tess Overdyk, IHM
Tim Nelson, Siemens
Ernest Street, EWJ

Jackie Prione, Orasure
Suzanne Allison, CRL
Glynis Arnall, CRL
Kimberly Erin, CRL
R. Duncan Jenkins, CRL
Daniel Kolbow, CRL
David Kuntz, CRL
Mona Modi, CRL
Jim Robertson, CRL
Melinda Smotherman, CRL
Veronica Stewart, CRL
Mike Stogner, CRL
Robert Steve Valverde, CRL
Ila Bhatt, CRL
Megann Agne
Alison Stockdale
David Anderson
Ann Adcook
Ann Chappie
Robert Bard
Barry Kurtzer
Betty Emerson
Kimberly Blake
Pamela Childers
Christine Moore
Alicia Cundiff
Ken Edgell
David Evans
Neil Fortner
James Ferguson
Janet Fose
Jennifer Collins
Josephine Kenny
Janet Kornmann
Mary Brown-Ybos
Michael Peterson
Jeff Morrison
Pat Pizzo
Paula Childs
Paulette Fitzgerald
Glynda Phelps
Claus Pruemper
Doug Rheinheimer
Jenny Richard
Sami Jamokha
Janet Toomsen
Mike Bunch
Greg Capps
Melissa DiThomas
Nick Hartman
Linda Shreet
M. Hayes
Morrison Reed
Richard Lipov
Cheryl Taylor
Vicky Looney

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January 26, 2011

Call to order

Dr. Janine Cook, the Designated Federal Official (DFO) of the Drug Testing Advisory Board (DTAB), called the meeting to order at 11:00 a.m. EST. Because of the nor'easter, the published agenda was not strictly followed. Dr. Cook explained the public comment process, provided housekeeping announcements for the onsite attendees, and instructions regarding Adobe Connect for those attendees participating remotely.

Welcome and Opening Remarks

Dr. Cook, as Acting Chair of DTAB, welcomed everyone. She elaborated on how the mission of DTAB, as written in the DTAB charter, meshed with the mission of the Substance Abuse and Mental Health Services Administration (SAMHSA). The Department of Health and Human Services (HHS) has the authority for administering the Federal Drug-free Workplace Programs and the Secretary has delegated that authority to SAMHSA.

Each member of the DTAB and the Division in Workplace Programs (DWP) introduced him or herself.

Ms. Carol Rest-Mincberg, the Acting Director of DWP, discussed the legal basis for drug testing and the charge of the DTAB.

Ms. Fran Harding, the Center for Substance Abuse Prevention (CSAP) Center Director, welcomed the Board members. She elaborated on SAMHSA's reliance on the DTAB to apply the latest scientific evidence, legal considerations, and consumer advice in their considerations of the important agenda items. Ms. Harding explained why DTAB resides in CSAP. She elaborated on the uniqueness of this regulatory workplace drug testing program, with its permanent and separate legal authority that does not require a periodic reauthorization, which is managed by SAMHSA on behalf of the Office of National Drug Control Policy (ONDCP). The Drug-free Workplace Program is the largest universal prevention program within SAMHSA, targeting 400,000 federal employees in testing designated positions and more than 12 million workers in the federally-regulated industry.

Dr. Rick Broderick, SAMHSA's Deputy Administrator, also thanked the Board for providing advice and guidance to SAMHSA as SAMHSA administers this regulatory responsibility.

Mr. Ed Jurith, General Counsel for the Office of National Drug Control Policy (ONDCP) in the Executive Office of the President, explained how a drug-free workplace and drug testing are integral parts of any comprehensive and successful national drug control strategy. He related his lectures at the American University Law School on drug policy in the law to the historical importance of the Drug-Free Workplace and drug testing in dealing with drug abuse in America. He stressed the invaluable contributions of the Drug-Free Workplace Program and the DTAB in making our nation and workplaces healthier and safer. Mr. Jurith challenged the DTAB to build on this progress, to advance technologies, and to be on the cutting edge of policies and practices that reduce the consequences of drug use and abuse, especially as it explores the standardization of oral fluid testing methods. The Obama Administration has set a goal of reducing the prevalence of drugged driving by ten percent by 2015. ONDCP Director Gil Kerlikowske has adopted this initiative and believes that the standardization of oral fluid testing in drug testing labs is important in detecting the presence of drug use by drivers.

Federal Drug Testing Updates

DOT Drug Testing Update

Mr. Jim Swart, of the Department of Transportation (DOT), emphasized how DOT Secretary LaHood believes that this program is the cornerstone of safety at the DOT and supports the components of this demand reduction drug-free workplace program, which includes the education, testing, and treatment for those who test positive. His office works with all the DOT agencies above ground, on the ground, underground, and on our nation's waterways, including the Federal Motor Carrier Safety Administration, Federal Transit Administration , Coast Guard, Federal Railroad Administration, Federal Aviation Administration, and Pipeline and Hazardous Materials Administration. DOT agencies conduct inspections and audits. The drug testing data since 2005 indicates that laboratory positive results are on the decline. Recently, amphetamines positives have nudged above cocaine for the first time in history. Marijuana is the most prevalent, and rising, drug that is used. DOT has implemented new testing procedures, lowered the cutoff levels for cocaine and amphetamine, eliminated the initial test for morphine as a means to obtain 6-AM or heroin positives, and are testing for MDMA. DOT is interested in prescription medication use, alternative specimen testing, medical marijuana issues, and developing a database of employee violations. He indicated DOT's full support of the DTAB efforts. Mr. Swart identified the DOT program managers. He also identified his staff members and thanked them for their dedication.

Federal Drug-Free Workplace Programs

Mr. Hyden Shen, of DWP, provided a broad overview of the 25-year history of the Drug-Free Workplace Program (DFWP) and its relationship to the DTAB and drug testing. The DFWP is authorized by Executive Order 12564, Public Law 100-71, and the Mandatory Guidelines. The Executive Order directed agency heads to establish specific programs for a drug-free workplace, create employee assistance programs, train supervisors and their employees on a drug-free workplace, establish deterrent drug testing programs, and identify testing designated positions. Public Law 100-71 provided guidance to ensure consistency throughout the program and to put into place specific guidelines. PL 100-71 has two key components: without a plan certified by the HHS Secretary and a report to Congress, the agencies are not allowed to use appropriated funds for federal drug testing, and the development of Mandatory Guidelines by HHS to establish laboratory procedures, technologies, a chain of custody, and lab certification standards and procedures, and to specify the drugs for which employees may be tested. The Anti-Drug Abuse Act of 1988 established the Office of National Drug Control Policy. In 1991, the White House designated ONDCP as the overall lead for the Federal Drug-Free Workplace Program and Chair of the Interagency Coordinating Group Executive Committee. The Committee is comprised of representatives from HHS, the Department of Justice, and the Office of Personnel Management. On behalf of ONDCP, DWP staffs both the Committee and the DFWP.

(Break)

DoD Drug Testing Update

COL Timothy Lyons, of the Armed Forces Medical Examiner, provided the Department of Defense (DoD) updates. DoD tests for more drugs than the federal civilian program. Recent changes include screening specifically for 6-AM (100% screen) beginning in 2004, dropping barbiturates from the testing panel, adding oxycodone/oxymorphone (20% random pulse testing) in 2005, and dropping LSD and MDEA from the test panel. Currently, testing at the six DoD laboratories includes marijuana, cocaine, designer amphetamines, and 6-AM at 100 percent testing. Oxycodone, oxymorphone, codeine, morphine, and PCP are pulse-tested at a target rate of 20 percent. Any specialty testing, including prescription drugs, synthetic cannabinoids, mephedrone, steroids, and oral fluids, is forwarded to either DoD's toxicology lab or the medical examiner. The most recent change to DoD's cutoffs was lowering the confirmation cutoff for amphetamine and methamphetamine to 100. Prevalence testing involves random selection of specimens that screened negative at the laboratories and testing those specimens for other analytes that are not currently part of the program to determine the positivity rate. If the positivity rate exceeds 0.25%, then DoD considers adding that drug to the test program. Prevalence testing analytes include LSD; prescription drugs, including salosin; benzodiazepines; hydrocodone; and methadone. Two drugs exceeded 0.25%: benzodiazepines and hydrocodone whose positivities were 80% related to valid pain and/or sleep management drug prescriptions. Nonmedical use of prescription drugs is a true readiness and safety threat for the DoD. Trending for the six million specimens per year tested at the six DoD laboratories include amphetamine-only positives predominately related to Adderall use. DoD has applied for funding to increase oxycodone/oxymorphone screening, to begin screening for hydrocodone/hydromorphone, and to add five benzodiazepines to the random testing profile. Positives results will be cross-referenced with DoD's pharmacy database to determine which are due to valid prescriptions and which will require confirmation.

Highlighted Changes: The Mandatory Guidelines for Federal Workplace Testing Programs (73 FR 75122, November 25, 2008)

Mr. Charles LoDico, of DWP, began by outlining the history of the Guidelines from 1988 through 2008. Next, he highlighted the substantive changes to the 2008 revised Mandatory Guidelines for Federal Workplace Drug Testing Programs. The format of the 2008 Guidelines was changed to an easy to read, plain question-answer language with subparts organized by subject matter areas. He discussed the significant changes made to the following parts of the Guidelines: specimen collection, standards for collectors and collection sites, new analytes (6-acetylmorphine and methylenedioxymethamphetamine (MDMA) and its analogues MDA and MDEA) and lower cutoffs (amphetamines and cocaine), new technologies for confirmatory drug testing (GC/MS/MS, LC/MS, and LC/MS/MS), the new Instrumented Initial Test Facility (IITF) category, qualifications for the Medical Review Officers, and the Federal Custody and Control Form (IITF, Federal testing authorities, and new analytes changes). He explained the reasons for the 18 month implementation period for these Guidelines. Other supporting documents, including the Urine Specimen Collection Handbook, the MRO Manual, and the MRO Case Studies, were revised to be consistent with the 2008 Mandatory Guidelines.

Federal Drug Testing Updates

NRC 10 CFR Part 26 Fitness for Duty Program

Mr. Wayne Chalk, of the U.S. Nuclear Regulatory Commission (NRC) Fitness for Duty in the Regulatory Programs, presented NRC's mission: to license and regulate the Nation's civilian use of byproduct, source, and special nuclear materials, to ensure adequate protection of the public health and safety, to promote the common defense and security, and to protect the environment. Currently, there are 104 reactors at 65 sites or plants with 18 applications for new reactor construction under consideration. There are four components to NRC's fitness for duty program: drug and alcohol compliance as per Fitness for Duty part 26, background checks as part of the access authorization program, training and behavioral observation for the human factors interaction, and fatigue management as per 10 CFR Part 26.

Medical Review Officer (MRO) Certification

CDR Sean Belouin, of DWP, addressed the key Mandatory Guidelines changes in Section 13.1 regarding the certification of MROs and the annual approval by the HHS Secretary of MRO training and certification entities and boards for physicians performing reviews of Federal employee drug tests. On December 8, 2010, the HHS Secretary approved the following MRO certifying organizations that offer both MRO training and certification through examination: the American Association of Medical Review Officers (AAMRO) and the Medical Review Officer Certification Council (MROCC). Additionally, the HHS Secretary approved the following MRO certifying organizations that offer just MRO training, but not the certification: the American College of Occupational and Environment Medicine (ACOEM) and the American Society of Addiction Medicine (ASAM). This training offered by ACOEM and ASAM can be used as a prerequisite for certification testing offered through either AAMRO or MROCC. Federal agencies must ensure that MROs have been trained by one of the four organizations and certified by either AAMRO or MROCC.

Electronic Custody and Control Form (CCF)

Mr. Charles LoDico, of DWP, discussed the proposed adoption of an electronic CCF. The Office of Management and Budget (OMB) has requested that DWP investigate an electronic CCF prior to 2013 to reduce burden. OMB's Government Paperwork Elimination Act encourages the Federal government to use electronic signature alternatives. For the 2010 proposed CCF, many commenters expressed a desire for an on-demand CCF and provided the associated benefits. There are two pertinent HHS electronic document policies: one from the FDA describing the criteria under which electronic signatures are considered equivalent to full handwritten signatures and the other from the Office of the Secretary concerning adoption of national standards to protect the confidentiality, integrity, and the availability of electronic protected health information. As part of the process, SAMHSA will seek public comment on the standards for electronic signature, non-repudiation of an agreement for digital signatures, third party software for managing Federal CCF information, the qualifications of a unique specimen identification number, the legally-binding equivalent of traditional hand-written signatures in a forensic arena, the security of data transmission over telecommunications systems and networks, and the integrity of the document content. The DTAB will be requested to review the proposed electronic CCF prior to its publication in a Federal Register Notice.

Alternate Matrices

Mr. Ron Flegel, of DWP, reviewed alternate matrices for drug testing as published in the 2004 proposed Mandatory Guidelines. As stated in the 2008 Federal Register Notice, alternate matrices will require further examination and additional studies because of the significant issues raised by Federal agencies during the review process. Issues included scientific acceptability, the court and legal acceptability, community acceptability, FDA approval, cutoffs, specimen quantities, quality assurance and performance testing, the cost/benefit ratio, the different detection windows, reasons for testing for the different matrices, and the relatedness of the different matrices to each other for interpretation. Public comments concerning the 2004 proposed rulemaking numbered 285. Discussion concerning oral fluid included collection method, wait time, collector examination of donor mouth, collection observation period, collection device, volume indicator on device, split specimen collection method, specimen volume, the nature of the specimen, lack of dignity with collection, increased collection time, biohazard, specimen standardization, specimen stability, reasons for testing, marijuana contamination issues, collection with or without urine, and specimen validity testing. Hair discussion included location of collected hair on body, specimen amount, collector assessment of collection amount, gender bias, hair color bias, normalized for melanin, environmental exposure contamination, specimen validity testing, collector observation, distinguishing synthetic/substituted from real hair, and cutoffs. Sweat discussion included environmental exposure, donor questionnaire, privacy, gender of collector, stigma, length of time to wear the patch, and specimen validity testing. Issues raised that affected all matrices included what analytes to test for, fairness to individuals tested using different matrices, different drug detection windows, the complementary nature of the matrices, detailed guidance on the selection of the appropriate matrices, and the relationship of cutoff values between matrices. There were expressed concerns that it was not equitable to test Federal employees using different matrices with different detection windows.

Public Comments

Mr. Robert J. Bard is a regulatory attorney who expressed his concern as to the lack of progress by Federal agencies on the use of hair as an approved matrix. He stated that the Federal agencies have a duty and legal responsibility to protect the American public, in general, and to aid regulated industry, through the drug testing program. Most private employers are free to choose the drug testing methods and matrices they wish to use in their drug testing program. Currently, federally-regulated industries must use urine specimens for required drug testing. The urine specimen has problems, including specimen control and privacy. The legal system has embraced the use of hair testing as a method of evidentiary requirements introduced in Daubert versus Merrill Dow. The science is sound. Major Kevin J. Christner offers a strong rationale for the use of hair testing in the military to avoid the problems that are seen in urine drug testing.

Mr. Bill Corl is the Chief Operations Officer for Omega Laboratories, one of the major U.S. hair testing laboratories with over ten years of hair testing experience. He stated that the Federally-regulated industries need the approval to use the best available technology to fight illegal drug use and abuse in the workplace, including hair testing for pre-employment and random testing. Hair testing is a secure, reliable testing method that is difficult to adulterate, unlike urine. Hair testing has a longer detection window compared to urine. It is easily collected, transported, and stored and less biohazardous than urine. Given that hair testing is widely accepted in most industries; in state, Federal, and local courts; and is scientifically proven, why has it not been brought to the forefront to complement urine testing?

Mr. David Goncalves is General Manager at DrugPak LLC, which markets a drug testing management software utilized by over 100,000 employers and over three million DOT-covered employees. He expressed his delight in the progress towards the adoption of the electronic chain of custody form. He stated that an electronic CCF has been vetted in terms of security, non-repudiation and thoroughly tested in the free market and overwhelmingly accepted in matters of national security, personal privacy, and safety. He believed that the drug testing industry is ready for the electronic chain of custody as is DATIA's Electronic Data Standards Committee. DrugPak supports DTAB in this effort and offers its resources, expertise, and cooperative spirit to directly aid in the process of establishing open standards for the electronic transfer of drug and alcohol testing information.

Dr. Murray Lappe is a physician, a Medical Review Officer, and founder of National Medical Review Officers, the largest MRO service organization in the world, which handles more than eight million drug test results each year. Between 1990 and 2000, his employees handled more than 100 million CCFs, which added four dollars to the cost of every drug test because of printing, mailing, faxing, merging, and storing the CCFs. He stated that the manual paper CCF form increased errors and was the rate limiting factor in the reporting of drug test results in a timely manner. His company developed e-screen with its electronic CCF and error checking capability to eliminate errors, bottlenecks, paper wastage, and reduce costs in the drug testing process. To date, they have processed more than ten million CCFs using e-screen with no legal challenges or affidavits. Ninety percent of the cost of processing the CCF has been eliminated.

Ms. Abigail Potter, with the American Trucking Associations (ATA), stated that safety is one of their top priorities. Carriers want to ensure their drivers are the safest by using drug tests and having alternative specimens, particularly hair, to test their drivers. They found a benefit to performing both urine and hair testing despite the high financial costs because they can reduce their accident and liability risks. ATA strongly recommends that regulations be developed for hair testing. Ms. Potter stated that Ellen Boyd of the Women in Trucking Organization is also a proponent for hair testing because many women have direct observation and discrimination issues.

Mr. Stephen Lee, Executive Vice President and Chief Science Officer for OraSure Technologies, provided public comment on oral fluid testing in Federal workplace drug testing programs. He described how OraSure has been the market leader in oral fluid drug testing in both worksite and criminal justice applications since the FDA approval and deployment of the Intercept Oral Fluid test system. Currently, Intercept is used to analyze over two million specimens per year. The factors that drive the use of oral fluid testing are its simplicity, convenience, relative resistance to specimen adulteration, and its precedent for future legal defensibility. Data from 2005-2009 indicate that the cutoffs established using the Intercept test system are effective in detecting drug use at rates similar to those obtained with urine testing. In partnership with Roche Diagnostics, OraSure is developing oral fluid assays for analysis on random access, automated laboratory instruments. OraSure is also developing a new and improved version of its oral fluid sample collector to increase the reproducibility of sample volume collection, to increase the total volume of sample collected, and to indicate when adequate sample has been collected. Mr. Lee expressed a desire to work with DTAB on the oral fluid initiative.

Ms. Vandehei, of Schneider National, represented Schneider, the parent corporation of four major interstate carriers which operates in excess of 13,000 tractors and 35,000 trailers, employs more than 12,000 drivers, utilizes the services of over 1,800 independent contractors, and logs an average of about six million miles per day. Urine drug testing is not without its flaws, including the ability of the donor to suborn the test. Schneider National has been conducting hair testing on its driver applicants since March 2008. To date, they have conducted 19,349 hair drug tests, of which 793 tested positive (4.1%); 728 of those applicants received a negative result using urine (0.34%). Thus hair testing has kept 700 drug users out of a Schneider truck. Pre-employment hair testing has resulted in a 58% reduction in their random testing rates and 83% reduction their post-accident positive test results. Schneider proposes implementing hair testing for pre-employment and random drug testing because of the longer window of detection. Urine drug testing is still the best option for post-accident, reasonable cause, and return-to-duty follow-up testing because it aids in determining whether the driver was under the influence at that given point in time. They would recommend using both specimen matrices to create a more comprehensive drug testing program.

Mr. David Whiteside, Senior Director of Compliance with J.B. Hunt Transport, represents one of the larger trucking companies with about 11,000 drivers. He has almost 46,000 paired hair and urine drug test results which he would offer to DTAB. He recommends oral fluid testing to detect the drugged drivers on the roadside and hair testing for pre-employment because of its longer detection window and its less chance of adulteration and substitution. Concerning external contamination, he shared a letter to the editor of Forensic Journal of Analytical Toxicology from Marc LeBeau and Madeline Montgomery. He does not believe that truck drivers have any legitimate reason to have cocaine exposure.

Dr. Dave Kuntz, Executive Director of Analytical Toxicology at Clinical Reference Laboratories (CRL) in Lenexa, Kansas, announced CRL has been conducting external clinical trials for the new semi-quantitative and qualitative KIMS technology homogenous assays from Roche Diagnostics and OraSure Technologies. The homogenous assays were compared with the currently approved micro-plate assays using a mix of repository and spiked samples; all discordance results were resolved by LC/MS/MS. The homogenous assays had excellence performance agreement of greater or equal to 95%t with the microplate assays and greater than 99% with LC/MS/MS. The homogenous assays improve laboratory workflow. He urged DTAB to review the existing technologies and the new assays in development as formal Guidelines are established for oral fluid.

Dr. Cook adjourned the meeting at 3:00 p.m. EST.

January 27, 2011

Call to order

Dr. Cook called the morning session to order. She again provided housekeeping announcements for those attending on-site and web conferencing instructions for those attending remotely. She read one public comment from the day before.

Dr. Steven Soifer, the CEO of the International Paruresis Association (IPA) and an Associate Professor of Social Work at the University of Maryland, represented the non-profit organization for people who suffer from shy bladder syndrome, the social anxiety and chronic pelvic floor dysfunction disorder. Currently, there are an estimated 17 million Americans (7%) who suffer from shy bladder. In 2004, IPA submitted public comment on the proposed new regulations on alternative testing matrices in which the IPA reiterated its position that it is not opposed to drug testing, but is asking for alternative testing for those who are unable to provide a voluntary urine specimen due to Shy Bladder Syndrome. SAMHSA drug testing rules require exclusively urine testing and do not permit alternative specimen testing for those who suffer from paruresis or other medical conditions, which may cause an unexplained inability to produce a urine sample. Currently, a failure to produce a urine specimen equates with refusal to test. IPA requested that DTAB realize that the problem of paruresis is real and assure that reasonable accommodations will be built into the testing rules, such as the use of hair, saliva, or oral fluid in lieu of urine for anyone unable to produce a urine sample within the two hour time limit. Per Law S.3406 or the ADA Amendments Act, disabilities now include major bodily functions, including those of the bladder. Thus, it is illegal to discriminate against anyone with bladder problems and reasonable accommodations must now be provided.

Oral Fluid Matrix - Historical Perspective

Dr. Michael Walsh began with a brief history of the HHS Guidelines development, starting in September 1986 when President Reagan signed Executive Order 12564. The initial version of the Guidelines was issued in February 1987, which contained the standards for collection, laboratory testing, etc., but it did not include laboratory certification. Public Law 100-71 outlined the prerequisites that must be completed before any appropriated funds could be used to drug test any Federal employee. One of those prerequisites was to revise the Guidelines to include a laboratory certification program and to publish in the Federal Register the elements of this program for public comment. The final notice of the new Guidelines was issued in April of 1988. Later, DOT, NRC, and other federal agencies adopted these Guidelines for their own regulated industries. Over the next 15 years, from 1988-2004, the Guidelines were fine-tuned. In 2004, SAMHSA proposed changes to the Guidelines to include alternative matrices - oral fluid, hair, and sweat. The Final Notice in 2008 stated that urine would remain the only approved specimen matrix for Federal programs because of public comment and Federal agency concerns. These comments indicated that the technology for hair, oral fluid, and sweat was not sufficiently mature to include in the Federal program at that time. Over the last three years or so, more research has been done on oral fluid and the science and technology for detecting drugs in oral fluid seems to have reached the point where further consideration appears to be merited. Remaining issues concerning oral fluid include specimen matrix, reason for the test, how often testing occurs, the required window of detection, the tested drugs, the immediacy of the results, the availability of devices/assays, and where testing will occur. Advantages of oral fluid include its collection is less invasive than urine, it provides evidence of very recent exposure, and it contains the active drug rather than the metabolite. The cons include that the window of detection is shorter than urine, the collection method is critical, and the contamination issues. Testing methodologies include ELISA, heterogeneous and homogenous immunoassays, GC/MS and LC/MS/MS, and point-of-collection tests, with or without readers. In a study evaluating 10 different on-site point-of-collection tests, only two devices performed well. In another study of unregulated drug data of two million urine and 650,000 oral fluid tests from a single large MRO source, overall oral fluid positivity rate was a 4.3% with a MRO-verified positivity rate of 95.6%, meaning only 4.4% were reversed in the MRO process. For the MRO-verified positives, the positivity rate was 60% for marijuana, 24% for cocaine, and 6.4% for methamphetamine, followed by amphetamine, opiates, and PCP. Comparing urine and oral fluid results, overall positive rates were 4.15% in lab-confirmed results in urine and 4.3% in oral fluid; more cocaine and methamphetamines were detected in oral fluid than urine. MROs were reversing more urine positives than oral fluid. For both specimens, the majority of the MRO reversals appear to be due to prescription use of opiates and amphetamines. The recent significant changes in technology provide an opportunity to improve the Program and increase efficiency and cost-effectiveness, all the while maintaining the quality control, legal defensibility, and confidence in the program.

Oral Fluid Matrix - Current Perspective

Specimen

Mr. Denny Crouch of Aegis Labs discussed the oral fluid specimen, which is also referred to as saliva, oral fluid, oral fluids, whole saliva, mixed saliva, etc. The three major glands that produce up to 1.5 liters a day of saliva are the submandibular, the sublingual, and the parotid. Oral fluid production can be stimulated by mechanical (chewing) or chemical (citric acid) means or non-stimulated. The pH (6-8) of oral fluid is roughly one pH unit less than blood. Saliva is primarily 98-99% water. Analytes found in oral fluid include electrolytes (sodium, potassium, chloride, and bicarbonate); calcium; immunoglobulins; steroids; various enzymes, especially amylase; DNA; viruses; etc. Immunoglobulins are important because IgG and IgA have been suggested as markers of specimen validity. Drugs can also be present since oral fluid is an ultrafiltrate of the blood. Drugs enter into saliva via active transport or diffusion, with diffusion dependent on the lipophilicity of the drug, its degree of ionization (pKa) and its bound and conjugated state. Because drugs are present in low concentrations, lower cutoffs are required and assay analytical sensitivity is critical. Oral fluid collection volume is much less than urine. In urine, drug metabolites and sometimes the parent drug are primarily detected. In oral fluid, the parent drug is primarily detected. In a study of the relationship between codeine concentrations in oral fluid and plasma, in the initial time points, the saliva/oral fluid concentrations were much, much greater than the plasma concentrations, probably due to residual codeine in the mouth. It is not until two to four hours post dose that there is reasonable correlation, allowing possible prediction of a plasma concentration from an oral fluid concentration. This study also found that stimulation of oral fluid caused an increase in the pH. In a second study to determine the effects of various collection techniques on oral fluid concentrations, there was a pronounced affect from stimulating oral fluid on the decreasing concentration of drugs, implying that the collection technique does affect concentration which is reflected in the duration of detection. Drug recovery varied by collection method and drug. Another issue is whether there is a validity measure for oral fluid collection. Is IgG is a good indicator of dilution and is there a good chemical marker for validity testing and, if so, at what concentration? Future topics for discussion include specimen definition (saliva, oral fluid, whole saliva), volume of specimen needed for testing and cutoffs, collection devices, criteria for percent recovery and volume, allowance of spitting as a mode of collection, cutoffs, tested drugs and metabolites, specimen validity, collection volume indicator, and the effects of stimulation. Advantages in the collection of oral fluid versus blood or urine include observed collection, less invasive specimen collection, ease of collecting multiple specimens, oral fluid drug concentration reflective of blood drug concentrations, no special facilities or requirements for the collection site, specimens that are easily transported and analyzed, and complementary information to what is obtained with urine, hair, sweat patches, etc.

Drug Analytes/Cutoffs

Dr. Marilyn Huestis of NIDA has been doing research on oral fluid for years. It is important to remember that identical results will not be obtained from the different matrices; each matrix provides unique information. Positivity rates vary by matrix and are related to the detection window which is completely driven by the selected cutoff. Different cutoffs have been proposed for oral fluid, including the proposed 2004 SAMHSA, the DRUID, the Tailloires Expert Group, and Belgian, French, and Australian legislative cutoffs. Advantages of oral fluid include less invasive collection and direct observation collection, so adulteration may be less of a problem. Other factors that affect drug concentrations are the physiochemical characteristics of the drug (lipophilicity, pKa, protein binding, ionization, molecular size, half-life), the specimen matrix, specimen viscosity, the route of drug administration, the oral fluid pH, time since administration, specimen collection method, oral fluid stimulation, analyte stability, within and between individual variability, drug contamination of the oral fluid cavity, drug recovery, elution solvent, buffer matrix analytical interferences, immunoassay cross-reactivities, assay performance (analytical sensitivity, specificity, and precision), detection windows, specimen processing, and chronic versus acute dosing. Dr. Huestis presented data from controlled clinical studies involving methamphetamine, MDMA and its metabolites, opiates, cocaine, and cannabinoids. Although PCP can be measured in oral fluid, there are no controlled studies.

Methodologies (Collection Devices, Screening Immunoassays, Confirmatory Tests)

Dr. Frank Esposito of RTI International provided a general overview of the methodologies used for oral fluid collection devices, screening immunoassays, and confirmatory tests. Currently available oral fluid collection devices include the neat oral fluid collection device; the passive pad that is simply placed in the mouth of the donor with a timed collection or with a volume indicator; the chewable pad, with or without impregnated compound to stimulate oral fluid secretion; the active swabbing with a pad, with and without a volume indicator; and other collection devices, including an oral cavity rinse. The devices may or may not use a transport buffer to serve as a preservative and to elute the drug. The screening immunoassays used to detect the parent drugs and metabolites in oral fluid require greater analytical sensitivity. There are two types of immunoassays for oral fluid: the heterogeneous Enzyme-Linked Immunosorbent Assay (ELISA) and the homogeneous assay. Cutoffs for oral fluid are less than urine due to lower concentration of drugs and metabolites in oral fluid.

Manufacturers' cutoffs are not standardized. The 2004 proposed Guidelines for oral fluid recommended the determination of immunoglobulin G (IgG) concentration on every specimen. Some scientists believe that the specimen validity testing is not needed for the oral fluid specimen due to the observed collection process. GC/MS was the only confirmation method permitted for urine drug testing under the Mandatory Guidelines from 1988 to October 2010. New technologies (LC/MS, GC/MS/MS, and LC/MS/MS) are now permitted for urine drug confirmatory tests. Oral fluid testing will require these new technologies. The confirmatory analytes for oral fluid include two parent drugs not included in urine - THC and cocaine parents. The proposed confirmatory cutoffs for oral fluid are lower than those for urine.

Methodologies (Collection Devices, Screening Immunoassays, Confirmatory Tests)

Dr. Courtney Harper is from the Food and Drug Administration (FDA), which regulates human and animal drugs; biologics, such as vaccines and tissues; food and food products; cosmetics; and also medical devices. She works for the Center for Devices and Radiological Health (CDRH), which regulates in vitro diagnostic medical devices used for diagnosis, screening, risk assessment, prevention, or surveillance. These devices are used in a broad range of settings, including central laboratories, over-the-counter use, and point-of-care tests. CDRH offers both pre-market and post-market regulation of laboratory tests and performs compliance actions. CDRH oversee devices from the time that they are developed, to the time that they are evaluated for clearance or approval, and then, once they are on the market, they continue to monitor them and evaluate how they perform. In that premarket review setting, they examine analytical and clinical performance and labeling. In the clearance approval of a drug test, their goal is to verify the labeling. Submitted analytical data include accuracy, precision, linearity, performance around the cutoff, recovery, cross-reactivity, matrix-dependent interferences, and interference studies on common over-the-counter drugs and compounds of similar structures. With a point of care test, accuracy and precision assessment in the hands of the intended user is required. For over-the-counter studies, lay users are employed. The approval bar for screening tests is generous because positive results should be confirmed because of false positive and negative results. Approval failures include false positive results, incorrect cutoffs, poor recovery of drug following pre-analytical steps, and false negative results at very high drug concentrations. One issue is when there is no well recognized cutoff, such as a SAMHSA-recognized cutoff or literature-recommended cutoff. CDRH has cleared many drugs for oral fluid testing, including mostly central laboratory-based tests and one or two point of care oral fluid tests. The advantages of oral fluid testing are that collection is easily observable, the specimen is easy to collect, and these tests are often just as easy to run as a urine test. Challenges include the effect of the collection method on test results, the nature of the specimen for confirmation, how and when the confirmation specimen is collected, the variability in the specimen collection method, and the cutoff. It would be helpful if standards, suggestions, or guidelines existed to ensure uniformity and comparability between results. FDA offers the Device Classification Database, which allows the user to research the different types of tests that FDA regulates by product code. In the section called Device Advice, they provide information about how FDA regulates medical devices. The 510(k) Releasable Database is where the data summary that was used to clear any particular test since 2003 is found. In summary, rapid oral fluid tests for drugs of abuse are a promising opportunity for drug testing but are not without their challenges. FDA is really interested in helping companies overcome those challenges and also providing input to the DTAB.

Proficiency Testing

Dr. Frank Esposito of RTI provided RTI's experience with their two (SAMHSA-sponsored Oral Fluid Pilot and the RTI Center of Forensic Sciences proficiency testing (PT) programs) synthetic oral fluid PT over the last four years. From 2000-2006, SAMHSA's National Laboratory Certification Program (NLCP) funded an oral fluid pilot PT program for 16 laboratories, which received a total of 15 cycles of PT samples. 6-AM, codeine, PCP, and THC had more consistent performance between laboratories than did amphetamine, MDA, MDMA, morphine, and methamphetamine. Synthetic oral fluid PT material was stable for all analytes for at least one year when stored frozen. There were significant decreases in the variability, expressed as mean percent CV, both within and between laboratories over the course of the study. Some analytes did have subsequent increases in variability in the latter cycles, illustrating the laboratory's challenge of maintaining its performance over time. An important finding over the course of the program was a large variation in reported results. Comparing the oral fluid with urine PT performance, oral fluid variability was generally comparable to the urine with the exception of BE. The second PT program involved 34 laboratories, 24 from the U.S., 2 from Canada, and 8 from Europe. These PT samples were contained three to five analytes each spiked into synthetic oral fluid with three cycles of five samples each shipped annually. Screening was mostly by immunoassay with five different commercial reagents being used. There was a wide range of initial testing cutoffs offered by the manufacturers for these analytes; positivity rates were dependent on the manufacturer cutoffs. Confirmation was by mass spectrometry. The variability of laboratory oral fluid results, as measured by the mean inter-laboratory percent CV for each analyte, was less than 20%, except for THC. By comparison, the mean percent CVs for all analytes in urine is less than 10%, which can be attributed to the additional experience that labs have in analyzing urine over oral fluid. In addition, the NLCP urine program is a remedial-based program, requiring laboratories to investigate quantitative errors, whereas the current oral fluid program is the self-improvement based program with no remedial actions or follow-ups.

Best Practices Experience

Ms. Barbara Rowland of Quest Diagnostics in Lenexa, Kansas is the Director of Laboratory Operations. Quest Lenexa tests about 2,500-3,500 oral fluid specimens a day. Quest uses the OraSure Intercept Drug of Abuse Specimen Collection Device collection device which is retained in the donor's buccal cavity for about three minutes to collect about 400 uL oral fluid. The donor places the pad in the specimen vial, which contains 800 uL buffer (times three dilution), caps the specimen vial, places the tamper evidence seal across it, and signs the chain of custody. Split specimens, if requested, are collected simultaneously. At the laboratory, the specimen is processed similar to urine specimens. The device is inserted into a specimen storage tube and centrifuged for two to three minutes to elute the oral fluid out of the device into the storage tube. The original collection device remains inserted into this storage tube and serves as a cap for the oral fluid and preserves the original tamper-evident seal and identification. For initial testing, Quest uses the Intercept micro-plate EIA (96-well ELISA). The confirmation methods are liquid/liquid extraction for amphetamines and THC and solid phase extraction for PCP, opiates, and cocaine. Derivatives are HFBA for amphetamines, BSTFA for THC, methoxyamine and BSTFA combination for opiates, and HFIP for cocaine. Confirmation instrumentation includes GC/MS for amphetamines, cocaine, and D/L isomer and the Dean's Switch for PCP, THC, and opiates for extra sensitivity. The non-negative specimens are stored frozen for a year. Laboratory challenges with the oral fluid specimen are specimen volume, whether or not to test for THC acid to eliminate contamination issues, split versus simultaneous collections, retests between the different labs with different limit of detections, and automation.

Data

Dr. Barry Sample of Quest Diagnostics provided data from Quest's routine workplace drug testing specimens to compare the trends in positivity rates between urine and oral fluid. Between January 2005 and June 2010, there were 4.9 million oral fluid tests and 32.6 million non-regulated urine specimens included in the summary data. By testing reason, 74% of the urine and 81% of the oral fluid specimens were pre-employment tests, 13% and 9% were random, respectively, and both urine and oral fluid were 6% for post-accident tests. Cutoffs varied by specimen type and whether for screening or confirmatory testing. Confirmation methodology was a mix of solid phase and liquid/liquid extraction, either with or without derivatization, but all were by GC/MS analysis. Oral fluid screening was by the OraSure Intercept system. The overall positivity rates, holding relatively constant over the last five and a half years at a little over 4%, between urine and oral fluid are really quite comparable with only a 4.7% difference that is explainable because of the inclusion in the urine data of barbiturates, benzodiazepines, and other prescription drugs. For amphetamines, there are 62% more positives in urine than in oral fluid, presumably related to Adderall prescriptions. For methamphetamine, there are 43% more positives in oral fluid than in urine with declining trends for both. For cocaine, there is a 45% difference with similar trending. Marijuana positives were nearly 9% more in oral fluid than urine. For opiates, there is a 72% difference in positivity rates for oral fluid versus urine, which is related to the inclusion of hydrocodone and hydromorphone in the oral fluid panel. There were significantly more positives for the 6-AM heroin marker in oral fluid as compared with urine. For PCP, positivity rates are very low and quite similar and seem to track together quite well. In summary, both oral fluid and urine provide insights into an individual's recent drug use and are exhibiting similar trends. While there are some differences in the positive prevalence rates, they are remarkably similar and usually related to cutoff.

Dr. Cook adjourned the meeting at 12:15 p.m. EST.

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

/SIGNED/

Janine Denis Cook, Ph.D., DABCC
Designated Federal Official, DTAB
Acting Chair, DTAB

These minutes were formally considered, amended, and approved by the Drug Testing Advisory Board using email.