DRUG TESTING ADVISORY BOARD (DTAB)

Exploring the Science and Experience of Testing for Prescription Drugs in the Non-Regulated Workplace

August 19, 2008

Sugarloaf and Seneca Conference Rooms
One Choke Cherry Road
Rockville, Maryland 20857

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Proceedings

DR. BUSH: Welcome to the open session meeting of the Drug Testing Advisory Board. My name is Donna Bush. I am the Designated Federal Official for this Board, and I call this Board to order.

I also have some housekeeping notes for you. The doors out to the hallway look like this, a single door. The doors to a closet look like this, a double door. Which door you choose determines where you will end up. The bathrooms and the kitchens with vending machines for cold drinks and light snacks are out the single door.

We thank those of you who called ahead with the necessary information to prepare a visitor badge for you. The sticky visitor badge you have on right now is good for today only. It will get you back into the building after lunch, so keep it and leave it affixed. If you leave the building, you will need to go through the security screening process again, but please return that sticky visitors badge to the guards on your way out at the end of the day. If you do not plan to come back after lunch, then return the badge before you leave this morning.

There were several pieces of information at the sign-in desk this morning. These include a roster of the DTAB members and a shuttle schedule. The shuttle circulates back and forth between the Shady Grove Metro Station and the Substance Abuse and Mental Health Services Administration (SAMHSA) Building, with a few additional stops into the King Farm business and restaurant area during lunchtime. For those of you with a car, there is a list of local restaurants. A copy of the Federal Register Notice (FRN) announcing this meeting is also available.

When you signed in, you were asked to sign that you have received or read the FRN, which announces this meeting and includes the meeting standards of conduct. I'll read the FRN now for the record. SAMHSA would like to ensure that Advisory

Committee meetings proceed in an orderly fashion, are conducted in a safe and secure environment, and that the right of free speech is protected and that the ability of SAMHSA Advisory Committees to accomplish their objectives is not disrupted. Therefore, the following procedures will be followed by DTAB. Attendees may be subject to security screenings, such as presenting identification, passing through metal detectors, and having briefcases and packages inspected. Any interested person who wishes to be assured of the right to make an oral presentation during the open public hearing portion of the DTAB meeting must register with Mrs. Hersh before the meeting. We have two people who have done that. Those who have not registered before the meeting will only be invited to speak at the discretion of the Chair and should submit their requests to the Designated Federal Official, which would be me, on the day of the meeting. Open public hearing participants who are designated to speak may be questioned only by the Chair or other DTAB members. Audience members may not present comments or questions to the committee unless recognized by the Chair. Attendees at the meeting are asked to maintain order and not display behavior that is disruptive to the meeting, such as shouting from the audience or loud outbursts. We ask that attendees not approach the DTAB table area during the meeting without permission from the Chair or the Designated Federal Official. The DTAB Chair or Designated Federal Official will note for the record any disruptive behavior and will ask the person to cease the behavior or else leave the meeting room.

This meeting topic, “Exploring the Science and Experience of Testing for Prescription Drugs in the Non-Regulated Workplace” is an expanded meeting topic for us. We wanted to use the model that our Food and Drug Administration (FDA) colleagues use at large public meetings to make our intentions for conducting the meeting clear.

Now, we know that there will be questions from the public. We have index cards and sheets of paper for you to write your questions on. Return the index cards to the registration table. We'll handle questions in the following way: they'll be brought up to us, we'll determine who best can answer them and how to answer them, and we will answer them in a systematic way and as time permits. According to the agenda, any relevant questions will be addressed either at noon or 4:00 p.m. as part of the DTAB panel discussion.

For those sitting at the table with microphones, the microphones are high-tech, and we need to turn them on and off as we use them. Too many microphones on at one time will cause background noise and may shut the system down. This will hamper our ability to create the public transcript that is so important for this meeting.

At noon, there will be a DTAB panel discussion. For the morning speakers who are seated in the first rows of the audience area, we will ask them to return to the table in front of the Board's convened area. On that table are microphones with long leashes. Responses should be spoken into the microphones so that we can capture all comments for the public record.

Mr. Chair, those are all the housekeeping announcements I have. I'll turn it over to you.

Welcome and Opening Remarks – Robert Stephenson

MR. STEPHENSON: Again, good morning, everybody. I want to thank everyone who is in this room for taking the time and having the interest to come and participate in this meeting. As Donna Bush had said, the issues that brought us together are so far beyond the normal scope and prior history of what we have done. I guarantee you that the group of people that are convened here as the members of our Drug Testing

Advisory Board have all the skills and experience necessary to hear the information that is going to be presented, to begin to filter it, and ask some really tough questions. Whether or not all those questions come out today is not key. What is important is that the process is started, and it will be a part of an ongoing exploration of this very complex set of procedures, experiences, and datasets that we will hear about today.

This meeting is an example of wonderful teamwork and collaboration, not only inside our agency with our sister center, the Center for Substance Abuse Treatment (CSAT), and Dr. Wes Clark who's here with us, but also with the Office of National Drug Control Policy (ONDCP) and Dr. Bertha Madras, who's also here sitting to my left. We have a wonderful set of experiences that will be shared from our Food and Drug Administration (FDA), Drug Enforcement Administration (DEA), and other colleagues that have their own particular perspective and oversight responsibilities for data and systems analysis.

I'm going to let you know, and I have to say this carefully and respectfully, that there is a Proposed Final Notice for Revisions to the Mandatory Guidelines that has been cleared through the Department of Health and Human Services (HHS) and delivered to the Office of Management and Budget (OMB). It's currently listed on OMB's website as undergoing review. I can't say anything more than that at this time because it's inappropriate to do so because of the ongoing internal review. It is listed on a public access website, which indicates that it has been there since the first of August.

At this time, I would like to acknowledge a staffing change that is important and everyone should recognize. I want to congratulate Jim Swart for being named as the Director of the Office of Drug and Alcohol Policy and Compliance in the Department of Transportation (DOT). Years ago when a similar event happened to me, I said be careful what you ask for because you might just get it. We really appreciate all the good

work and progress the Department of Transportation has had with us, and Jim has been a wonderful team player.

That covers all I need to do this minute. With that, we are going to give Mike Baylor a speaking role for his first job.

DR. BUSH: As the moderator, Mike Baylor will take care of the speakers and make sure their presentations ready for projection. He has a five-minute card to alert the speakers as their time limit approaches.

We have such an ambitious agenda. As a way of apology, I'm so sorry we gave our speakers only 20, 25, or 30 minutes to speak, when, in fact, they have hours worth of experience and information that they could constructively share. However, in the context of framing this meeting, we wanted to convey to the public the many facets of drug testing for prescription drugs, including the technology, the policy and the outcome, the medical review officer review, what happens with employers, and how employers handle information. Because there are so many facets to this, we have arranged for about 25 speakers in two days. Because moderating this meeting is a difficult job, we gave it to Mike Baylor. He will help us run meeting this constructively.

MR. STEPHENSON: Mike, please set some of the ground rules.

DR. BAYLOR: The speakers will deliver their presentations from the podium. I will project their presentations and then they'll speak. At the conclusion, we will transition to the next speaker.

DR. BUSH: There is a pointer as part of the slide changer.

DR. BAYLOR: Right. Forward, back, and a pointer.

DR. BUSH: One more thing I want to mention. You'll see that some individuals, particularly the board members here at the table, have a blue folder that has copies of the presentations in it. We have many speakers and much information. Because we

received revisions at the last minute and there was no way to know how many people were going to be here, how many copies to make, and how to make sure that we made copies of the final versions, we are asking you to just listen. Also, it would be distracting if you had 25 packets of slides in front of you. All the slide presentations will be included as part of the transcript that we will post up on our website.

We are in a holding pattern for one minute; Bob's making a phone call.

Any questions from the members of the Board or those at the table?

We will go around and introduce ourselves, beginning with Lisa. State where you are from so that members of the audience and our transcriber will have an idea of who's where. Thanks.

MS. MOAK: Good morning. I'm Lisa Moak, formerly with Kroll Laboratory Specialists, now an independent consult.

MS. PIZZO: Pat Pizzo, Director of Toxicology, Kroll Laboratories.

DR. NIPPER: I'm Henry Nipper. I'm Director of Toxicology and a member of the faculty at Creighton University School of Medicine in Omaha.

DR. KUNTZ: David Kuntz, Executive Director of Analytical Toxicology, Clinical Reference Laboratory in Lenexa, Kansas.

DR. TURK: Bob Turk, Center for Toxicology Services in Houston, Texas.

MS. GORDON: Ann Marie Gordon, Laboratory Manager, Office of the Chief Medical Examiner, San Francisco.

MS. ESTAPE: Estela Estape. I'm Dean and Director of the Clinical Research Programs at the School of Health Professions, University of Puerto Rico.

MS. COLLINS: Jennifer Collins, MedTox Laboratories in Saint Paul, Minnesota.

MS. HARDING: I'm Fran Harding, the Center Director for CSAP.

DR. BUSH: Donna Bush, Drug Testing Team Leader, SAMHSA, CSAP.

MR. STEPHENSON: I'm Bob Stephenson, Director, Division of Workplace Programs, Center for Substance Abuse Prevention and SAMHSA.

DR. MADRAS: Bertha Madras, Deputy Director for Demand Reduction, White House Office of National Drug Control Policy.

DR. BAYLOR: Mike Baylor, Co-Director, Center for Forensic Sciences, RTI International.

DR. MITCHELL: John Mitchell, Co-Director, Center for Forensic Sciences, RTI International.

MR. McCUNE: Tim McCune, Fitness for Duty Program Manager, Nuclear Regulatory Commission.

MR. SWART: Jim Swart, Office of Drug and Alcohol Policy and Compliance, and I'm the Director.

DR. CAPLAN: Yale Caplan, Consultant, Toxicology, and Consultant for DOT.

DR. GUTIERREZ: Alberto Gutierrez, Food and Drug Administration.

DR. CLARK: Westley Clark, the Director of the Center for Substance Abuse Treatment (CSAT) in SAMHSA.

MR. STEPHENSON: At this time, it's an honor and pleasure to introduce Frances M. Harding, who is the new Director for the Center for Substance Abuse Prevention. She's recognized as one of the nation's leading experts in the field of drug and alcohol policy and author of several widely published articles on prevention.

Prior to becoming the CSAP Director, she served as the Associate Commissioner of the New York State Office of Alcoholism and Substance Abuse Services. She's responsible for development of policy and guidelines for drug, alcohol, and gambling prevention and treatment and recovery program. She is the President of the National Prevention Network, which is an organization of state, alcohol, and other

drug abuse prevention representatives that provide a national advocacy and communication system for prevention. State prevention representatives work with their representative state agency directors regarding alcohol and other drug abuse to ensure the provision of high quality and effective alcohol, tobacco, and other drug abuse prevention services in each state.

She is a board member of the National Association of State Alcohol Drug Abuse Directors, Inc., which is a not-for-for profit and private organization that serves scientific and informational purposes. Its mission is to foster and support the development of effective alcohol and other drug abuse prevention and treatment programs throughout every state.

She's the first non-researcher to receive the prestigious Science to Practice Award from the Society of Prevention Research. Frances.

Welcome and Opening Remarks – Frances Harding

MS. HARDING: Good morning. I know one way to get here from my new house in a new area, and it was blocked. Thank goodness for GPS, but I learned you can't program a GPS system when you're driving. Next time you meet, I will at least know how to get here from my home, which will give me more time to meet the Board.

Welcome to all of you. I hope, before the end of tomorrow, to have at least said hello to all of the Advisory Board members. I thank you. My job here this morning is to say good morning and to welcome you to my first Advisory Board meeting of yours.

Today and tomorrow we will focus on and learn about the range of issues around prescription drug use and abuse in the workplace, community, and the home. This meeting is very timely, considering all of the news articles and the issues that are arising around prescription drug use from a prevention perspective. There is a rise in

prescription drug misuse on the college campuses across our country. This was surprising to me. We knew that the misuse of prescription drugs was on the rise across our communities and our schools; I had no idea that the college and university systems were seeing the same issues.

The misuse of prescription drugs contributes to many dysfunctional issues in the workplace, including multiple accidents, family problems and, of course, in some cases, death. Over the next two days, we're hope to focus on four major issues and possible outcomes: what we know about the incidence, prevalence, and trends of the prescription drug problem in general; what can be tested for; what the drug test results can tell us; and what we'll learn from the experience of others who are currently using expanded drug testing in the professional setting.

You have a very full agenda. I would like to, on behalf of Dr. Terry Cline, also recognize and welcome some of our presenters and guests for today, including Dr. Bertha Madras, the Deputy for Demand Reduction from the Office of National Drug Control Policy. I had a brief meeting with Dr. Madras, and it was very exciting. The two of us have a connection and passion for this field; I've met someone who actually matches my energy level when speaking and getting involved in the subject matter. I also would like to recognize my colleague, Dr. Westley Clark, who is the Director of the CSAT here at SAMHSA.

I will not going to take anymore of your time. You have a lot to do. I will turn this over to Bob. I look forward to reading the results and the outcome of your two day meeting and will continue to work with you in the future, not only on prescription drug use issues but other issues in the workplace that are so dear to us. Thank you. Good morning.

DR. STEPHENSON: Thank you, Frances. Unfortunately, Center Directors don't

have an opportunity to spend much time in any one place because they're expected to be in multiple places, often at the same time. We welcome you and would like to have you stay as long as you can, but I know you have an Executive Leadership Team meeting this morning.

At this time, I will introduce Dr. Bertha Madras, who was nominated in July 2005 to serve as the Deputy Director for Demand Reduction in Office of National Drug Control Policy (ONDCP).

The United States Senate unanimously confirmed her nomination. She is a well-qualified person; there was no political dissent over her confirmation. It was one of those few instances where everybody agreed this is a good person for the job.

Dr. Madras is focused on strategies, programs, and policies aimed at reducing the demand for illicit drugs and promoting best practices for intervention and treatment. Prior to joining ONDCP, Dr. Madras was Professor of Psychobiology in the Department of Psychiatry at Harvard Medical School. At Harvard Medical School, she supervised the Neuroscience Research Program and taught substance abuse and addiction to medical school students.

Her research focused on how drugs affect the brain. She developed new brain imaging agents and potential medications to treat addiction, Parkinson's Disease, and other brain disorders. One of her discoveries, a class of agents that damages living brain cells affected by methamphetamine and Parkinson's disease, was recently highlighted in *Better World Report* as one of 25 technology transfer innovations that changed the world. What a wonderful accomplishment. I mean that most sincerely.

She served as Associate Director of Public Education in the Division on Addictions at Harvard Medical School. She received awards from the National Institute of Health (NIH), has 17 patents with her collaborators, and other distinctions. She's

authored over 130 scientific manuscripts and book chapters and recently edited a book titled *Cell Biology of Addiction*. She also directed the creation of an exhibit, play, and CD for exhibit at the Museum of Science in Boston titled: *Changing Your Mind: Drugs and the Brain*.

At this time I'd like to welcome Dr. Madras to make her opening comments.

Welcome and Opening Remarks – Dr. Madras

DR. MADRAS: Thank you very much. I want to thank Frances Harding, the Director of CSAP; Bob Stephenson, Director of SAMHSA's Division of Workplace Programs; and Donna Bush, the team leader for drug testing for catalyzing a collegial and critical meeting today. I thank SAMHSA and its Division of Workplace Programs for organizing what looks like to be a very key, two-day Drug Testing Advisory Board meeting on the issue of prescription drug use and workplace drug testing.

I'm particularly pleased to see the agenda packed with a breadth of expert speakers on this topic and so many people in the audience who I know have profound knowledge and expertise as well. I am also delighted to see Federal agencies here, including the FDA, Nuclear Regulatory Commission (NRC), the Department of Transportation (DOT), the Department of Defense (DoD), and Ron Shippee, who has done a stellar job on organizing drug testing in one of the most daunting and complex areas of our Federal Government.

I'm here to offer the Federal Government perspective on the magnitude of the prescription drug abuse problem in the United States and the efforts we're making to combat it. I'm also here to address some of the challenges we face, which many of you are able to discuss in great depth as well as to offer some solutions. This meeting in part was catalyzed by a meeting we had at ONDCP, in part because of my own acute

sense of stress over the prescription drug problem.

We have seen a reduction in youth drug use in our nation, 24 percent, since 2001. And yet, drug abuse is a growing problem with regard to prescription drugs, which makes this meeting so timely. Prescription drugs are America's second most abused drugs as measured by prevalence with marijuana being first. For the past three years, using SAMHSA-generated National Survey on Drug Use and Health (NSDUH) data, the numbers of new initiates into prescription drug abuse as compared to marijuana have numerically been higher, even though statistically they are not. Of particular note is that among the 18 to 25-year-olds entering the workplace, prescription drug abuse rose 19 percent from 2002 to 2006. Most of this increase was driven by non-medical use of opiate analgesics, otherwise known as painkillers.

Where do people get these drugs? What is most disconcerting is that the vast majority gets them free from friends and family. If you factor in the amount that is removed without permission from medicine cabinets or bought from friends and family, 70 percent of our population acquires prescription drugs from friends and family. These are not shady deviants in back alleys in downtown urban areas with drug sellers and dealers. These are loose pills that are being passed around, sold, or removed from uncontrolled supplies in medicine cabinets or on tables.

We know that SAMHSA’s Charlene Lewis will be presenting in much greater detail the problem of prescription drug abuse in this country and, therefore, I will not present any more details on this issue.

What are the consequences of this? Between 2004-2005, the number of people seeking treatment for prescription pain medication increased nine percent to more than 64,000 admissions. We're beginning to see a slight decline in people seeking treatment for heroin and an increase in those seeking treatment for opioid analgesics. What we're

seeing, in fact, is a crossover between prescription drug abuse and illicit drugs. We don't know what that exponential or gradual incline will lead to eventually, but we do know that now is the time to do something proactive about this problem.

In the past 10 years, the number of teens going into treatment for addiction to prescription pain relievers has increased by more than 870 percent. This figure is of serious concern and specifically targets a population that is most vulnerable to addiction. Kids who start using drugs before the age of 14 are 6 times more likely to become addicted than if drug use is initiated past the age of 18.

We've also seen an escalating rate of death due to prescription drugs, primarily opioid analgesics.

We face a complex problem, a problem that has consequences to every sector of society, including the workplace, academic institutions, parents, and the criminal justice system. Since every sector of our society is affected by this, every sector of society needs to contribute to evolving and precipitating rapid solutions to this problem.

Some of the strategies involve law enforcement and legislation. The Federal Government has made multiple efforts to reduce the supply of prescription drugs and to intervene with those who are addicted. We are committed to balancing the need to reduce the diversion and abuse of prescription drugs with the need to protect access to pharmaceuticals by those with medical need.

ONDCP has partnered with key state stakeholders and legislatures to encourage and assist in the passage of legislation and implementation of prescription drug monitoring programs. Multiple US Government agencies, including the FDA, the DEA, and the Department of Justice (DOJ), have taken steps to address pharmacy distribution, to address physician education, and to address so many needs that are being identified very rapidly. ONDCP and SAMHSA have partnered in this meeting.

ONDCP and NIDA have partnered in another meeting to try to define prescription drug abuse. It is not easy and far more complex than illicit drug or alcohol abuse.

Think about these following scenarios. A person escalates a dose because he/she doesn't have adequate pain relief, but it goes contrary to the prescription that is written by a physician or outside of the boundaries of that prescription. Think about a student who buys Ritalin or Adderall from a college classmate because he/she has to study for exams. Think about young people who are using opioids in order to fall asleep and to alleviate stress. And then think about people who escalate opioid doses and doses of psychostimulants that are used for attention disorders in order to get high.

There are so many scenarios involved with prescription drug abuse. Think of abusing one's own legitimate prescription as opposed to abusing pills that are taken into pharming parties, P-H-A-R-M-I-N-G, where a fishbowl is set out, everyone who has raided medicine cabinets of parents and grandparents dumps a load of various drugs of unknown physiological and pharmacological effects into it, and everyone reaches in.

There are multiple scenarios for this, so the definitions are far more complex and daunting. FDA and ONDCP are working together to develop some guidance on this as well as guidance on how to ask the questions.

As I said earlier, every sector of society needs to engage in this issue. Some strategies require labor-intensive education of the public, including parents, students, people in the workplace, the elderly, and healthcare professionals, including doctors, dentists, pharmacists, nurses, and social workers, with everyone engaged because the level of awareness is still not adequate to meet the extreme consequences that can arise from abuse of these classes of drugs. Every sector of society is affected.

What are some of the types of issues that we have to engage in with regard to education? For example, with teens and with people in the 18 to 25-year-old category,

which is our most vulnerable population and also the population at highest risk for using, the vast majority perceives prescription drugs as being safe because the doses are controlled, they are medically approved, and they are produced under the most stringent of circumstances. They are not adulterated or contaminated as street drugs are. They are clean, and they are legitimate medications. We need to address this perception.

What do parents think? The vast majority of parents in our country do not engage in discussions with their family members regarding to prescription drugs as a form of abuse. In fact, they will much more readily engage in discussions on cocaine, marijuana, or heroin than prescription drug abuse.

Last year, ONDCP, the FDA, and the Environmental Protection Agency (EPA) joined together to release new guidelines for the proper disposal of prescription drugs. This is an effort to try to reduce supply within homes and households. We face far greater needs and need far greater strategies. We need to change attitudes, and we need to educate medical professionals. This is a prescription drug strategy that is ongoing.

Some strategies call for testing. This is the focus of the two-day meeting that we are here to learn from. There are two different forms of testing. There is verbal, and there is biometric testing. The Federal Government and our partners in the private sector can make significant contributions to both. Verbal testing can be conducted in a form of screening. If a test is positive, a person can be offered a brief intervention. We now have good evidence that screening and brief interventions have an enormous effect on future drug use. We also are aware, from verbal and biometric screenings which identify people who are abusing alcohol or illicit drugs, that these people are at high risk for abusing prescription drugs as well. Therefore, we encourage as many

sectors of society who are engaged in a public health approach to the problem with regard to verbal screening, to be on high alert for people who engage in illicit drug and/or alcohol abuse because these are the high-risk category of people who are going to also engage in prescription drug abuse, though not necessarily because the profiles are not identical; they do not overlap completely, but they certainly do overlap.

We come to drug testing itself, and we know that drug testing can work as a deterrent and as a signal of the need for assistance for these individuals. We face a myriad of questions that need expertise to address.

Developing a blood alcohol concentration range, which was used to identify people at risk for accidents that were driving in an intoxicated state or in a workplace when intoxicated, was a relatively simple task. It is a single drug. It is readily quantified using Breathalyzer tests. This response relationship is crisp and clean. When one reaches 0.08 percent, there is a rampant rise in accident rates on the highways. For that reason, blood alcohol concentration cutoffs have been relatively stable and standard over the years.

Biometric testing appears to be straightforward with regard to legal drugs because if anyone tests positive, there is a simple algorithm. There's a simple response or policies that one can have under those conditions. With regard to drug concentrations, first and foremost, we have to know what the range of drug concentrations exist within people who are using the prescriptions as prescribed by physicians. We understand, for example, that tolerance to certain types of drugs, such as opioids, can confound those correlations between impairment and blood levels enormously because opioids are a class of drugs that promote a form of biological adaptation which is far, far more extensive in some individuals than can be, for example, with alcohol.

Much more complex is that scenario when a person tests positive and has a legitimate prescription. Are they and can they be impaired? Are they, in fact, eligible for certain types of work if they have a legitimate prescription that will turn into a level of impairment? What are the levels that affect workers' safety? What are the ranges? If so many of the blood tests come up positive because individuals have prescription drugs, how do we address the daunting costs that are associated with it?

The challenge associated with selecting testing for and differentiating between illicit and licit use of prescription drugs used in our society is something we have to address. We also have to address what are concentrations that are intoxicating, and we have to address policies that are effective, appropriate, and just for the individual that has a legitimate reason for taking these drugs.

These are the challenges that we face in the next two days. These are challenges we are going to face as a society for the coming years. We know that all our Federal agencies, as well as people who represent multiple sectors of our society, such as the drug testing industry, healthcare professionals, and parents, individuals, teenagers, young adults, elderly, and every person, have to contribute in one way or another to alleviating this growing challenge to our society.

I look forward to hearing your presentations. I thank you all for taking the time to be part of this discussion. I look forward, above all, to the solutions that are likely to emerge from this meeting that can be implemented in the near future, as well as in the long-term. Thank you.

MR. STEPHENSON: Thank you very much, Dr. Madras. Before we go any further in the normal agenda, I need to correct an administrative oversight error and do so with an apology.

Colonel Shippee, could you please come forward and join us at the table?

DR. SHIPPEE: (Off microphone)

MR. STEPHENSON: At this time, I'd like to begin the process of our Federal updates. This is how we conduct business in the Drug Testing Advisory Board and have for years. We look to our Federal partners, who have their own authorities and their own programs but who do similar kinds of work, for harmonizing programs and policies where possible.

First is Jim Swart from the Department of Transportation. Jim, would you like to give your updates?

Federal Drug Testing Updates

Department of Transportation

MR. SWART: (Slide 1) Yes. Thank you, Bob. I bring greetings from the Secretary of Transportation to all my fellow DTAB members and to the audience.

(Slide 2) We have several regulation and policy updates for you. This has been a usy summer for us in terms of these issues. In an effort to begin and continue the process of stopping job hoppers in the transportation industries from going from one position after testing positive to another without benefit of the required treatment and evaluation process, we have issued in interim final rule that was issued on June 13. This rule permits employers and third-party administrators for owner/operators, without regard to perceived or real consequences in regulation Part 40, to report to the state licensing authorities to get truck and bus drivers off the road. Accordingly, we want to ensure that when the state has a law that requires or urges employers or third parties to report that information, that there are no confidentiality issues within Part 40. Reporting to the states is encouraged, and we’re urging the states to remove those licenses and to take action.

The final rule that will be effective on August 25 and was issued on June 25 has implications in many different areas. For laboratories, all DOT specimens will be tested for specimen validity, adulteration products, and substitution products using HHS protocols, HHS laboratories, and HHS designated procedures.

Also, all laboratories are required to submit to the DOT on a semiannual basis their DOT testing results to help us better understand what those results are and which laboratories are doing which particular types of testing. For laboratories and medical review officers, we are attempting to close that endless loop that medical review officers face with invalid test results, and we're hoping to streamline the results reporting to make it clear to medical review officers, laboratories, and employers what they are to do with certain results.

To stop the cheating at collection sites and the numerous attempts to beat the urine drug test, we've implemented some new, direct observation procedures. Those observation procedures are for invalid results with no medical explanation and obvious attempts to cheat at collection sites, as well as for an optional requirement for follow-up and return-to-duty testing for those who have tested positive or have cheated on the test in the past.

We support Congress' activities, and Congress is certainly supportive of activities to take devices used to cheat the drug test off of the market and to make it illegal to sell and manufacture those. We will do our part by taking action against those who would thwart the drug testing process.

We've changed and updated our collection and staff guidelines and employer handbook. There is a website available to find all these documents. The new employer handbook is an online document with links to many other parts of our regulations in the DOT, to agency regulations, and to many of the HHS documents that employers and

their service agents need.

Finally, on July 31, we issued an interpretive question and answer document that looks at four different things: two related to collection sites, one related to the alcohol testing form itself, and one is the new procedures for medical review officers in reviewing pH results in the 9 to 9.5 range. The MRO procedures were based on information we had received from laboratories, medical review officers, and certainly some of the scientific reviews and an HHS-sponsored study. This document prompts medical review officers to take into consideration temperature and time since collection in making a decision as to whether an individual with an invalid result related to pH does indeed have a legitimate medical reason.

(Slide 3) The Government Accountability Office (GAO) made recommendations to the Department in May of this year. There were five recommendations, two for DOT and three for Congress. DOT is supportive of these and considering ways to make these happen now, and not just within the Federal Motor Carrier Safety Administration, but within all the DOT agencies. We are investigating how to be more cooperative with our safety audits, share information, and rate and rank some of the service agents as being more critical than others for revisits, et cetera. We are working smarter, more efficiently, and more cooperatively within DOT. We support everything that the GAO asked Congress to consider, such as the ban on products and civil penalty authority, not only for Federal Motor Carriers, but for all the DOT agencies in order to ensure service agent compliance. Certainly, we want to encourage states, with our new interim panel to suspend and revoke those licenses of drivers who tested positive or refused a drug test.

(Slide 4) Finally, an update on who my staff and what they do. Bob Ashby is our Chief Counsel and has been that for quite some time. Patrice Kelly is our Acting Deputy Director for Policy. Mark Snider is our Acting Deputy Director for Administration. Bohdan

Baczara is our Policy Advisor. All of us know and understand drug and alcohol issues. We hope that we've been responsive to anyone who calls in or e-mails us for information. The two people responsible for keeping us in line and making all of our administrative and budget decisions work are Vicki Bellet and Maria Lofton. Thank you.

MR. STEPHENSON: Thank you, Jim. Colonel Shippee, would you like to provide your updates?

Department of Defense

COLONEL SHIPPEE: Yes. I don't have any slides but I do have some bullet points. You're going to hear from Lieutenant Colonel Lyons from the Armed Forces Institute of Pathology (AFIP) tomorrow.

My office is under the Assistant Secretary of Defense for Health Affairs. I use the AFIP as my technical board in the same manner as SAMHSA and HHS use this Board.

This topic on prescription drug use is very timely and is an important topic to DoD for a number of reasons. There's a huge increase in pain medication use, such as anti-depressants and benzodiazepines, related to combat action. Tomorrow, Tim will show you some of DoD's prescription drug prevalence data.

I am responsible for managing and funding DoD's laboratory drug testing program and assessing the burden that drug testing places on the medical review officer (MRO) and the laboratory structure. DoD supports six military laboratories, including the Army facilities at Fort Meade and Tripler, Hawaii; the Navy facilities at Great Lakes, San Diego, and Jacksonville; and the Air Force facility at Brooks.

These six DoD laboratories are a true joint testing program because of standardization across all facilities. This was not easy an easy accomplishment because the individual services were reluctant to relinquish control. The Navy recently

completed a facility study assessing the impact to laboratories affected by the Defense Base Closure and Realignment (BRAC). The preliminary report from an unbiased independent contractor stated that DoD saved about $21 million through in-house drug testing. The report concluded that the joint testing program is very successful and recommended that laboratory standardization continue.

Two of the laboratories are rather specialized. The Great Lakes laboratory handles both the military accession and MEPS (Military Entrance Processing Station) testing, which totals about 350,000 annually. The Great Lakes accession personnel report to the United States Military Entrance Processing Command (MepCom).

Fort Meade is the only dual certified, both by DoD and the National Laboratory Certification Program (NLCP), forensic drug testing laboratory in the nation. Fort Meade is subject to three DoD and two NLCP inspections a year; about every two months, inspectors are on-site. Currently, all specimens from the 135,000 DoD testing-designated positions in the Federal government are centralized to Fort Meade.

DoD has a laboratory information management system (LIMS) that was developed 12 years ago. This very successful LIMS software allows for efficient data handling and transmission of testing results from the laboratory to the Brigade Commander in Afghanistan, Iraq, or wherever in a timely manner. The LIMS data is interfaced with the Defense Manpower Data Center (DMDC) in Monterey, California, allowing for the storage of all the military data into a central repository. Because of this central database, the data can be analyzed by many different variables, such as demographics, including service unit, age, gender, et cetera. When Congress requests a deployment report, I can now respond quickly and efficiently.

DoD foresaw this prescription drug issue based on prevalence data. One problem with assessing this issue was our inability to access the MRO information that

was retained by the service and was not in the DMDC repository. The MRO information is now accessible. Data from the LIMS is transmitted to the MRO for review, the MRO review is transmitted back to the LMS, and then finally merged into DMDC in a very timely manner. The end result is a nice, clean, scrubbed data assessment, which is reflected in our fiscal year 2007 report. For instance, the MRO unknown category decreased to only 11 percent of the 21,000 positives last year. Our goal is to decrease the MRO unknown category even further through the use of scrubbed data.

DoD performs about 4.5 million military and about 135,000 civilian tests a year. We are unique in the regulatory drug testing industry because we run our own military drug testing laboratories, have observed collections, and set our own drug testing policies, which allow us to be very flexible in our drug panel. To change a drug testing panel, a Federal Register Notice is not required. Based on DoD's BTAB (Biochemical Testing Advisory Board) and AFIP's technical assessments, I make a recommendation to the Assistant Secretary of Defense (ASD) for Health Affairs and present my recommendations to the services for their agreement. Because DoD's drug panel must change to meet the threat, I can implement a new drug into our drug-testing panel in 30 to 60 days.

Because of our large drug testing volume, DoD can leverage the in-vitro diagnostics (IVD) industry. For example, DoD recognized the ecstasy wave in the mid-1990s and was subsequently informed by the Criminal Investigation Command (CID) that ecstasy was a growing issue. Our ecstasy drug testing requirements were communicated to IVD manufacturers who developed an ecstasy screening kit. By the time the ecstasy wave peaked in 2000, the DoD laboratories were already certified for ecstasy testing, ecstasy was included in our drug-testing panel, and analyses were being performed on incoming specimens. Because of the availability of heroin in

Afghanistan, DoD now performs 100 percent testing of all specimens for heroin. Again, we met with IVD industry representatives who provided to us a heroin screening kit. Currently, the DoD drug panel contains D, L-amphetamine and methamphetamine analyses. Since all the DoD laboratories are certified for this isomeric analysis, results are reported as D-amphetamine and D-methamphetamine. All specimens are screened for ecstasy, D-amphetamine, D-methamphetamine, tetrahydrocannabinol (THC), cocaine, and heroin. Because DoD cannot afford to perform 100 percent testing on all abused drugs, we pulse test for codeine, morphine, phencyclidine (PCP), oxycodone, and oxymorphone. Vicodin is becoming a growing concern, and the services are requesting screening tests for it. Currently, no screening kit is commercially available.

We are considering a study whereby we would perform 100 percent screening for specific prescription medications and then compare the laboratory results with the prescription database before we pursue other actions. By leveraging our technical ability and our software system, we hope to overcome the burden that will be placed on the laboratories and MROs.

Lysergic acid diethylamide (LSD) and barbiturates were recently removed from our routine drug test panels. For instance, there was one positive LSD result in the last five years. But, these tests are not dropped from the radar. Tim will talk tomorrow and provide details about the DoD-unique prevalence studies that are performed in conjunction with AFIP.

Overall, we had 1.2 percent overall positivity rate (21,000) last year in active duty Guard Reserve personnel compared with the DoD-set two percent maximum positive goal, which was codified this year. If we can retain our overall positivity rate below the two percent maximum, we are doing our job of deterring drug use through our drug

testing program.

Between fiscal years 2003 to 2007, the cocaine positivity rate rose from 19 percent to 39 percent. Marijuana use stayed constant at about 46 percent. The ecstasy positivity rate, which was seven percent in 2002, decreased to three percent in 2007 with a peak occurring in 2000.

With oxymorphone, the data is limited because it is derived from pulse testing of only 20 percent of all laboratory specimens. The MRO-verified positivity rate for oxymorphone is 1.4 percent, implying illicit drug use. A year ago, this information about illicit drug use verified from the MRO database was unavailable. The interface of these two databases is a tremendous improvement.

Through DoD and AFIP's interactions with the British, we have learned about the individual-specific, sub-cutoffs for marijuana and cocaine that are reported to their command. We are also considering providing similar sub-cutoff results to the services by unit, not by individual's name, which would permit identification of drug usage within service units. By identifying drug use trends, service policy may change.

Our new website is available at http://www.tricare.mil\DDRP. Posted on our site is the annual report, all of our policies, and a historical record of all information available from early in the mid-1970s.

Bob, thanks for your time.

MR. STEPHENSON: No. Thank you for sharing. This is what it means to have those who share a common question and a common passion come together periodically. I'd like to ask for Tim McCune from NRC to provide some updates from Nuclear Regulatory Commission.

10CFR Part 26 Fitness for Duty (FFD) Program

MR. McCUNE: (Slide 1) I'm Tim McCune, the FFD Program Manager at the Nuclear Regulatory Commission. The scope of 10 CFR Part 26 is any NRC licensee that uses, possesses, stores, or transports formula quantities of special nuclear material. Primarily, that's the nation's two category one nuclear facilities, NFS Erwin and BWXT Lynchburg, Virginia, as well as all of our power reactor community.

(Slide 2) What have we done with the new update to the rule? It's been about 20 years. We have strengthened the drug and alcohol testing provisions. We have enhanced validity testing of urine specimens to detect tampering, dilution, and substitution. The cutoff levels were changed for a number of reasons. In the current rule, licensees are allowed to deviate from the cutoff levels, and some are actually testing at the 50 nanogram per milliliter level for marijuana, which is now the new NRC cutoff.

We have an innovative process for alcohol testing involving a sliding scale to determine blood alcohol positive results. This process would detect someone in a random alcohol test after he'd been on shift, for instance, for 11 hours of a 12-hour shift. We have a sliding scale to determine blood alcohol positives.

Lastly, all workers on the FFD program will be trained at the supervisory level. Certainly, everyone subject to the rule will receive training, but the supervisors will be trained in behavioral observation and the detection of substance abuse, including prescription drug abuse.

Finally, we've enhanced the prescription drug provisions. In our policy section, Part 26, at 26.27, we require all licensees to develop policies in accordance with the rule that will mitigate the effects of drug and alcohol abuse as it applies to prescription drugs. Those licensee policies will be reviewed to make sure that it's ingrained in every

licensee's policy statement.

In the sanctions section at 26.75(f), the sanctions in this section do not apply to misuse of prescription or over-the-counter drugs, except if the MRO determines that misuse of the prescription or over-the-counter drug represents substance abuse. It is incumbent on the MROs and the substance abuse experts to be trained to detect substance abuse and to screen for that as a part of the sanctions section. Per section 26.187, a substance abuse expert can make a determination of fitness when an individual may be impaired by alcohol, prescription drugs, or over-the-counter drugs. There is a requirement for training of substance abuse experts who make determinations with respect to abuse of prescription and over-the-counter drugs.

And lastly, in the determination of fitness section, a determination of fitness must be made when there is acceptable medical explanation for a positive result, but there is a basis for believing that the individual could be impaired while on duty. Again, it is incumbent on the MRO and the substance abuse expert to make a determination regarding what could be substance abuse and what is just an expected positive as a result of a prescription drug.

(Slide 3) We've also implemented more stringent sanctions. If an NRC licensee subject to Part 26 is caught attempting to subvert the testing process or refusing a test, he/she will never work in the nuclear industry again. Except for this requirement in the NRC, the strongest requirement is five years for any other infraction. We justify this on the basis that there are ways to beat drug and alcohol tests, and we needed to send a very strong deterrent message, and we've done so with the rule. We also have a five-year denial if an individual resigns to avoid removal for an FFD violation. We've had people retire and say, “Well, I’m quitting” to circumvent the system. A five-year denial is for the second confirmed positive; in the current rule, it’s three years. A permanent

denial is for any FFD violation following a five-year denial. Also, the requirements for reauthorizing an individual terminated unfavorably for FFD reasons were strengthened.

(Slide 4) We are all very concerned about fairness within our programs and the protection of workers' rights. The opiate cutoff level was raised from 300 nanograms to 2,000 nanograms per milliliter. This was done to mitigate positives and as part of our strategy for addressing prescription drug use.

The requirements for independence of the MRO staff function from a licensee management were strengthened. We had some indications that MROs and their staffs who are funded by licensees were not completely independent from the licensee. In other words, the MRO staff was working only part time for the MRO. We had some incidents where it was evident that the MRO was not able to conduct his business of being an impartial arbiter in the drug-testing program.

In the current rule, licensees are allowed to depart from the HHS panel as well as to test at different cutoff levels. We strengthened that allowance in the new rule by saying that any deviation in those two areas must be verified by a certified forensic toxicologist to instill more rigor in the program.

(Slide 5) We've also found ways, in terms of relaxations, to save the industry money in an appropriate way. Because there were so few blood alcohol tests, this was eliminated as an option for donors. Only one alcohol breath test is required initially and a second to confirm a positive. Saliva devices are allowed, instead of breath, for the first test of those who choose to do so. Lastly, the requirement for licensees to report their fitness-for-duty testing performance data is once every year.

(Slide 6) We've been asked why we don’t incorporate the HHS guidelines. The HHS guidelines are an excellent place, from a technical perspective, from which to build the NRC program, but fundamentally, we have different missions. We are consistent

with the HHS guidelines in our rule-making update of 2004. The differences are related to NRC's mission, which is to ensure that our nuclear facilities are run safely. That is why we have sanctions for lifetime exclusion, for instance, for cheating.

(Slide 7) Implementation of the rule takes time in the NRC, as it does in other regulatory agencies. The rule was published in March of this year with three implementation periods: drug and alcohol is one year; the fatigue requirements are 18 months; and Subpart K, which is FFD or drug and alcohol testing during construction, has already taken effect; it had a 30 day fuse from March.

Industry is developing the guidance documents and sending them to us for endorsement, which is actively in progress. The guidance is endorsed through a regulatory guide that will undergo public scrutiny, public review, and most likely, public meetings.

The inspection guidance in the NRC was revised. The inspections are primarily conducted at our four regions, and training programs for our regional inspectors were developed.

About three years ago it occurred to me that we were getting hundreds of pages of data from our licensees every six months, which is an extraordinary waste of time to manually type the data into a database and then analyze it. After about 3.5 years of working with the industry and with our Office of Information Services, we expect to go online next year with the licensees, whereby they'll be reporting the data electronically.

Now, the data that we're going to be receiving will have much greater granularity than we're now getting. In response to Federal government data requests, we can analyze our database by worker population, by licensee, by time, and by drug. The data will be reflected on our public website at http:\\www.nrc.gov.

(Slide 8) That concludes my presentation. Are there any questions?

MR. STEPHENSON: Regarding NRC's focus on updating its program and policy, why is this so relevant now? What is transforming the nuclear industry in this country, and why are these updates so time and mission-critical?

Nuclear Regulatory Commission

MR. McCUNE: The resurgence or renaissance of the nuclear industry is a result of the increased pressure to evaluate what the energy industry has done to our environment. Relatively speaking, the nuclear sector program of generating power is one of the most environmentally friendly. What that essentially means is we're building reactors. The part of our new rule that's the most contentious is drug and alcohol testing during the construction of reactors. Never in the history of the NRC or our sister agency, the Department of Energy (DOE), has there been a drug and alcohol testing program that's been federalized that deals with construction. All types of questions had come up regarding who should be tested, when should they be tested, and how should they be tested. Our Part 26, Subpart K, did address that. We're working with the industry and guidance to iron out any other details.

I want to thank Bob and his organization for providing a study last summer of voluntary reporting of industry drug use. As it shows, for the 18 to 25 age group, there is a testing rate or a voluntary admission of drug use of approximately 18 percent. The NRC is running a little less than one percent in contrast to DoD's two percent. We expect that to increase greatly with the testing of that age group for construction.

DR. MADRAS: In the most recent Federal Interagency meeting regarding drug testing in Federal agencies, we implemented a program of evaluating who should be eligible for testing on an annual basis. Has that proven to be an exceptionally daunting task for NRC?

MR. McCUNE: Yes, quite frankly. In the first public meeting when we announced the requirements in this area, the industry said in a public meeting that they thought that they should be subject to only the same kinds of drug and alcohol testing programs as any other part of the construction industry. I referred to it as their Toys-R-Us policy. We're not building normal industrial facilities. We felt very strongly, and it's been quite a challenge to get the industry to agree to test workers. At one point, the industry informed us that they were concerned that they could not get enough construction workers that would be able to comply with the policy. That's not a good justification for not having the policy in place, obviously. We are at a 50 percent testing rate for all construction workers that are building nuclear reactors. The more critical positions, those positions that are quality assurance (QA), quality control (QC), security, and management, will be in the full FFD program. The industry would like a one percent testing rate in the first year with the option to drop the 50 percent testing rate even further. Personally, I'm not supportive of that.

MR. STEPHENSON: Thank you very much. At this time, I'd like to turn the proceedings over to Mike Baylor.

Tim, thank you very much for your presentation. We're very pleased that he was able to take the time to be here with us. Mike.

DR. BAYLOR: The next speaker will be Mark Weber, the Director of Office of Communications, the Substance Abuse Mental Health Services Administration, on Smart Rx.

MR. STEPHENSON: It's going to be Brad Stone, who is presenting in place of Mark and knows this topic very well.

Smart Rx

MR. STONE: Thank you, Bob.

(Slide 1) I’m to talk about the Smart Rx program, which is a program that was developed last year. In the Office of Communications, one of our main goals is to communicate a message particularly to the target group that needs to hear it. One of the challenges we've had over the past few years is that, although in many instances drug use has gone down or remained pretty steady, one area of concern has been the increasing use of prescription drugs for non-medical uses. It was a unique problem that calls for a unique solution, which is targeting a message to the particular group that could really influence, not only the availability of those drugs, but how they were maintained, stored, and disposed of.

The Office of Communications decided to team up with one of the primary marketing firms in the prescription drug area. Catalina is one of the leading firms responsible for the messages communicated with prescription drugs. After discussion between Catalina and the Office of Communications, it was decided to provide information to people who picked up those drugs that are most subject to abuse, to provide them with information first of all about how those drugs could be misused if they fall into the wrong hands, and what could be done to make sure that that didn't happen.

(Slide 2) We instituted a six-month prescription drug informational pilot program that ran from the end of 2007 to the first few months of 2008. The core of the program, called PatientLink, the trade name of the Catalina information sheet, targeted patients picking up the following categories of prescriptions: hydrocodones, benzodiazepines, sleep aids, and OxyContin. Based on data, these drugs were selected because they are most problematic in terms of misuse. Based on abuse rates, 26 states across the country were targeted. In total, the program involved 6,300 pharmacies throughout the United States.

(Slide 3) Information was distributed as leaflets with each having a specific

theme: one dealt with how to safely maintain one's supply of these drugs, another one dealt with the importance of disposing them properly, and then the third dealt with keeping track of who may have access to the drugs. Now, all these leaflets had the common theme of informing the persons who received these prescriptions about the potential dangers of these drugs.

(Slide 4) Through this program, a cumulative total of about 15 million leaflets were distributed over this period, and the cumulative total of individual patients who received them was well over seven million.

(Slide 5) Regarding how those seven million people used the information, analysis by Catalina determined that 85 percent, or slightly over six million people, read the material they received with their prescription. (Slide 6) With further analysis, they determined that 80 percent found the content useful, 48 percent kept the materials for future reference, and 26 percent of those who kept the materials shared the content of the leaflet with at least one person.

(Slide 7) The material had a great deal of credibility with the people who read it. This slide presents a ranking of how people rate the source of information for pharmaceutical products. These leaflets ranked very high, slightly below the information that one would receive directly from a physician or directly from a pharmacist.

(Slide 8) Catalina's program has the potential of reaching 120 million households. It can target stores individual consumers who tend to buy in certain patterns.

(Slide 9) This program, although it was relatively small in size and lasted only about six months, produced such interesting and positive results that ONDCP has entered into an arrangement with Catalina to have a broader program of this type.

(Slide 10) In summary, the program was very successful. It targeted the group in the population that could really have an effect on this problem and it did so for a very,

very low price. This program was able to obtain the best of both worlds because not only was it able to very effectively target a critical audience that could have a direct impact on this problem, but by publicizing the program itself, we had considerable media coverage on the general problem of prescription drug use. Indeed, both the Associated Press and Reuters wire services, as well as a whole slew of other major media, covered this program and told of its benefits, but in doing so, highlighted the problem of prescription drug abuse.

That's the end of my program. Thank you.

MR. STEPHENSON: Before we move on, I think Dr. Madras has a question or comment.

DR. MADRAS: Yes. Is there any interest from other sectors of the Federal Government, the private sector, or the pharmaceutical industry in perpetuating this?

MR. STONE: In addition to ONDCP, I'm not aware of any other government entities. However, some parts of the private sector, particularly some trade associations, have noted the success of it and have contacted us for some information about it.

DR. MADRAS: Do you have any outreach measures with regard to changing patient’s behavior rather than just awareness?

MR. STONE: We are working on with Catalina to see if there are any other indicators of whether patients followed through on some of the advice given in the leaflets, particularly with regard to storage and disposal information.

DR. MADRAS: Is there any indication of unintended consequences? For example, patients become alert to the fact that these drugs could produce a high?

MR. STONE: We haven't seen any data to indicate that. The concept of raising awareness about the risk of prescription drug abuse is an issue that ONDCP has looked into. We haven't seen any data, particularly with this program, that would indicate that it

somehow had a counterproductive effect.

DR. MADRAS: Is there any indication that promoting the concept that these drugs could produce addiction would enhance the impact and power of the message rather than just the statement that kids are using them to get high?

MR. STONE: We look very carefully at the messages that we were imparting. In this program, if it continues in whatever form, that would be a very good message to consider.

DR. BAYLOR: The next presentation is Prescribing Trends for Opioids, Benzodiazepines, Amphetamines, and Barbiturates from 1998 to 2007. The presenter is Sean Belouin, Lieutenant Commander, United States Public Health Service, Division of Workplace Programs, the Center for Substance Abuse Prevention, Substance Abuse Mental Health Services Administration. Dr. Belouin.

Prescribing Trends for Opioids, Benzodiazepines, Amphetamines, and Barbiturates from 1998-2007

DR. BELOUIN: Good morning. Today I'm presenting on prescribing trends for 15 commonly prescribed controlled drugs that fall within the pharmacologic classes of opioid analgesics, benzodiazepines, stimulants, and barbiturates. All these products are further classified as schedule controlled substances with a rating of C2 through C5. The 15 drugs chosen for these analyses are based on their use relative to all other prescribed controlled drugs, potential for abuse, and potential for diversion from individuals for whom the prescriptions were intended.

(Slide 1) I would like to thank in advance Nick Reuter, from the Division of Pharmacologic Therapies, CSAT, for his assistance in this presentation. A very special thanks to Dr. Hina Mehta, who’s here with us today, and Dr. Vicky Borders-Hemphill,

both PharmDs from the Office of Surveillance and Epidemiology, FDA, for completing all the requests for compiling and analyzing the data for this presentation. This presentation could not have been completed without their assistance and the close cooperation and partnership that exist between FDA and SAMHSA.

Several types of analyses were performed that looked at prescription drug data spanning the last 10 years, from 1998 through 2007. The drugs analyzed were oxycodone, hydrocodone, methadone, Fentanyl, codeine, propoxyphene, alprazolam, lorazepam, diazepam, clonazepam, temazepam, amphetamine, methamphetamine, butalbital, and phenobarbital.

To make the analyses more accurate and complete, we combined brand and generic drug data for each drug to give a more complete picture, for example, Percocet, OxyContin, Endocet, Percodan, Tylox, OxyIR and OxyFast. Some are brand names that contain oxycodone in addition to formulations that contain generic oxycodone. Some of these brands and generics contain not only oxycodone alone but also contain acetaminophen or aspirin in combination. Thus, to be complete and accurate, all products containing oxycodone, brand, generic, or combination products, such as oxycodone plus acetaminophen, have to be combined and accounted for to get a more accurate and complete picture.

We created a breakdown of each drug prescribed by strength. For example, hydrocodone comes as 2.5, 3.5, 4.5, 5, 7, 7.5, and 10-milligram strengths. We then analyzed the total number of prescriptions dispensed for each drug for each year over the last 10 years from 1998 through 2007.

We also analyzed the demographics by breaking down each drug into how many prescriptions were filled for men and how many for women and how many prescriptions were filled for various age ranges using 10-year intervals to get a sense of which age

range the drug product was most utilized.

Finally, to get a more complete picture, we further analyzed the total number of tablets, capsules, patches, milliliters, et cetera, which we refer to as extended units, that were dispensed for each drug for each year for 1998 through 2007. This would reflect the volume of just how much drug product was being dispensed on a year-to-year basis.

Now, what this presentation does not attempt to do is draw any conclusions or explain the reasons behind the prescribing trends over the last 10 years. I'm deferring to Dr. Westley Clark, CSAT Center Director, to help shed light on this issue. He'll be presenting in the afternoon session at 1:45 p.m.

The analyses conducted utilized Verispan's Vector One National Database, also known VONA, and IMS Health/IMS National Sales Perspectives Retail and Non-Retail Database, both of which were utilized to compile and analyze the data. The Vector One Database measures retail dispensing of prescriptions or the frequency with which drugs move out of retail pharmacies into the hands of consumers in the form of prescriptions, information on the physician specialty, the patient's age and gender, and estimates for the number of patients that are continuing on or beginning new therapy.

Vector One integrates prescription activity from a variety of sources, including national retail chains, mass merchandisers, mail order pharmacies, pharmacy benefits managers, and their data systems and provider groups. Vector One receives over two billion prescription claims per year representing over 160 million unique patients. Since 2002, Vector One has captured information on over eight billion prescriptions, representing 200 million unique patients. Prescriptions are captured from a sample of approximately 59,000 pharmacies throughout the United States. The pharmacies in the database account for nearly all retail pharmacies and represent nearly half of retail prescriptions dispensed nationwide.

Verispan receives all prescriptions from approximately one-third of the stores and a significant sample of prescriptions from the remaining stores. For prescription drug sales data and market share, IMS Health/IMS National Sales Perspectives was utilized. These data are based on national projections in the outlets within the retail market, including the following pharmacy settings: chain drug stores, independent drugstores, mass merchandisers, food stores, and mail service. Outlets within the non-retail markets include clinics, nonfederal hospitals, Federal facilities, HMOs, long-term care facilities, home health care, and other miscellaneous settings.

When viewing these data, it is also important to keep in mind the overall increase in US population. In 1998, the US population was approximately 270 million, and in 2006, the US population was approximately 299 million. This equates to an overall increase of 29 million or 10.7 percent increase in nine years.

The slides being presented contain a fair amount of information. Given the presentation time limits, I will stress only a few of the major points. Keep in mind that when looking at the prescription volume that I'm presenting for each of these drugs, it is the volume dispensed that impacts consumers directly. That's the biggest focus, and the slides reflecting actual drug volume dispensed will come at the end of the presentation, along with a slide representing each drug ranked nationally out of a possible total of 7,500 prescription drugs on the US market.

The first set of slides focus on the total number of prescriptions for each of the previously mentioned prescription drugs, the actual increase or decrease in prescription drug volume, and the percent increase or decrease in prescription drug volume.

(Slide 2) Here in Figure 1, the total number of propoxyphene and codeine prescriptions from 1998 through 2007 is shown. Volume decreased year-to-year for a total decrease of 8.4 million propoxyphene and 11.6 million codeine prescriptions,

representing a 36.5 percent decrease for codeine and 27 percent decrease for propoxyphene.

(Slide 3) Figure 2 is a very busy slide. What cannot be emphasized enough in this slide and the following slides are both the rapid and very significant increase in prescription volume for the majority of these drugs.

Total methadone prescriptions increased by 3.7 million from 1998 through 2007, with a percent increase of nearly 800 percent. Amphetamines increased by 463 percent or 11.7 million prescriptions. There was a 409 percent increase for Fentanyl for 4.5 million prescriptions for the same time period. As for the benzodiazepines, there was 114 percent increase in clonazepam, which represents 10.9 million prescriptions; 30 percent increase in temazepam or 1.9 million prescriptions; a 24 percent increase in lorazepam, which represents 4.2 million prescriptions; and a 17 percent increase in diazepam represented by 2.1 million prescriptions.

Those drug prescriptions that decreased were phenobarbital, which decreased by 22 percent or 820,000 prescriptions; butalbital, which went down 61 percent, or 381,000 prescriptions; and finally, methamphetamines, which decreased by 65 percent or approximately 36,000 prescriptions. Methamphetamine prescriptions have greatly fallen out of favor over the decades and have since been replaced by a dramatic rise in amphetamine prescriptions.

(Slide 4) In Figure 3, from 1998 to 2007, alprazolam increased overall by 17.6 million prescriptions, or 71 percent, to 42.4 million prescriptions in 2007. Oxycodone increased by 26.4 million prescriptions, or 166 percent, to 42.2 million prescriptions in 2007.

(Slide 5) Finally, in Figure 4, hydrocodone tops the list by increasing from 63.6 million prescriptions in 1998 to 123.3 million prescriptions in 2007, which is a net

increase of 59.7 million prescriptions by 2007 compared to 1998, which is a 94 percent increase.

(Slide 6) Figure 5 is a summation of the slides one through four that you just saw. It's important to keep in mind that when looking at these slides, one has to view them by considering the increase or decrease in prescription volume, as well as the percent change, to get a more complete picture of the prescribing trends. You cannot show volume without percent change and vice versa without skewing the overall picture.

(Slide 7) In this slide, the sales data for these prescription drugs indicates that the majority of distribution, 80 percent, is within outpatient pharmacy settings. The only exception was Fentanyl whose distribution through outpatient pharmacy was only 21 percent, with 78 percent within inpatient settings. Outpatient settings comprised of chain pharmacies, independent pharmacies, food stores with pharmacies, and mail order pharmacies. Mail order, however, accounted for approximately less than 12 percent of all the manufacturers of selected prescription drugs. Mail order was not included in this analysis for the slide when determining prescription drug distribution.

Now, the next 15 slides reflect the total number of prescriptions dispensed by strength, the age range for which each product had the majority of prescriptions written, and the ratio between males and females receiving these prescriptions.

(Slide 8) Figure 6 shows the 30-milligram strength of phenobarbital being the most commonly dispensed, however, it has declined over the years. The ratio for males to females has been one-to-one, with the majority of prescriptions dispensed to children ages zero to 10 years for males and ages 41 to 50 for adult females. The exception occurred after 2006 in which female children zero to 10 years were commonly dispensed phenobarbital.

(Slide 9) Figure 7 shows that the 50-milligram strength butalbital is the most

commonly dispensed, however, use has been gradually declining over the past 10 years. The ratio of dispensed butalbital prescriptions for females to males is approximately four-to-one, with the majority of prescriptions dispensed to both male and females aged 41 to 50 years.

(Slide 10) In Figure 8, the 30-milligram strength of codeine is the most commonly dispensed; however, its use has been declining year-to-year. The ratio of codeine prescriptions for females to males is 1.7-to-1.0, with the majority of codeine products dispensed to males and females age 41 to 50. However, after 2005, the range for males changed from 51 to 60 years of age.

(Slide 11) In Figure 9, the 65-milligram strength for propoxyphene was more commonly dispensed and has fluctuated over the last 10 years while the 100-milligram strength has steadily declined. The ratio of dispensed propoxyphene prescriptions for females to males was 2.4-to-1.0, and the majority of propoxyphene was dispensed to adults age 51 to 60 for females and aged 71-plus for males.

(Slide 12) Figure 10 shows a gradual decline in 5-milligram methamphetamine prescription use with total prescriptions totaling less than 20,000 in 2007 for the 5-milligram strength. The ratio of use between female and males was approximately one-to-one, with the majority of prescriptions dispensed to both males and females aged 41 to 50 years. Again, methamphetamine prescriptions have greatly fallen out of favor over the decades and have since been replaced by a dramatic rise in amphetamine prescriptions.

(Slide 13) Figure 11 is the amphetamine slide, which shows a rapid rise in amphetamine prescriptions with 20 milligrams being most commonly dispensed. The ratio for males to females is 1.7-to-1.0, with the majority of amphetamine prescriptions dispensed to adolescent males and females aged 11 to 20 years. Again, from Slide 2

that you saw earlier, the average increase in all amphetamine prescriptions rose from 2.5 million in 1998 to 14.2 million in 2007, a 463 percent increase.

(Slide 14) Figure 12 shows that the 30-milligram strength of temazepam was most commonly dispensed followed by the 15-milligram strength. The ratio of females to males is 1.7-to-1.0, with the majority of prescriptions dispensed to males and females aged 71 and over.

(Slide 15) In Figure 13, the 5-milligram strength of diazepam was most commonly dispensed with the ratio of females to males being 1.6-to-1.0. The majority of all diazepam prescriptions dispensed to males and females were age 41 to 50 years.

(Slide 16) In Figure 14, the 0.5-milligram strength of clonazepam was most commonly dispensed followed by the 1.0-milligram strength. The ratio of females to males is approximately two-to-one, with the majority of prescriptions dispensed to both genders age 41 to 50 years.

(Slide 17) In Figure 15, 1.0-milligram lorazepam is most commonly dispensed followed by 0.5 milligrams, with the ratio of females to males of 2.4-to-1.0, and with the majority of prescriptions dispensed for both genders age 71 years and over.

(Slide 18) Figure 16 shows alprazolam, 0.5 milligram, most commonly dispensed with a ratio of females to males 2.3-to-1.0. The majority of dispensed prescriptions for males and females occur between ages 41 to 50.

(Slide 19) In Figure 17 shows the 50 microgram strength of Fentanyl most commonly dispensed, closely followed by 25 micrograms with a ratio of females to males of approximately two-to-one. The majority of all Fentanyl prescriptions are dispensed to females are age 71 and older and males age 41 to 50 years. Again, from Slide 2 that you saw previously, the average increase in all Fentanyl prescriptions rose from 1.1 million in 1998 to 5.5 million in 2007, a 409 percent increase.

(Slide 20) In Figure 18, 10-milligram methadone was most commonly dispensed with a significant increase over the last 10 years. The ratio of females to males was approximately one-to-one, with the majority of prescriptions dispensed to both genders, age 41 to 50 years. Again, from Slide 2, the average increase in all methadone prescriptions rose from approximately 468,000 in 1998, to 4.2 million in 2007, a nearly 800 percent increase.

(Slide 21) In Figure 19, oxycodone, five milligrams, was most commonly dispensed with the ratio of females to males approximately of one-to-one, with the majority of oxycodone products dispensed to males and females age 41 to 50 years. Again from Slide 3, the average increase in all oxycodone prescriptions rose from 15.9 million in 1998 to 42.2 million in 2007, 166 percent increase.

(Slide 22) Now, the last of the 15 drugs being analyzed is hydrocodone, as shown in Figure 20. We can see the hydrocodone 5 milligram is the most commonly dispensed strength and the ratio of females to males prescribed hydrocodone is 1.4-to-1.0 with the majority of hydrocodone products dispensed to both genders age 41 to 50 years. Again, from a previous slide, the average increase in all hydrocodone prescriptions rose from 63.6 million in 1998 to over 123 million in 2007, a 94 percent increase over 10 years.

The next three slides will show some general statistics of total prescriptions dispensed sorted by gender from 2002 through 2007.

(Slide 23) Figure 21 reflects opioids dispensed for both females and males; hydrocodone is most commonly dispensed drug followed by oxycodone. The use of propoxyphene has steadily declined in use over the last 10 years.

(Slide 24) In Figure 22, which reflects benzodiazepine dispensed, alprazolam is the most commonly dispensed drug in females followed by lorazepam. In males,

alprazolam is also the most commonly dispensed drug; however, clonazepam follows second. Overall, females fill more prescriptions for benzodiazepines compared to males.

(Slide 25) In Figure 23, which represents amphetamines and barbiturates, there was approximately a 30 percent increase in amphetamine use for males from 2002 through 2007; however, there was 111 percent increase in use for females over the same period. Referring back to Figure 11, amphetamine use is still close to a two-to-one ratio of males to females.

In the next set of five slides, the volume of drug product will be shown. Prescription volume gives only half the picture; without the volume of drug product being dispensed, the data is incomplete. To accurately represent trends and prescribing practices, both prescription volume and drug product volume dispensed must be presented. Extended units refer to the number of units dispensed for a given product for a given period of time. This takes into account individual tablets, capsules, milliliters, patches, et cetera.

(Slide 26) In Figure 24, there has been a small decline in actual volume of codeine and propoxyphene, 12.4 and 12.1 percent, respectively, with total codeine dispensed at 1.7 billion extended units and approximately 1.9 billion extended units dispensed for propoxyphene in 2007.

(Slide 27) In Figure 25, the number of units being dispensed for methadone increased from 56.5 million units in 1998 to 758 million units in 2007, a 922 percent increase. This represents 521.5 million more units dispensed in 2007 than in 1998. Fentanyl increased over the same period by 800 percent, or 74 million units, and amphetamines by 345 percent, which represents approximately 500 million more units dispensed in 2007 than in 1998. Clonazepam increased by approximately 120 percent

from 1998 to 2007, which represents 641 million more units dispensed in 2007 than in 1998. There was a 27 percent increase in lorazepam, or 236 million units over the same period; a 35 percent increase in temazepam, or 70 million units; and a 16 percent increase in diazepam, or 92 million units. There were decreases in butalbital, phenobarbital, and methamphetamine volumes, with phenobarbital showing the greatest decrease in volume at 103 million units, or 24 percent.

(Slide 28) In Figure 26, alprazolam increased 83 percent from 1998 to 2007, which represents almost 1.18 billion more units dispensed in 2007 than in 1998. Oxycodone increased by 314 percent over the same period, which represents over 2.27 billion more units of oxycodone dispensed in 2007 than in 1998.

(Slide 29) Finally, the last of the 15 drugs is hydrocodone. When looking at hydrocodone in Figure 27, hydrocodone units dispensed increased 172 percent from 1998 to 2007, which represents over 4.6 billion more units dispensed in 2007 than in 1998.

(Slide 30) Just keep in mind that Figure 28 is another summation slide of all the drug products and the number of extended units dispensed from 1998 through 2007. Also keep in mind the Y-axis is in the billions of units dispensed.

(Slide 31) Lastly, this slide provides some perspective as to where these products rank in the prescription drug market. Out of approximately 7,500 drugs on the US market, all but four ranked within the top 200 dispensed drugs. Methadone is close to the top 200, ranking 203.To give you some perspective of the prescription volume involved when it comes to ranking these products, the combination product hydrocodone with acetaminophen ranks number one at 117 million prescriptions, which is followed by lisinopril, a high blood pressure medication, which is not shown on this slide. It was in the number two position at 61.7 million prescriptions. In 2007, there were

over 55 million more prescriptions of hydrocodone with acetaminophen than there were prescriptions for lisinopril.

Again, this presentation does not attempt to draw any conclusions or explain the reasons behind the prescribing trends over the last 10 years. I'm deferring to Dr. Westley Clark, CSAT Center Director, to help shed some light on this issue later this afternoon.

The data presented reflect prescription volume and prescription product dispensed, however, this does not reflect how much dispensed product is consumed by the individuals for whom the products were prescribed or the potential for a diversion after dispensing. That concludes it.

DR. BAYLOR: Thank you, Sean. We'll now take a 15-minute break and resume promptly at 10:47.

(Break)

DR. BAYLOR: The next speaker is DeMia Peters, a chemist at the Office of Diversion Control, Drug Enforcement Administration (DEA). She'll be speaking on the National Forensic Laboratory Information System. DeMia.

National Forensic Laboratory Information System (NFLIS)

MS. PETERS: (Slide 1) Good morning. You just heard about pharmaceutical drugs and how the number of prescriptions has increased over the last 10 to 11 years. As the number of prescriptions increased over the past 11 years, the number of seizures on the law enforcement side has also increased.

(Slide 2) The National Forensic Laboratory Information System (NFLIS) accumulates drug analysis results from state and local crime labs all over the country. The database consists of roughly 8 million cases and drug items that date back to 1998.

Currently, 276 of our nation’s 320 state and local laboratories have joined the NFLIS system, and we have just over 250 reporting regularly.

(Slide 3) This slide depicts a census of the regions and the laboratories that report and the coloring for the state laboratory systems and the local or regional laboratories that we also have reporting to the NFLIS system.

(Slide 4) 95 percent of the state laboratory systems and 86 percent of the local systems report to the NFLIS system, which gives us approximately 91 percent of all laboratory cases from the state and local laboratories across the country.

(Slide 5) The primary purpose of the NFLIS system is to take chemically-verified data, which are cases and seizures from law enforcement activity, and compare them and supplement the information from databases such as the Drug Abuse Warning Network (DAWN) and NSDUH and the DEA system STRIDE (System to Retrieve Information From Drug Evidence), which is comparable to the NFLIS system, and support our Federal, state, and international regulations of drugs.

(Slide 6) Other uses for the NFLIS include the support of the supply-side data for the Federal, state, and local authorities. We provide information on drug trafficking to our counterparts on the state and local level, and we identify changing distribution levels geographically and over time. We also try to identify emerging drug trends that we would not see from the larger cases that we collect on the Federal level.

(Slide 7) In this table are listed the top 25 identified drugs that were analyzed in 2007 by the state and local systems across the country. The arrows are pointing out that 14 of the top 25 drugs are actually pharmaceutical drugs, and that does not include pseudoephedrine, which is listed with the three dots because it's an over-the-counter product and is not a controlled substance.

(Slide 8) Narcotic analgesics make up a large part of what is seized by law

enforcement entities. Hydrocodone is number one, followed closely by oxycodone for the narcotic analgesics. Hydrocodone is now the number one prescription drug in the country. For narcotic analgesics, most of these drugs were just presented on our top 25. Everything down to hydromorphone, which represents about two percent of all narcotic analgesics, was presented on the top 25. Taking those same numbers for the distribution of narcotic analgesics and dividing them by region of the United States, while hydrocodone is large in the South, oxycodone is more prevalent in the Midwest. However, both oxycodone and hydrocodone are prevalent throughout the United States.

(Slide 9) This graph and the graphs to follow present the hydrocodone data; the drug data are presented per 100,000 population for those 15 and older across the United States and have been normalized by region.

(Slide 10) The South leads all regions in the United States for hydrocodone use. The West, Midwest, and Northwest are running about the same and are converging in 2007 on the amount of hydrocodone used.

(Slide 11) For oxycodone, this changes a little bit and moves more towards the Northeast. You don't see the convergence in 2007, and the regions are spread out a bit more.

(Slide 12) For benzodiazepines, for lorazepam and above, these four items were all on that top 25 of the most seized and analyzed drugs identified by the NFLIS system.

(Slide 13) The South continues to lead in what is being seized and analyzed by the NFLIS system, and it's above any other region in the seizure and analysis of alprazolam.

(Slide 14) This mixed slide compares some of the larger drug volumes that we've been seeing. One DEA Schedule One drug, which is 3,4-methylenedioxy-*N*-methylamphetamine (MDMA), that's listed here just for comparison. Comparing illicit

drugs, such as MDMA, with the amount of pharmaceutical drugs that are seized and analyzed in the forensic laboratories, the pharmaceutical drugs are outweighing illicit drugs such as MDMA. Hydrocodone, oxycodone, and alprazolam have more items being analyzed by the laboratories than MDMA.

(Slide 15) On the Department of Justice (DOJ) diversion website for NFLIS is a presentation on our 2007 annual report. This presentation is available for download, as is our midyear and other reports, including our annual special report. Two years ago, we did a pharmaceutical report that looked at narcotic analgesics and benzodiazepines, and that's available for your download at this website as well: http://www.deadiversion.usdoj.gov/nflis. Thank you very much.

DR. BAYLOR: Thank you, DeMia. The next presentation is, “Prescription Drug Misuse: What Can the National Surveys Tell Us?” presented by Dr. Charlene Lewis, Senior Advisor Office of Applied Studies at SAMHSA.

Prescription Drug Misuse: What can the National Surveys tell us?

DR. LEWIS: (Slide 1) First of all, I want to thank Bob and Donna for inviting us to be here today. The Office of Applied Studies (OAS) loves to present their data. It's a great privilege to be able to do it today.

I first want to describe three of our national surveys, including their commonalities and their differences. First, all three surveys are in the field all of the time; these are continuous data collections. Secondly, the data collections are reported on the basis of a calendar year, so the 12 months that are 2006 in NSDUH are the same 12 months that are in DAWN or in Treatment Episode Data Set (TEDS).

What is different about the three surveys is that the populations covered are quite different and, to some extent, the nature of the survey drives the definitions that we use

to collect drug information inside the surveys themselves. First, I will discuss the 2006 National Survey on Drug Use and Health.

(Slides 2-3) NSDUH is a nationally representative sample of people, both for the country as a whole and within each state and the District of Columbia. It polls the civilian, non-institutionalized population aged 12 and older. The data are collected through a face-to-face interview, which takes about an hour and is completely confidential. It's a computer-assisted interview where the respondent uses a laptop and a set of headphones. Annually, we screen about a quarter of a million homes and select from those homes around 67,000 respondents.

(Slide 4) NSDUH does a good job of telling us about the prevalence of illicit drug use inside the country as a whole. The slides I brought today will give you an idea of the context of where prescription drugs fall within the continuum of illicit drug use within the country.

(Slide 5) We have about 20 million people who are current users, that is, in the past month users of illicit drugs. Of those, marijuana users constitute the majority or the largest portion of that population, with marijuana being the most widely used illicit substance in the country. People who are misusing or abusing prescription drugs now number about seven million throughout the country.

(Slide 6) Just to give you again an idea of the proportion, we have far more current users of marijuana than we do psychotherapeutic drugs. However, I would draw your attention to the differences in the prevalences from 2004 to 2006. We've had a statically significant increase in the number of psychotherapeutic drugs users, which has not happened with any of the other drug categories such as marijuana.

(Slide 7) Non-medical use of a prescription drug in NSDUH is defined as using a prescription intended for someone else or using a prescription drug just for the feeling or

the sensation that it causes.

You are particularly concerned with certain classes of drugs. For pain relievers, there was a statistically significant increase from 2004 to 2006 in the percent of people who are current users non-medically of prescription drugs, which is not so with other drugs, such as stimulants, sedatives, and tranquilizers.

(Slide 8) There's been some media attention as to where people get these drugs and concern about use of the Internet as a source of obtaining illegal prescriptions. What NSDUH tells us is that well over half of all people who are currently using prescription drugs non-medically get it from a friend or a member of their family, whether the drugs are given to them or whether they simply take the drugs from them. Of those friends and family members who are inadvertently or advertently dispensing these drugs, the majority of those have gotten that drug from a legitimate physician.

(Slide 9) Regarding the general state of illicit drug use in the country, NSDUH can help us identify where in the population we're seeing the greatest problem with certain types of drugs. In the age group of adolescents who are 12 to 17, we've seen a significant decline in illicit drug use since 2002.

(Slide 10) This is not so in the age group of young adults who are 18 to 25. Specifically, these young adults show a marked increase in their use of prescription pain relievers and prescription tranquilizers.

(Slide 11) NSDUH also shows us who are starting to use new drugs or who are becoming initiates into drug use. (Slide 12) In 2006, there were more new users of prescription pain relievers than there were for marijuana. (Slide 13) Interestingly, on average, whereas adolescents tend to initiate their substance use with inhalants or marijuana, it isn't until about the age of 20 that the average age of initiation for pain relievers, stimulants, tranquilizers, and sedatives is seen. We'll keep coming back to this

18 to 25 year-old age group because they're very important.

(Slide 14) Using the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria, NSDUH also provides us with measures of abuse and dependence on illicit substances. (Slide 15) For a national perspective, the most commonly abused substance in the country is alcohol, whether it is alcohol alone or alcohol in combination with some other drug. (Slide 16) However, the most commonly abused illicit substance is marijuana followed by cocaine. Pain relievers, however, are now in third place as a common substance of abuse.

(Slide 17) What happens to those people who are abusing or dependent on prescription drugs, other illicit drugs, and alcohol? Hopefully, they end up in treatment. TEDS is another of our major data collection activities. In TEDS, I will focus specifically on those prescription pain relievers that we saw in NSDUH.

(Slide 18) TEDS is client-level data on people who are admitted to specialty substance abuse treatment. The information comes primarily from facilities that receive some amount of public funds. We estimate that our coverage nationwide is somewhere in the vicinity of 80 percent, which translates into about 1.8 million admissions to treatment annually. As a word of caution, an admission and a person are not necessarily the same thing since a person may be admitted to treatment once, twice, or three times during the year; there's not a one-to-one correspondence.

(Slide 19) TEDS collects a variety of information, including the demographics of the person entering treatment and that individual's drug use history. We collect three substances of abuse at admission, though these may not be a full enumeration of everything that the person is using when he or she comes in to treatment. We also collect age at first use, frequency of use, and how that substance is being used, along with a variety of variables about the treatment that's planned to address the drug

problem.

(Slide 20) TEDS has some limitations that are relevant to you because we do not collect drug brands the way DAWN does, for example, but we collect generic categories, such as opiates other than heroin. We do have 16 states where opioid analgesics are collected on a name brand basis. I will present some data about them just to give you a flavor of what you can learn from a small sample of states.

(Slide 21) First of all, from NSDUH, we know the most prevalent substances bringing people into treatment are alcohol, followed by marijuana, cocaine, and heroin. The opioid analgesics in 2006 represented four percent of all treatment admissions. Remember, that's four percent of 1.8 million, so the number is fairly substantial.

(Slide 22) TEDS has been a stable dataset since 1992. For those of you who like to play with data, a concatenated dataset is available that allows us to study from 1992 to 2006. We can trace the entrance into the marketplace of certain drugs. For instance, OxyContin was introduced in 1996, and there is a steady increase in the number of treatment admissions that involve opioid analgesics since about 1999.

(Slide 23) The increase in these prescription drug admissions to treatment is not related to an overall increase in treatment admissions. We've seen about a 12 percent increase in total admissions and a 4 percent increase for heroin, but a 367 percent increase for prescription drug abuse as a primary substance of abuse.

(Slide 24) Sixteen states report on specific opioid analgesics as seen on this map showing these states spread out from Maine to Nevada. (Slide 25) From their reports, we assembled this chart, which shows that, head and shoulders above all the rest, oxycodone is mentioned as the substance bringing people into a treatment episode, whether as a primary, secondary, or tertiary substance of abuse. Nothing else really seems to come close, at least in those 16 states.

(Slide 26) In perspective, overall, there's been 168 percent increase in admissions with opiate analgesics as part of the package of substances being abused, but a 1,500 percent increase for oxycodone. This has tremendous ramifications in the treatment field for employee assistance programs (EAP) and for other folks who are concerned about the characteristics of clients coming into forced treatment programs for changing their approach to treating people with dependency issues.

(Slide 27) Maine, Massachusetts, Rhode Island, Delaware, Maryland have the highest rates per 100,000 for treatment admissions for opioid analgesics. There seems to be a geographic component associated with this particular substance of abuse.

(Slide 28) Similarly, if we look at the urbanization factor, the highest rates of treatment admission occur in those areas, which we would consider to be less urbanized, outside of metropolitan statistical areas (MSAs), in small cities, or outside of MSAs, where there are no cities.

(Slide 29) By the time these people enter treatment, whether they have a primary or a secondary problem with opiates, they quite frequently also have problems with other drugs, such as alcohol, marijuana, cocaine, heroin, and stimulants.

(Slide 30) The bubble of usage, regardless of the route of the administration, occurs starting around the age of 19 and going to about the age of 25, whether you're taking these substances orally, inhaling them, or injecting them.

(Slide 31) Because TEDS is a very stable dataset, we can look across the last decade and look at the characteristics of clients coming into treatment for opioids. There are more males than females, and patients are predominantly white. The age of the person entering into treatment has shifted dramatically. In 1997, only 20 percent of the people entering into treatment were under the age of 30; now it's closer to 50 percent.

There is an upswing in the number of new users, people who have been using

these substances for three years or less, and an increase in the number of people who are taking them through inhalation rather than orally or through injection.

(Slide 32) Most of you are familiar with DAWN, so I will just hit a few highlights here for those of you who aren't. (Slide 33) First of all, DAWN is a national probability sample of community-based hospitals that operate 24-hour emergency departments from which we determine annual estimates of drug-related visits to these emergency departments.

(Slide 33) Annually, there are about 115 million visits to emergency departments across the country. Approximately 12 million of these records are sampled every year and every chart is reviewed end-to-end. On average, three percent of cases are drug-related. From these, the national estimates are derived.

(Slide 35) Non-medical use in DAWN parallels to some extent the definition that is also used in NSDUH. The definition here is to exceed the prescribed or recommended dose, to use somebody else's prescription, to be poisoned by someone with a malicious purpose, or attendant to substance abuse as defined by the DSM-IV.

(Slide 36) As with the TEDS statistics, there are a few more female visits to emergency departments than male visits, which may be related to with female health-seeking behavior. But again, the bubble for the greatest rate of emergency department visits occurs between the ages of 18 and 25. Consistent across all three surveys is that this age group is particularly at risk for the abuse of these pharmaceuticals.

(Slide 37) There has been a tremendous increase between 2004 and 2006 in the number of emergency department visits, which were attributable just to pharmaceuticals. Similarly, there has been a 36 percent increase the number of visits attributable to those pharmaceuticals in combination with another illicit substance. Between 2005 and 2006, there was a 22 percent increase in visits attributable to

pharmaceuticals and alcohol.

(Slide 38) What happens to these people who show up in these emergency departments? Little over half of them get sent home, go to jail, or they leave against medical advice. Around 45 to 46 percent receive some kind of follow-up care, whether that's referral to a treatment program or admission into a detoxification unit. The percentage attributable to death is quite small.

(Slide 39) For those of you who would like further information, all of this information and much, much more is available on our website http://www.oas.samhsa.gov/. You can call our office help line and somebody will actually answer your questions for you, or you can contact the SAMHSA Clearinghouse and get the publications from there. Thank you.

MR. STEPHENSON: Thank you very much. Charlene. We really do appreciate that you were able to present. You have a great personal history, passion, and a depth of knowledge, which makes it interesting to share what you know with the rest of us.

Just looking around the room, I want to ask a question. How many of you have found a theme around prescription drug issues? Is there anything new that we presented that you didn't know before that goes beyond what you intuitively understood? For members of the Board especially, is this perceived to be of value for you?

PARTICIPANT: Definitely.

MR. STEPHENSON: Okay. Hopefully, it’s mirrored in the general audience too. That was our intention, and it looks like we’re being able to carry off the mission. Mike.

DR. BAYLOR: The next presenters are Dr. Paul Starr, Specialist, Poison Information, Maryland Poison Control Center, University of Maryland School of Pharmacy, and Dr. Alvin Bronstein, Associate Professor, University of Colorado School

of Medicine, Medical Director Rocky Mountain Poison Center, Director of Surveillance National Poison Data System, American Association of Poison Control Centers.

National Poison Data System (NPDS): Real-Time Documentation and Surveillance

DR. STARR: To begin with, I'd like to thank the Advisory Board for inviting us here and giving us the opportunity to present our data system, which seems to be right in line with all the other systems that we've heard about.

(Slide 1) Ours is a real-time surveillance system that has the capabilities of finding very, very acute and chronic trends or long-term trends.

Our system can be correlated with the goals of the Advisory Board. Before we go on as to the exact potential for the data, I'd like to talk about poison centers because that's where the front-line documentation begins with this data.

(Slide 2) The general public and health professionals phone an emergency call line that fields both emergency exposures and drug information calls. Both have full access to these regional poison centers. There is an immediate download, every 11 minutes, to a central surveillance database. These data include, as part of medical record demographic information, the date, time, type of call, and exposure duration. For exposure duration, we deal with acute, chronic, and acute on chronic, such as someone on pain medication who has overdosed or started abusing or someone with a toothache who is taking a medication that’s been previously prescribed for another condition. Other data collected includes the cause of exposure, whether it’s intentional or unintentional, and the symptoms, severity, and the course of action. A course of action involves where it's managed, how it's managed, and recommended treatment.

(Slide 3) There are 61 regional poison centers throughout the continental United

States. In order to be certified, these centers have to meet certain parameters, one being that they're accessible 24/7. We never close, and the data is always being transferred to the national database. All centers receive varied funding support, ranging from federal to state to private sector in terms of donations and possibly hospital budgets. It's an ongoing financial battle, and it's something that we, as with other organizations, have to deal with on a year-to-year basis. The poison centers are all computerized; all medical records and all calls are documented on the computer for immediate download.

The regional poison centers all serve the same mission or a similar mission as the central organization, which is to maintain and improve patient outcomes, to prevent poison exposures, and to reduce healthcare cost. For every million dollars spent on operational costs, we save seven million dollars in healthcare costs.

(Slide 4) We wear many hats. Our predominant hat is to provide treatment recommendations and triage information to the public and health professionals. We also provide poison prevention education, not only to the public but also to healthcare professionals. We do an amazing amount of evidence-based research from retrospective and prospective studies on data that we will be talking about, which include the data collection component of this operation.

Data collection is done as a medical record. The medical record not only contains a computer online form that codes for certain parameters, but it also requires a written documentation on all exposures. The written documentation usually follows, for those who are familiar with medical charts, SOAP (subjective, objective, assessment, and plan) notes.

(Slide 5) Poison Centers are staffed by pharmacists and nurses who are specially trained in the field of toxicology. They must be certified; they take a national

exam every seven years. Most of the training occurs on the job. There is actually some research being presented that the pharmacists and nurses who take these calls are actually starting to turn gray. We're a small community and our experience is just growing by the day.

Each center has a director of operations and specialists who are either credentialed like me who are either board-eligible or board-certified by the American Board of Applied Toxicologists. There are about 100 of us in the country.

In order to be a certified poison center, a center must also have a medical toxicologist who is usually board-certified, not only in toxicology, but also in emergency medicine. We also have professional and public educators whose sole job is to coordinate and educate the sectors that they are assigned to and also put out, as does the central office, immediate recalls and information about current trends that affect public policy.

There are specialized consultants, including people who specialize in all four fields of toxicology and information technology (IT) personnel, that we have access to as a poison center. In our case, we have a very special situation in that we have people trained in drug abuse who serve as social workers, taking drug identification (ID) calls throughout the day, for approximately six hours every day. They also have the opportunity of asking questions.

(Slide 6) This slide shows the Maryland Poison Center. These are our workstations. We have a couple of specialists there; the gentleman to the right is actually a social worker taking drug ID calls.

(Slide 7) These are some of the general data from our yearly report. We are a medium-sized center. In 2007, we received over 35,000 exposure calls out of the 65,000 to 66,000 total calls received. The rest of the calls are for drug information, drug

ID, and animal exposures.

(Slide 8) Our exposure reasons are similar to the DAWN categories. I left out malicious because it's a very small number. About 15 percent are intentional, implying a fair percentage of abuse and misuse, and 80 percent are unintentional.

(Slide 9) For the place of management, 72 percent are usually handled and treated in a non-healthcare facility and about 25 percent end up in a healthcare facility.

(Slide 10) Our statistics show certain groups of drugs by age group. Only in the 6 to 19 year age group did stimulants and street drugs fall into the top 10 drug classes that are included in exposures. Alcohols, which include a fair amount of different alcohols, really don't apply. Antidepressants rank fifth in the 6 to 19 age group but are third in the over 20 year age group. In the population exposures that include sleep medicines and antipsychotics, the ranking is fourth for the 6 to 19 year age group and second for the over 20 age group. Analgesics were ranked first in both the 6 to 19 and the over 20 age groups.

And at this point, I'm going to hand the microphone over to Alvin so that he can introduce and spend more time on the system.

DR. BRONSTEIN: (Slide 11) Thank you, Paul. I want to thank the committee for allowing me to come today to present and Ron Flegel for arranging this.

I want to talk about the National Poison Data System (NPDS), to which all of the 61 US regional poison centers contribute their data. (Slide 12) As mentioned, there are 61 US poison centers that cover all 50 states, Puerto Rico, the US Virgin Islands, plus three specific jurisdictions. They all upload data to the national system with a median time to upload of every 11 minutes.

For years and years, we published a static annual report. Now with our online data system, we can look at data for the last hour or through the last day; the data are

always current. That doesn't necessarily mean real-time, but any time anyone looks at the data, the data is current.

(Slide 13) We categorize the cases into two flavors, information and exposure cases. We had 2.4 million exposures in 2006, 2.6 million exposures in 2007, and so far this year through the end of July, we had 1.5 million exposure calls and over one million information-type calls. Information calls have no victim because no one's exposed.

(Slide 14) It is a real-time database. We can compare the data to historical means. We currently have online in the system the data back to the year 2000, but the data actually go back to 1983.

(Slide 15) We can flag cases as they are uploaded for case-based surveillance. If someone wanted to see cases for Vicodin or hydrocodone, for instance, by death, by age, by outcome, or by intent, we can flag those cases as they hit the system. If needed, we have the capability to speak with the regional poison center that took that case to obtain more information or to confirm what the patient actually took. We also can do surveillance looking by volume-type definitions for surveillance. For call volume plus clinical effects, we hardcode 131 clinical effects that are used throughout the cases to describe the clinical status of the patient. We also have our case-based definitions.

(Slide 16) The system is online; accessible from any computer in the world with proper credentials at https://www.npds.us/logon.aspx.

(Slide 17) This slide depicts data from 2006 back to 2000. The upper line in red represents the exposure calls. The data are very periodical, with calls peaking during the summer months, decreasing around Christmas and New Year's, and increasing again, like the little P waves in an EKG (electrocardiogram). The big blue line shows the information calls. The rate of rise of information calls is much steeper than exposure calls. The green line on the bottom represents animal exposure calls, which run about a

two to five percent.

(Slide 18) For drug ID calls, there is a relatively steep rise. The blue line on the bottom represents drug ID calls from police agencies. These data can be used to look more closely to parallel what's on the street as drug diversions and from people swapping drugs. The number one call for drug ID is hydrocodone. But curiously, number four in the overall picture is antibiotics because people do swap these drugs because it's cheaper to swap then going to the doctor. There's so much data here, and, of course, this is real-time.

(Slide 19) We can also use NPDS to track outbreaks, such as contaminated water supplies. Last year, we received over 12,000 calls last year from the salmonella-contaminated peanut butter recall. We picked up and tracked Fentanyl exposures with clenbuterol. What the system really offers is situational awareness.

One of the issues that I've seen today at the meeting is all of our definitions need to be conformed, so we define things the same way everybody else does and prepare our statistics in the same way so we can compare apples to apples, and hopefully, that is something we can all work on.

(Slide 20) This slide shows a call volume example of the calls we received last year for the peanut butter recall, illustrating our ability to track trends. This same technology can also be used to track drug diversions or to investigate at drug information calls or clinical exposures.

(Slide 21) This slide shows workplace calls for a variety of drugs. Oxycodone comes in three flavors: oxycodone by itself, oxycodone plus acetaminophen, and oxycodone plus aspirin. Overall in the poison system, we had over 13,000 oxycodone exposures in 2006 and slightly more last year, with about one percent of the calls from people in the workplace. These data can be mined for more information looking at

various issues.

(Slide 22) In summary, NPDS is a national, real-time exposure tracking system with data contributed by the 61 US poison centers. We use it to track outbreaks, including the recent problem with the nutritional formulation with selenium. We've used it to track Fentanyl, spinach, and other agents. We think that collaboration and coordination between the Poison Centers, the FDA, Environmental Protection Agency (EPA), SAMHSA, Centers for Disease Control and Prevention (CDC), et cetera, can be very helpful.

We have the fledgling national adverse event (AE) reporting system; we can gather adverse events in near real-time if they're called into the poison centers. We think it can be used to enhance the workplace monitoring and drug trending.

(Slide 23) I thank you very much for your kind attention.

DR. BAYLOR: Thank you, Dr. Bronstein. The next presenter will be Dr. Gordon Smith, Professor of Epidemiology and Preventive Medicine, National Study Center for Trauma, and EMS. Dr. Smith.

Drugs and Trauma Center Patients: What Do We Know About Involvement of Prescription Drugs?

DR. SMITH: (Slide 1) Thank you. I also would like to thank Ron Flegel for inviting us here. He asked us to do a presentation on what's known about the involvement of prescription drugs. I almost felt like titling my slide “not much”.

I really want to show you how some of the work that we've done on illicit drugs and alcohol could potentially be used to develop a system to understand prescription drugs and the injury risks involved.

We are the research unit associated with the Shock Trauma Center, which is the major trauma center in Baltimore, and part of a very organized regional trauma center.

We receive almost 7.5 thousand admissions a year just for trauma. Most admissions are motor vehicle crashes and work-related injuries, with many of them flown in by helicopter from around the state and brought in by ambulance.

(Slide 2) What do we know? Our trauma center has done work in the past to document alcohol involvement. If I were giving this talk 15 years ago with regard to alcohol, I would admit that back then we didn't even know the alcohol involvement in people admitted to the hospital. We have accumulated good data over the years on alcohol and fatalities but not much data on the nonfatal injuries because people weren't tested.

Shock Trauma has a very aggressive alcohol-testing program, and as a result, we know much about alcohol. A big part of our program includes verbal screening questionnaires for alcoholism, such as the CAGE and the AUDIT (Alcohol Use Disorders Identification Test), to diagnose people with drinking problems, and brief interventions to prevent the recurring injury. We have done some interesting studies on the proportion of people who are discharged with an alcohol problem and then end up dead a few years later. Hopefully, we want to reduce that.

Studies have proven the response relationship of alcohol and injury risk. With regard to the other drugs, the evidence is much less convincing. I will discuss that, using data on illicit drugs as an example of how we could move forward on some of these issues.

(Slide 3) As part of our work, we look for alcohol, people with alcoholism, and alcohol abuse diagnoses. We also look for drug dependence in the same studies. In a study that I did with Carl Soderstrom a number of years ago, we asked the question, "What is the prevalence of people with substance abuse disorders coming into our trauma center?" For 18 to 20-year-olds, their lifetime dependence is 24 percent and

their current dependence is 19 percent. These people meet the DSM-III criteria, at the time we did the study, for substance abuse dependence, including amphetamines, cocaine, marijuana, opiates, and phencyclidine. The dependence rate was surprisingly high, which interested us and explains why we are interested in looking at these over time.

(Slide 4) Carl Soderstrom also investigated this incredible increase in cocaine and opiate use by trauma center patients over time. This is based on a large number, 53000, of trauma patients from 1984 to 2000.

Alcohol testing is done in almost 100 percent of our cases. There's the rare case that slips through or something happens to the blood, and it doesn't get tested. All the drug results are based on urine screens. We do detailed urine screens for many drugs on all of our admissions. Some of the cases don't get admitted, are sent home, may not have a urine sample collected, or the specimen doesn't get saved; that's one of the issues in the future we'd like to work on.

(Slide 5) This slide depicts the decreasing trend for alcohol, which is a success story. The alcohol involvement in trauma patients has gone down from 30 to 20 percent over the time period of the study. Unfortunately, there is the increase in cocaine and an increase in the opiates. We don't have more recent data but we are trying to obtain funding to do more data analysis. Hopefully, our funding will be increased based on some of the very convincing data we seen from some of the surveys.

(Slide 6) We have collaborated with Mike Walsh of The Walsh Group on a two-phase study on the involvement of these other drugs. Because of cost limitations, we only tested for a limited number of drugs. Mike Walsh's goal was to evaluate the feasibility of using a rapid test on urine to document drug involvement in various injury types. I have the references for the two publications, which you can to look up yourself

or get copies from either Mike or myself.

(Slide 7) The study involved analyzing admissions to Shock Trauma in Baltimore, which come from all over the state. The key to this study was that only routinely collected specimens from trauma patients were used. We were not specifically collecting specimens for drug testing but instead taking them from the routine clinical specimens. Drugs were tested for in urine, and the blood is used for alcohol.

(Slide 8) In the next slide, we documented that only 34 percent of the people that came into the trauma center were found to have no evidence of alcohol or drugs. The rest of them had either drug only or drug involvement with alcohol.

(Slide 10) We find evidence of these drugs but is it really an injury risk? Our data may provide a snapshot of drug usage in the population, particularly if you do innocent victim-type driver studies with people not involved in causing crashes. In this study, we looked at crash culpability or fault. There are two basic groups of crashes. In one group are those crashes where the person was primarily responsible for causing the crash, in other words, they were at fault based on police officer determination and review by our expert panel of the police report data from the vehicle collision. The other group consists of the innocent victims. For example, you are driving down the road and all of a sudden a huge hole appears in the road and you drop into the ocean; there would be nothing on your part for fault. Or, someone veers over into your lane and crashes into you. The person that veers over into your lane is determined to be at fault, and you are the innocent victim. This innocent victim represents a random sample of the general driving population and can provide some useful information to determine what drugs drivers are on.

The drug testing results were for alcohol, cocaine, and marijuana. Blood alcohol was determined by a blood test, while cocaine and marijuana results were obtained

from a urine specimen.

(Slide 11) One of the problems we have in the trauma center is that sometimes opiates are given for pain relief in the field and also in the immediate resuscitation area. With our electronic capture of the emergency medical services (EMS) record, in the future we can document specifically what drugs have been given and over what time course. Unfortunately, we weren't able to do this in this particular study.

The key to this study is this linkage of the data. Our center is part of the Crash Outcome Data Evaluation System (CODES) study of the National Highway Traffic Safety Administration whereby we can link together the ambulance and the EMS logs, the hospital record data, and the police crash reports for each individual case, allowing us to assemble complete patient records for these estimates.

(Slide 12) For example, in the cocaine positive graph are the results of those who were culpable versus those that were not responsible. For those who were cocaine positive, a much higher proportion was found to be responsible for causing the crash versus the innocent victim. For those who are cocaine negative, a lower proportion was responsible for causing the crash. An odds ratio can be calculated. For instance, if you are urine cocaine positive, you are 2.3 times more likely to be responsible for causing the crash then you were if you had a negative cocaine level in your urine.

(Slide 13) Alcohol is by far the greatest risk for odds of being culpable of a crash - six times more likely for men and almost nine times for women. For the same blood alcohol level, women experience more impairment. Cocaine showed a two-fold increase. Interestingly for urine marijuana positives, the relative risk was one, in other words, no significantly increased risk if you have marijuana in your urine. Since this result is not for serum marijuana bioactive products, it only provides some evidence that you have been smoking marijuana at some time in the past, which is related to how high

the level was and how fast it was cleared from your body.

(Slide 14) What are some of the limitations of this current research? One of the big problems is that of numbers because the rates for each individual drug, particularly with prescription drugs, are low. What is needed is either larger numbers of trauma centers collecting the data over a short time period or just one large center collecting data over a longer period of time. In contrast, alcohol is a single drug, and that's why it's much easier to study.

The toxicology specimens are drawn for the clinical treatment of the patient, not for legal reasons. Thus, we have very high rates of testing for alcohol; but the rates of testing for other drugs is close to 50 percent because it relies on collecting urine samples. It is administratively more difficult to collect urine samples on all admitted patients, particularly those in short stay. We would prefer to do serum drug testing, which I'll talk more about later.

Two limitations for drug testing in urine are: urine doesn't accurately reflect the serum levels at the time of the injury and noting the presence of the drug in urine does not necessarily imply an increased injury risk.

(Slide 15) Most studies are based on the prevalence of drugs only. Quantified serum levels are needed, and there are big debates in the literature as to what are toxic levels and what serum drug level reflects impairment. With alcohol, there is a very clear cutoff level at 0.08 or 80 milligrams per deciliter for impairment in almost everybody. It's much more difficult to estimate risk for drugs. Case control studies are very expensive and very difficult to conduct, and that's why we are doing culpability analysis with regard to motor vehicle crashes.

There is this very high rate of prescription drug use in the population. Fifty percent of the population over the age of 18 took at least one prescription drug during

the previous week. Seven percent took five or more prescription drugs. In estimating risk, the prevalence in the general population must be known. With opiates, about two percent of the population is using regularly, that is, five days per week for six weeks, and 3 percent were using it less frequently.

(Slide 16) This is a slide from a *JAMA* (Journal of the American Medical Association) article showing the use of prescription drugs during the preceding week by age and sex. About 50 to 60 percent of the population has any drug use, and about 5 percent of the population is using five or more drugs. I thought drug use would vary dramatically by age. The elderly are taking multiple drugs, but it was surprising to me how many people in the younger age groups, 18 to 44 and 45 to 64, who were also taking these drugs.

Is drug use putting people at increased risk of injury while driving, particularly with regard to crashes? That's really what I see as an important research question.

(Slide 17) I'll bring this to a conclusion and suggest future initiatives. As I mentioned earlier, we know a lot about alcohol and risk, and screening tests are available. These screening tests are very effective and have led to brief interventions in the trauma center that have clearly been proven to reduce alcohol consumption and also to reduce recurrent injury. There is biochemical testing readily available for alcohol. Patients with high blood alcohol concentrations are immediately referred for alcohol counseling services in the hospital.

For illicit drugs, the whole area is much more unknown. There is some good data on prevalence information, but it's much less complete, and the causal role of injuries is much less clear.

When we come to prescription drugs, even much less is known. The elderly have been shown to be at particular risk from sedating medications, such as

benzodiazepines, and there have been a number of studies showing that the benzodiazepine risk is clearly associated with hip fracture risk and falling, for example, in the elderly. These issues must be kept in mind as we think about how are we going to collect better data on other drug involvement.

(Slide 18) What are the recommendations for studying these drugs in trauma center patients? We clearly need comprehensive data on serum drug levels. Because of the cost involved, one strategy is to do initial urine drug screens, and then perform serum levels for selected drugs. The issue is what are the at-risk levels of serum drug concentrations? When do these drugs actually propose an injury risk as opposed to just a routine therapeutic level? What about interaction with other drugs and alcohol? For instance, for motor vehicle crash risk, if marijuana use is associated with alcohol use, then there is a very significant increase in crash risk. The risk is little less convincing for marijuana only.

What we need are analytical studies to estimate risk. There were some very classic case-controlled studies done for motor vehicles and alcohol. How can we replicate these for some of the other drugs? We've been taking shortcuts in using these culpability studies.

There’s also this whole unknown area about the differences between on- and off-the-job injuries. What about workplace injuries and drug involvement? That's another black box that I'm particularly interested in and doing some follow-up work on.

(Slide 19) We have extensive data systems in Maryland, including police crash reports, the EMS logs, the emergency room data, the hospital records, the statewide trauma registry, our toxicology registry, and the medical examiner data. The medical examiner tests all injury fatalities for alcohol and drugs, including a number of prescription drugs. We would like to see these data sources built into a comprehensive

system to better grapple these issues.

(Slide 20) What opportunities do we have? We need to develop comprehensive testing, including serum drug levels, on all admissions. Admission blood is collected and stored in the freezer until the patient is discharged from the hospital. We need appropriate funding, resources, and the necessary permissions to utilize and analyze these specimens. The results by particular groups would be saved and linked to our trauma registry and the other information.

We also want to utilize the medical examiner data and specimens. We wish to save those bloods to test them for other substances at a later date.

We now have good documentation on the drugs given in the field by emergency medical system personnel. We can link those drugs, as well as any narcotics given for pain relief or resuscitation in the trauma system, to the time of blood collection.

How do we tackle this issue of legal use versus illegal use? We obtain a detailed patient history of current medications. The assumption, from looking at the patient's chart, is that the medications are for legal use because that's the way the questions are asked and that's the way the classic medical history is obtained. We need much more detail in this area of inquiry because we are able to perform patient histories to identify people at risk for substance abuse.

People can readily obtain legal and illegal drugs. We have also done work to specifically target this testing with regard to work injuries. I've just finished a study on how to better identify work-related injuries in the trauma center. We have an established system with research nurses on call 24 hours a day for range of different studies, and they are incorporating work-related injury screening questions. We could also incorporate some of these other measures as well as we go forward.

(Slide 21) The prescription drug issue presents a great opportunity for research,

but unfortunately, we currently don't know very much and so I can't inform on it. Hopefully in the future we will be able to do some more research on this.

DTAB Panel Discussion

MR. STEPHENSON: I'd like to ask a question of the panel. In the context of drug testing in the trauma centers, I have two questions that I don't have answers for or understand what the updates are. What is the relationship to Workman’s Compensation issues and the liabilities that would come up by having such tests done at the nexus, and even if you are able to differentiate work-related versus non-work-related? Second, with the emergency department and reimbursements for medical expenses through the individual’s insurance coverage or through his/her driving insurance, what is your knowledge of the experience regarding cost avoidance by having a clause which says, if these are the result of alcohol or drug use, then the insurance company’s not liable for the expenses? This was a major area of concern years ago, and I don't know whether state-by-state some of those barriers were knocked down or that more people could be courageous like Maryland to identify these barriers and at what cost.

DR. SMITH: This is a very good point. This is a big argument and matter of debate within the trauma community with regard to drug testing because in some states there are real problems with regard to that. Medical bills may not be paid, for example, for someone who is drug-involved.

There are a couple of issues there, one of which is that these tests are not done for legal purposes. They're done as part of clinical care and designed to test, for example, whether someone might have alcohol withdrawal problems or substance abuse issues; they're not actually conducted to legal standards. Clinical drug results are not upheld in court because there's not a chain of custody, et cetera.

Maryland and Shock Trauma have been very good about insurance over the years. Maryland, in particular, doesn't have been an issue with regard to the insurance, and cases are not denied with the insurance company.

Until relatively recently, the data was kept in a confidential database to protect the data. Maryland has solved the lack of reimbursement problem. Whether this is unique to Maryland, I don't know.

DTAB Panel Discussion

MR. STEPHENSON: Thank you very much. Do we have questions from members of the Board?

DR. NIPPER: As one of the previous speakers, Dr. Charlene Lewis, was leaving, I asked her if methadone was considered an opioid for the purposes of her talk. She said, “No, it wasn't, because methadone,” and this is a direct quote, “gummed up the data.”

I agree; methadone does gums up the data. It points out a problem that we are not all talking on the same page here. For example, in Nebraska, methadone has risen to the top as one of the major drugs found in our postmortem toxicology testing as a cause of death. And yet, we don't know a lot about it. I’m suggesting that one of the things that may arise here, and which has been alluded to by others, is the need for talking the same language, listing the same things, and thinking about drug tests as not just being point of collection (POCT) but as reliable toxicology data that are confirmed. There’s a need for standardization among the different agencies and groups.

MR. STEPHENSON: Any responses?

DR. SMITH: Certainly, in the medical examiner data are fatality cases with drug involvement. I wish we had that same quality data on the injured patient, for example, in

Shock Trauma. And I agree with you. It has to do with the money. One of my hopes and goals for me in the future is to raise funds to at least analyze certain groups, such as motor vehicles drivers, injured workers, and other particularly high-risk groups.

MR. STEPHENSON: There will be an opportunity to explore more about this because we are blessed by having a very good working relationship with CSAT, the Poison Control Centers, the CDC, and others that have dealt with overdose deaths and issues specific around methadone-related deaths and accidental poisonings.

We can discuss that later with Dr. Clark and at other discussion opportunities. It is an area of concern, and it's a part of the total picture. We're are trying to catch the full spectrum of prescription drug issues, and we'll worry about what the image is a little later, once we've gathered as much light as we can.

DR. BUSH: We must address analytical issues to parse out exactly what are we analyzing for and what are we capable of detecting test by test to assist that doctor in the emergency room (ER) who is saying, "I need to test for opiates and all kinds of prescription medicines that may be opioids". We come up short in many ways because of the available technologies and the capabilities of the laboratory.

MR. STEPHENSON: What a wonderful set of presentations we've had this morning. We are on time.

DR. BUSH: To each and every one of the speakers, thank you for taking the depth and experience that you have, distilling it down to 20 minutes, and giving us the best of the best.

MR. STEPHENSON: Yes.

DR. BUSH: Since we have no further discussion, it is 12:11 and we are scheduled to close the meeting at 12:15. We will close four minutes early to break for lunch. So officially, this session of the Advisory Board is closed. We will reconvene

here, same place, at 1:45. Your next speaker will be Dr. Wes Clark.

There are local restaurants for lunch. Should you need assistance, one of the Federal employees here will guide you and help you find a bite to eat. Thank you and see you back at 1:45.

(Whereupon, a luncheon recess was taken at 12:11 p.m. to reconvene at 1:45 p.m.)

A F T E R N O O N S E S S I O N (1:48 p.m.)

DR. BUSH: At this time, I'd like to reconvene and open up the session of the Drug Testing Advisory Board for this afternoon. Thank you.

MR. STEPHENSON: Our first presenter this afternoon is H. Westley Clark, MD, JD, MPH, CAS, FASAM. He's the Director of the Center for Substance Abuse Treatment, and as that, he leads the Agency's efforts to provide effective and accessible treatment to all Americans with addictive disorders. Dr. Clark's areas of expertise include substance abuse treatment, methadone maintenance, pain management, co-occurring substance use, and mental health disorders, all of the issues related to the variety of both medical and legal issues.

He is a wonderful advocate for many of the things we do in the workplace area. He's one of our heroes and has worked as a mentor and a colleague in these tough areas for years. Dr. Clark, thank you for presenting to us.

Prescription Drug Pain Management, Addiction, and Opioid Prescribing Practices

DR. CLARK: (Slide 1) You're welcome, Bob. It's always a pleasure to talk to such an impressive group. The issues that we're discussing are of critical national importance, both from a regulatory point of view and a clinical point of view.

(Slide 2) I like to start off my presentation with a quote from the President, who states that, “Alcohol addiction and drug addiction continue to challenge our Nation. An addiction to alcohol and drugs destroys family ties, friendships, ambitions, and moral conviction and replaces the richness of life with a single destructive desire. “

(Slide 3) The issue for us is that each year millions of patients in the United States are treated for a variety of serious medical problems related to prescription medications. Non-medical use represents a relatively small percentage of all the uses of these medications, but it is a problem that requires attention.

From a regulatory point of view, many people would like to believe that there is no pain and thus forget about pain management and clinical management. I can see a few gray hairs out there in addition to my own, and if you get up in the morning like I do, you realize that pain is a real phenomenon. This is not simply about public safety; it's also about public health.

(Slide 4) At the policy level, SAMHSA works to ensure that science, rather than ideology or anecdote, forms the foundation of our nation’s addiction treatment system. It's important for us to work together at the Center levels. The Center for Substance Abuse Prevention, which we've been working with; the Center for Mental Health Services because when we’re dealing with prescription opioid use, with prescription medications, and also with mental health phenomenon; Office of Applied Studies; and others within the organization are trying to promote the larger public health.

(Slide 5) Psychotherapeutic, principally pain, medications are the second most commonly abused substance. When used legally, they are therapeutic drugs. When used illegally, they become illegal drugs. Are we dealing with therapeutic misadventure, practitioners who mean well but don't have a clue, or people who misuse the medication?

(Slide 6) Alcohol is also an issue, which is not something that people commonly discuss when they're talking about pain management or prescription drug use. About 57 million people, or 23 percent of the population, admit to binge drinking, which is five or more drinks on a single occasion, and about 17 million people are heavy drinkers, having five or more drinks on a single occasion in the past 30 days. From overdose deaths, it is known that alcohol combined with benzodiazepines or opiates can be fatal.

(Slide 7) There are regional variations in pain relievers. The Office of Applied Studies looked at state-by-state or jurisdictional variations in the use of pain medications. Some jurisdictions have a higher prevalence rate than others. It doesn't minimize the problems in any specific jurisdiction, but it does raise the issues of the culture of communities and healthcare disparities. In a presentation in Montana from Healthcare Service, it was noted that a health plan approved pain medication in lieu of elective hip replacement surgery because it cost roughly 300 to 400 dollars a year to prescribe the pain medication where it might cost anywhere between 3,000 to 30,000 dollars for the surgery. To use pain medication as a therapeutic alternative creates a health disparity issue.

We are not dealing with just drug testing here. We are also dealing with decisions made by the healthcare delivery system to use prescription medications as an integral part of health allocation strategy.

(Slide 8) I've already pointed out the past month non-medical use of prescription drugs. In 2006, 2.1 percent of the population, age 12 and over, misused pain relievers for non-therapeutic use. These data point out that this is an ongoing, continuing problem. We need to do something about it, but we also need the resources to ensure that the strategies we employ are carefully crafted and not just instrumental strategies

that may cause more problems than they solve. The unintended consequences are issues that we need to address. Pain relievers are of major importance.

(Slide 9) In this slide on the estimated number of new non-medical users in the past year by type of drug, pain relievers began to increase over other substances around 1995 and have increased quite rapidly. The full reason for this increase is not clear, but clearly it's an issue. Dr. Madras suggested that some people feel that prescription drugs were better, purer, and easier to obtain. Indeed, we started asking questions.

(Slide 10) It is purported that the Internet is a source for prescription opiates, and while it plays a role, it plays a fairly minor role. People obtain pain relievers from the medicine cabinet. From a health disparities point of view, it is understandable. You go to the doctor, and the doctor gives you 14 days of pain medication. It turns out you only needed 3 days of pain medication, but you paid for those 14 days of pills. When was the last time you threw away money? If people see the pills as synonymous to money coming out of their wallet, they'll loathe discarding those pills, and so they keep them. They forget about them because, after all, they're not suffering now, and the pills sit. When a visiting neighbor, a friend, or a child sees this bottle of pills sitting there that is not being used, they remove the pills, and nobody even notices.

Where are these diverted prescription medicines originating from? According to our household survey, they are obtained from one doctor; it is not large-scale doctor shopping.

Why does the doctor prescribe it? For therapeutic reasons. What's the doctor's logic? A patient presents with a pain problem. How extensive is the problem? Well, it's an art form. If I prescribe a one-week prescription and the person comes back the second week, the insurance company says, “We don't want to pay you for two visits.

You just saw the person last week, why didn't you give them a two-week prescription?" I learn to write a two-week prescription even though the patient only needs one week. What do they do with the other week's worth of pills? It's that dynamic that we have to think about.

(Slide 11) Stimulant prescriptions increased seven-fold since 1991. Opioid prescriptions increased four-fold. Like the cartoon says, "We just don't tell you to starve a cold these days; we can prescribe an appetite suppressant for it."

The practice of medicine is changing. We use medications as an integral part of treatment. To the extent that our society encourages that, this becomes a cultural phenomenon. We need to be careful about stigmatizing behavior unless we're going to mount campaigns to educate practitioners.

(Slide 12) From our DAWN data, a number of medications, including methadone, hydrocodone, oxycodone, and buprenorphine, show up on the radar screen, in addition to illegal drugs like heroin.

(Slide 13) Poisoning deaths are a major issue. We have increased methadone poisonings. We attribute these poisonings to the misprescribing of methadone for therapeutic purposes and the increase in the use other opioids and other synthetic narcotics.

(Slide 14) The Federal Government is very interested. We are confronted on the Hill during Congressional hearings. There's pressure on FDA, DEA, NIDA (National Institute on Drug Abuse), and others to restrict drugs, using either FDA laws or the Controlled Substances Act. They want restrictions placed on practitioners through Federal laws and regulations.

There was a discussion, for instance, about reclassifying the schedule three combination narcotics. The doctors ask, "Okay, if you get rid of the schedule three

medications like Vicodin, then what will I do for pain?” Schedule two narcotics will be prescribed instead, and now we don't have a gradation of therapeutic options.

In the testing arena, we play a critical role. We know that state governments regulate medical practice, and there are a number of state laws that govern the use of controlled substances by physicians, pharmacists, nurses, dentists, and veterinarians.

(Slide 15) In the great state of California, a physician can be sued for not treating pain. The practitioner is confronted with that conundrum. Healthcare providers treat about 191 million Americans at least once every two years. Physicians are in a unique position to prescribe needed medications, to encourage compliance, and to identify problems as they arise. Unfortunately, this doesn't happen with the modern patient who has 15 minutes to work with his practitioner, provided you even see your practitioner. These are the systemic issues that, as we address the problem, we need to make sure that we're addressing also.

In a purely instrumental approach, we would say banish these medications. Anybody has allergic rhinitis or a common cold and had to go get some pseudoephedrine? You have to sign away your life to get the Sudafed, and that's a slight exaggeration. Only a small number, less than one million, of people use methamphetamine, which is a very dangerous, horrible drug. Over 50 million people have allergic rhinitis or get the common cold. Now there is a law that says you can't have access to Sudafed-containing products without a signature. In fact, drug companies have pulled away from using Sudafed.

The problem with policymakers is that they feel the need to do something, and so they do something. The unintended consequence is that phenylephrine doesn't work that terribly well, according to the literature. So, sick people are sniffling, wiping their runny noses on their palms, and then contaminating you by shaking your hand because

we're afraid of methamphetamines. We should be afraid of methamphetamine, but should we pursue solutions that in fact endanger the public health in our zeal and thus produce unintended consequences?

(Slide 16) We have to adopt appropriate strategies. There is the problem with prescription drugs acquisition. About 4.8 percent of the people age 12 or older uses a prescription drug non-medically. That's a large number of people. Of those 4.8 percent, 57.7 percent used hydrocodone and 21.7 percent used oxycodone products.

These products are available for use because people do suffer pain. Practitioners have a difficult time gauging the patient’s degree of pain. In fact, patients have a hard time gauging how much pain they’re suffering. When pain wakes you up in the middle of the night, you want a solution.

(Slide 17) We have addressed the issue of methadone-associated mortality in several meetings held in 2003 and 2007. There have been inadequate resources because of competing interests to address this in a systemic way, so we're using available resources in the best possible way we can.

We noticed the increased use of methadone for the treatment of pain. Because the unintended consequences of the mass media addressing OxyContin, a number of practitioners started withdrawing from the use of OxyContin and prescribed methadone instead. Health plans discovered that methadone is much cheaper than OxyContin, providing an added benefit. Doctors are afraid of OxyContin, and methadone is dirt-cheap. Methadone costs $0.58 a pill versus $10 for a OxyContin prescription.

Healthcare professionals and consumers need to be educated about the dangers of misusing prescription medications. SAMHSA’s Office of Communication had a program addressing disposing of and safeguarding prescription medication to reduce potential misuse. These efforts involve the consumers, and we want to make sure we

involve the consumers. Health plans must also involve the consumers because the consumers can play a critical role.

(Slide 18) We had a meeting to discuss Fentanyl-related overdoses and deaths. The drug dealers were using Fentanyl to cut heroin and/or the cocaine. Part of the epidemiology of substance misuse is the drive to alter mind and mood can be really overwhelming, particularly for young people. Young individuals, especially teenagers, are using “cheese” heroin, which is heroin cut with Tylenol PM.

We've focused on treatment strategies for prescription drug misuse and abuse. As part of an initiative, a curriculum was developed for emergency medicine and trauma surgery residents on Screening, Brief Intervention, and Referral to Treatment (SBIRT). Also, a training program on prescribing controlled substances was developed. Early in the process, we did have physicians who felt a little grandiose about what it is that they needed or didn't need. We suggested more training on abuse, and that was resisted by organized medicine.

(Slide 19) Our hope is that with meetings like this, we can form more cooperative partnerships with organized medicine, including pharmacy, to address these issues in a responsible way. We had an open dialogue meeting with the pharmaceutical industry, and the pharmaceutical industry is very interested in developing rational strategies, even though they may have a profit motive. There is a demand for the products, and the demand is secondary to our aging population.

The US population is aging. As a result, there will be more structural problems, and thus we will need good rationale. We had buprenorphine summits to get practitioners to recognize that they may need alternative strategies. We've had a difficult time convincing primary care practitioners to adopt the use of buprenorphine as a way of dealing with prescription drug abuse. There are over 500,000 ambulatory care

practitioners in this country, but only 15,000 physicians who have the eight hours of training necessary to prescribe buprenorphine. That's a problem. To address this, we are working the Prescription Action Alliance, which is a consortium of addiction experts, medical societies, and others; an advisory committee on the non-medical use of stimulant drugs; and the National Association of Drug Diversion Investigators.

(Slide 20) SAMHSA is just one of the many partners necessary to address these issues. SAMHSA controls methadone by regulating and certifying the treatment programs. This is our entry into the dialogue regarding methadone clinics getting implicated as the cause of the methadone diversion problem. We worked with state authorities to investigate. We discovered that it wasn't a methadone clinic problem. It doesn't mean that some methadone is not diverted; some methadone is. Methodone is prescribed to a high-risk, vulnerable population. We know that some people will engage in risky or illegal behavior. In the aggregate, this is about the misprescribing of methadone.

The DEA ensures medication security with regard to methadone. We at SAMHSA set the treatment standards and the requirements. We have an independent oversight with standards that are helpful to treatment. (Slide 21) We require accreditation of all methadone programs. There are accrediting entities, including Joint Commission on the Accreditation of Healthcare Organizations (JCAHO), the Commission on Accreditation of Rehabilitation Facilities (CARF), two states (Missouri and Washington), and the National Correctional Health Care Commission. (Slide 22) When we see data on methadone-related deaths as a percentage of all poisoning deaths, we become very alarmed.

(Slide 23) We need a more concerted effort because the draconian solution, as with Sudafed, is to ban or limit access to these things, which then adversely affects the

general population. We know the total prescriptions dispensed in outpatient retail pharmacies for methadone by strength increased over time. For instance, the 10-milligram pill increased more dramatically than the 5-milligram or even the 40 milligram dose. That's consistent with our belief that methadone is being used in non-methadone treatment, outside the methadone treatment clinic model.

(Slide 24) For pain treatment with methadone, there is no required risk management plan. The FDA modified the labeling in 2006, and the DEA added some voluntary restrictions on distribution of the 40-milligram dose.

We are working with the treatment community and with the regulatory agencies to come up with incremental strategies. With regard to addiction and dependence treatment, distribution is limited to certified, accredited, and registered programs. There is an initial dose limit. There are restrictions on dispensing. That doesn't mean that there are no problems, particularly when it comes to the pain treatment community, because methadone, when used for pain, is exempted from these regulatory devices. That's one of the conundrums. It's like buprenorphine. If you use buprenorphine for pain, even though it's not FDA-approved in the combination drugs, it is exempt from the regulatory reach of SAMHSA and the FDA.

(Slide 25) We convened a multi-disciplinary group in 2003 whose goal was to determine whether opioid treatment was a problem. Our conclusion was that it wasn't, based on their assessments. We are formulating recommendations to reduce mortality. We do know that there are some cardiac events secondary to the initiation of methadone treatment, and we're working on proposals to make recommendations about that.

(Slide 26) We also noted that when it came to methadone mortality, that there was an absence of uniform case definitions. That should be corrected. There should be

standards for toxicological testing, more useful data, and better training for healthcare professionals in addressing pain and addiction. This is a key construct. We do need to spend some resources as a society on making sure that people are aware of how to use pain medications, what to do with them, how to store them, and how to treat with them.

As a corollary, people place guns in locked boxes. We don't do that with very powerful narcotics, which can achieve the same end - people get killed. We want to address misperceptions about methadone, and we need public policies that need to respond to multiple needs.

(Slide 27) We are also concerned about the lack of reporting accuracy. We convened medical examiners, epidemiologists, and other experts to examine how methadone-associated deaths were classified. These are things that indeed have some impact on prescription drug abuse in general. Because prescription drugs are associated with mortality and morbidity, the question is, “How do they get there and how are people using them?” Based on our data, most people are getting them from the medicine cabinet.

Indeed, we have policies that discourage the diversion of prescription drugs; doctors are arrested for misprescribing. There are pharmacists who are arrested for misdispensing. Kids use the Internet, not to requisition drugs, but to understand which drugs to get from the medicine cabinet. Do I steal the diuretic or this pain reliever? On the Internet, I can find out that information; it's a wonderful source of information and disinformation.

The Internet is a lousy source of information for pain management. Many of the websites are inadequate. We should not abandon the Internet, but in terms of patient education, we must promote responsible websites and responsible information so that

we can address these issues.

(Slide 28) We need multiple sources of data to monitor methadone trends. The same is applicable to prescription drug use so that we can provide an accurate characterization of the issue. We commissioned independent epidemiologists to monitor data and perform special studies for methadone-associated morbidity and mortality, and we have an information specialist systematically tracking and evaluating published reports. On Pub Med and in published articles is a wealth of information about prescription drug abuse and pain management. Does the busy practitioner ever access that information? If it takes me three years to discover that I've been misprescribing or that I should've done something differently, then in the meantime, many patients will have had problems.

(Slide 29) Our recommendations include educating healthcare professionals on how to use methadone. The same is applicable to pain medications. I graduated from medical school back in 1973 when every drug was the same as any other drug, and there was no discussion about the misuse of pain medication. My hope is that younger doctors are learning radically different things, but that is not the case. The American Association of Medical Colleges (AAMC) told us that there’s so much competition for a place in the medical school curriculum.

If we don't do something now, as with Sudafed, the policymakers will do something because they don't know what else to do. When asked why they put a two-week limitation on Sudafed, they referred to the package insert that stated that only two weeks is needed, and therefore, a person only needs a two-week supply. People living in rural areas buy a month’s supply of medication because it's not only cheaper but it's also more convenient. We didn’t think about that because a 22-year-old who majored in political science is making decisions about who should get access to medications. This

isn't an ageist assertion. Policymakers, when presented with a threat and a challenge, will act out of necessity, and the decision they make is influenced more by the threat and the challenge and less by clinical and epidemiologic information.

A part of the needed education is a treatment protocol. We have sponsored workshops and symposiums on methadone, and we've hosted summit meetings. We offer achievement programs. We've developed a computerized patient intake questionnaire, and we're developing continuing medical education (CME) courses on the use of methadone to treat pain.

(Slide 30) We offer physician education, four to eight hours of CME, on: problems with patients who are prescribed opioids for persistent pain; whether or not to prescribe an opioid; the pharmacology with an emphasis on methadone; the steps to take if opioids are used in the treatment of persistent pain; the steps to take if opioids are not used in the treatment of persistent pain; the practical side effects of patient monitoring, including a prescription monitoring program, screening, lost prescriptions, et cetera; and when, why, and how to stop prescribing opioids and manage the patient with another treatment approach.

(Slide 31) We also offer this opioid prescribing CME that we planned with the State Medical Society. The program was test piloted it in Ohio and Virginia and then offered it in West Virginia, Massachusetts, Connecticut, and North Carolina. We hope to integrate it with other online courses and tie it to registration renewal. This is a policy decision that the system is thinking about, but no one has actually acted on it. The Hill is contemplating whether doctors must take continuing education to prescribe these very powerful drugs because there is an epidemic of deaths associated with them. We had some resistance from organized medicine, and our hope is organized medicine will cooperate and come up with some reasonable strategies that don't encumber the

practice of medicine, pharmacy, or nursing but at the same time take into consideration the problems associated with misprescribing and overdose deaths.

(Slide 32) We have promoted office-based opioid treatment. We've certified some 15,000 physicians out of the over 500,000 US ambulatory care doctors to use buprenorphine. About 57 percent of these are listed on our buprenorphine physician locator. We've trained almost 22,000 doctors, and we have 2,500 doctors who have indicated their intent to treat up to 100 patients each.

(Slide 33) There has been an increase in the number of patients that fill prescriptions for Suboxone, which is buprenorphine and naloxone, and only a small increase in Subutex, which is buprenorphine hydrochloride.

(Slide 34) We are training within medical schools and residency programs to address the issue. We will be announcing a medical residency education grant program; the results of our funding will be available sometime in the next three or four weeks. We want organized medicine to deal with this, so we've provided funds, $300,000 a year for five years, to selected residency programs to facilitate screening, brief intervention, and the use of pain medication. We're using the pain management and addiction vehicle to get this information across about managing patients with pain conditions who are addicted to opioids. We’re also using adverse events reported to emergency rooms and poison control centers.

We're concerned about diversion, not only about buprenorphine diversion, but diversion of other prescription drugs as well. There are a number of prescription drug-monitoring programs, including the Rogers program, jurisdictional programs, and the National All Schedules Prescription Electronic Reporting (NASPER) that we are authorized to do, but we were not given any money for. NASPER is one models of how we can obtain information from practitioners. Unfortunately, it is not real-time as it's

currently constructed. Real-time regional prescription drug monitoring at the pharmacy site is needed to provide information on practitioners who are misprescribing as well as information on clients or patients who are on multiple prescriptions. This is consistent with a system that is moving towards electronic health records and electronic prescribing. A NASPER-like system is a program that fits very nicely into what the system is saying it wants to do anyway.

(Slide 35) We are actively involved in resolving cases where medication interactions occur. Many programs now have policies about patients on methadone and benzodiazepines; the same is applicable to buprenorphine. This logic needs to extend to prescription opioids and benzodiazepines. There are considerable resources being devoted to resolving the false positive laboratory results from combination drugs.

(Slide 36) We recognize that buprenorphine, just as any other prescription opioid, has the potential for abuse. Buprenorphine is unique in the sense that more than one-third of the abusers reports that they took the drug in an effort to self medicate and to ease heroin withdrawal.

One health disparity issue is that many patients are unable to use buprenorphine because they don’t have a physician who has completed the required eight hours of training. This is eight hours; it's not 80 hours, eight days, eight weeks, eight months, or even eight years. It’s eight hours. For instance, MRO training to certifying people to interpret five drugs is 2.5 days. What about all the other drugs? Well, you don't need any additional education. That's a problem. We know that it can be abused, and we're working with the states to deal with it.

There are physicians that consider Subutex easily abused, but only six percent consider Suboxone, which contains naloxone in it, to be an abuse threat, but it does happen. If it can be abused, it will be abused. As a psychiatrist, I discovered that you

could buy Haldol on the street. If somebody is willing to divert Haldol, he is willing to divert anything.

(Slide 37) One reason for diversion is lack of physician access. Another is the financial barriers that prevent people from obtaining prescriptions from their physicians, the same financial barriers that are militating toward writing prescriptions that are larger than necessary. The insurance companies don't want you to see the doctor every week; they want you to see the doctor maybe once a month and have the doctor give you a bottle full of pills. That bottle full of pills sits there.

Patients are selling their buprenorphine to others dependent on opioids and may not hesitate to sell their drugs to non-opioid dependent users. These social and behavioral factors that contribute to diversion are applicable to other prescription opioids as well.

(Slide 38) Lax or inappropriate prescribing of a drug by physicians may be an issue, such as with Suboxone. Seventeen percent of doctors felt that some physicians were a bit cavalier. More than half the doctors questioned in New England, where Suboxone was most widely available as an addiction treatment, believed it was just as easy to buy illegally as methadone or other widely abused narcotics.

(Slide 39) This slide shows the average pill size of a retail prescription dispensed for buprenorphine. (Slide 40) With regard to buprenorphine, when we asked a high-risk population, i.e. individuals who are already addicted to drugs, in the past 30 days, how many days did you get drugs on the street? The baseline on entry was 13 days. Within 30 days, it dropped to 0.10 days, and at a six-month follow-up, it crept up to 1.72 days. People misuse opioids for many reasons, but it did have a positive benefit; there was a substantial reduction in street buying. (Slide 41) When we asked about the percent of patients acquiring drugs on the street, the baseline was 67 percent, which dropped to

four percent, and then crept up to 20 percent again. We are dealing with vulnerable people.

Whatever strategies we develop, we need to understand there will be people who like getting high, like being high, and will use whatever devices they can to get high. We don't want those individuals who legitimately need pain medications, specifically, prescription opioids, to be denied access to those pain medications. Many individuals have legitimate needs for prescription pain medications.

(Slide 42) When asked in the past 30 days, “Were you involved in any drug dealing, prescription fraud, or other crimes?”, there is a substantial reduction. Even addicts can behave responsibly if given a healthcare context that will permit it. Of course, there will always be somebody who wants to test the limits of the universe, but that happens regardless of whether you are prescribing the drugs legally or not.

(Slide 43) For the risk management of buprenorphine, the key elements of the FDA risk management program for monitoring abuse and diversion of buprenorphine include physician surveys, patient reporting, substance abuse treatment centers, Internet user groups, poison control, DAWN, and ethnographic studies. These elements are necessary for any strategy developed to deal with prescription drug abuse, particularly the opioids.

(Slide 44) You heard about SAMHSA’s Smart Rx prescription disposal. We need to continue getting these messages out because we have a high percentage of teens and young adults reporting that they have ready access to someone else's prescription from the family medicine cabinet. The Smart Rx recovery program addresses that.

(Slide 45) Smart Rx is having an impact and is helpful, but it's not a panacea. Whatever strategy we design, whether it is drug testing as an integral part of a strategy or whether it’s smart prescription disposal, it has to be comprehensively holistic. We

need patient, physician, and nursing and pharmacy education so that we can address these issues.

(Slide 46) We want to expand our training materials, which were developed through a blending initiative with the National Institute on Drug Abuse. This initiative is a unique partnership that uses the expertise of both agencies to apply research results, so we can improve treatment on substance abuse disorders. (Slide 47) CSAT addresses treatment, but we also realize we need to work with our partners at CSAP.

For buprenorphine, we created a Physician Clinical Support System (PCSS) in collaboration with the American Society of Addiction Medicine (ASAM). This is a free national service, staffed by 45 trained physician mentors, a PCSS medical director, and five physicians who are national experts in the use of buprenorphine. Physicians who prescribe or dispense buprenorphine can contact the PCSS for support via telephone, e-mail and/or at the place of clinical practice. These are the kinds of strategies that we need for prescription opioids, so that, indeed, a practitioner who is uncertain can consult with a qualified professional so that they can make decisions appropriately. This type of a service can be used for prescription opioids and other prescription drugs.

(Slide 48) We are developing strategies on therapeutic and non-therapeutic use of prescription drugs of abuse. We published an advisory and a treatment improvement protocol. These are free documents that we promote to outreach to practitioners in the field.

One of the problems with any kind of document is that practitioners are busy. I don't know how many of you have dusty journals. The dusty journal syndrome. You have all these wonderful journals. You look at the table of contents, and there are these wonderful articles. Maybe you get to read one or two; you're planning to get back to the others, and you don't. Then there are some journals that you never crack.

We need to change people's behavior. That is why we want CME and on-line courses to be are made mandatory.

Practitioners need to realize that a lot is at stake, especially how they are perceived by clients and patients, how they are perceived by the larger society, and how they can conduct their business as physicians, nurses, nurse practitioners, pharmacists, and others, including dentists, and in some jurisdictions, psychologists. This is a public health problem that requires comprehensive solutions. We all need to be actively involved in pursuing those solutions, but we failed to do that. We wind up in the Sudafed situation because we didn't deal with it. Now our 22-year-old person just out of undergraduate school with bachelors in political science will draft the legislation. If I were that ambitious 22-year-old just out of undergraduate school with a bachelor's in political science, I would draft the legislation the best I possibly can. It's not a criticism of that person, but a criticism of us as licensed practitioners reluctant to deal with reality. If we don't deal with reality, others will. Thank you.

MR. STEPHENSON: Are there any questions from the members of the Board? This whole issue is so important to look at. The aspect of what we are talking about with testing from the perspective of the other half of the whole system is appropriate use for medically indicated, properly dispensed and utilized medications by people in need. If we don't do that consistently with messages and policies, like Dr. Clark has suggested, then we are going to all regret it at some time in our own individual futures. It's up to us to look at the complex issues and deal with them realistically. Thank you very much for bringing that message.

Pharmacogenomics of Addiction

DR. HARPER: (Slide 1) Hello. My name is Courtney Harper, and I'm from the

Food and Drug Administrations' Office of In Vitro Diagnostics. In our office, we not only regulate drugs of abuse tests, but we also regulate genetic tests for pharmacogenetics, including genetic tests for drug metabolizing enzymes.

(Slide 2) Thank you for inviting me here today. I will present a brief overview of pharmacogenomics and relate that to drug abuse and addiction. I will also relate it to the idea of personalized medicine, which is an initiative of the Department of Health and Human Services. I will provide you with a couple of resources we have at FDA if you want more information about pharmacogenomics to relate it more to individual questions.

(Slide 3) Some of the confusion that people have around terms such as pharmacogenomics is that there is a lot of terminology out there that sounds very similar. This may be confusing to people who don't have a background in genetics or genomics. First, I just wanted to clarify some terms.

What are pharmacogenomics and pharmacokinetics? Pharmacogenomics is the overarching term for the application of genomes, which contain the person's genetic information, whether that is a person's DNA, the translator RNA, or the protein that comes out of the person's DNA, to the study of the variability in drug response. When we talk about pharmacogenomics, it often gets narrowed down to just the DNA, just the RNA, or just the proteins. For example, for the proteins, they'll refer to proteomics or metabolomics. For just the DNA, which is what is encoded in your own personal genome, they often use the term pharmacogenomics. When you hear those two terms, remember that pharmacogenetics is a subset of pharmacogenomics, but really, the study of those two fields is very similar.

Pharmacogenetics is the effect of a person's own DNA sequence on how they respond to drugs, including drug disposition, safety, how they tolerate the drugs, and

how efficacious the drugs are for them. A person has a single genome that he/she is born with and that genome encodes genes. Some genes encode for enzymes, and the enzymes perform certain functions.

Somebody with blonde hair versus somebody with brown hair has a genetic trait that is visually identifiable. You can see that somebody with brown hair has a different genetic profile than someone with blonde hair. This concept also translates into clinical medicine. There are certain genetic diseases where you can see the genetic difference, such as Down's Syndrome in which a person has an extra chromosome, and you can identify that person physically.

With pharmacogenomics and pharmacogenetics, though, people do have individual differences in the genes that encode enzymes related to drug disposition and drug pharmacodynamics. Unfortunately, you can't tell by looking at them what the gene differences are. This is difficult for physicians who are evaluating a person for drug therapy to determine the pharmacogenetics of that individual without specialized testing. Outwardly, a person may look like anyone else, but inwardly he/she may elicit a very different response to the same drug at the same drug dose.

(Slide 4) Pharmacogenomics testing is meant to detect inter-individual genomic variations. These variations, which aren't physically apparent, might affect the way drugs are absorbed or disposed, which is pharmacokinetics, or they also might impact the way that the drugs act on the body, which is the mechanism of drug action.

Today I will mostly speak about pharmacokinetics. I will focus on the drug metabolizing enzymes, but note that the genes involved in how a drug actually causes its therapeutic effect also are in this realm. This includes the genes that encode for proteins that transport drugs across membranes and the proteins that transport the drugs into the cells to their sites of action. It also includes the genes that code for co-

drug metabolizing enzymes, which break the drugs down from parent drugs into metabolites; drug receptors; and other proteins related to drug action.

(Slide 5) For pharmacokinetics drug metabolism, there is a group of enzymes called cytochrome P450 enzymes that are responsible for most of the drug metabolism occurring in patient livers. There are 57 different active genes in this group and 17 different families of genes. What can be confusing about the drug metabolizing enzymes in this family is that they are named very similarly; they're all called CYP followed by a number and then letters which represent the position of each gene in the genome. Each of these enzyme names with different letter or number combinations represents a different gene that encodes for a different enzyme that metabolizes the drugs differently. Each of these genes has overlapping specificity for certain drugs, but they also have individual responsibility for being primary metabolizers for clinically important drugs.

The reactions that they catalyze are varied, such as oxidation or hydroxylation of different drugs. The different enzymes, when reacting and binding to different drug classes and drug types, carry out these different functions.

(Slide 6) To give you an example, in someone with normal enzyme function, they will ingest a drug, such as dextromethorphan, and metabolize it via a primary metabolism pathway. In this case, dextromethorphan is primarily metabolized by cytochrome P450 2D6 (CYP 2D6) to yield the different metabolites of the drug. The reaction is driven in this manner because this reaction is more favorable than the reaction with CYP3A, which is still metabolically required further down in the pathway.

(Slide 7) When the CYP2D6 enzyme is somehow not functioning, that individual will have a build-up of the parent drug. Even if that person were to utilize the alternate metabolism pathway with the CYP3A enzyme, CYP2D6 is still required for the

secondary metabolism step. The parent drug accumulates as does certain metabolites that are different from the metabolites that normally build up. This is the manifestation of having a functional deficiency for this particular enzyme.

(Slide 8) With a genetic anomaly that causes a variation in enzyme function for a metabolizing enzyme, there are terms that are used, and these terms aren't necessarily intuitive. A person who is normal metabolizer is referred to as an extensive metabolizer. The extensive metabolizer has a normal gene on each of his/her two chromosomes, and so they have two normal copies. Extensive metabolizers represent the majority of the population.

With no functional enzyme, either the enzyme is absent because of a genetic variation that causes no enzyme to be synthesized or the enzyme that is present is nonfunctional. These individuals are called poor metabolizers.

In the intermediate situation, creatively called intermediate metabolizers, individuals have one functional and one nonfunctional gene. These people still metabolize the drugs, but since they have fewer enzymes than an extensive metabolizer, they may do so at a slower rate.

There are people who have duplications of the genes in their genome. Instead of having only two copies of the gene, they may have upwards of 20 or so copies of a single gene. These people have extra enzymes in their cells and are called ultra-rapid metabolizers.

(Slide 9) s I will present scenarios to illustrate poor and ultra-rapid metabolizers. In one scenario, which is the most common one, an active drug is inactivated by metabolism. Diazepam would be one example of that, whereby diazepam is the active drug, and when metabolized, it becomes inactive and cleared from the body.

With a poor metabolizer for CYP2D6, there is very good efficacy from diazepam

because the active parent compound remains in the body for a very long time. Accumulation of active drug may cause adverse reactions. A patient may be overdosed because the physician does not realize that the patient is a poor metabolizer. The patient may require a lower dose to achieve the same effects because of the build-up of the active parent drug in his/her system.

In the case of an ultra-rapid metabolizer, poor drug efficacy results because the active parent drug is rapidly metabolized and cleared from the body and so doesn't have time to achieve its full effect. With ultra-rapid metabolizer, the doctor may decide to give an increased dose of certain drugs to compensate for the fast metabolism.

(Slide 10) Another scenario is the pro-drug situation, whereby the parent drug is not the active form and needs to be metabolized into the active form. Codeine is a very good example of this. Codeine is metabolized by cytochrome P450 2D6 into morphine, which is the analgesic compound. For a poor metabolizer, drug efficacy is poor because the codeine is not metabolized into morphine very effectively. These people experience poor analgesic effects from codeine, and often codeine accumulates in their bodies. For the ultra-rapid metabolizer, efficacy is very fast and rapid, and thus may not last as long because it's cleared from the body fairly quickly.

(Slide 11) Here’s a case study related to being non-wild type CYP2D6 metabolizer of codeine. Remember, codeine is a pro-drug metabolized by CYP2D6 into biologically active morphine. This is also true for other prodrugs, such as oxycodone and hydrocodone.

(Slide 12) Ultrarapid metabolizers appreciate their analgesic response to codeine. However, there may be problems with ultra-rapid metabolizers. About a year ago there was case report about the death of an infant being breast-fed by his/her mother who was prescribed codeine. Upon investigation, it was learned that the mother

was an ultra-rapid metabolizer and had extra copies of this particular enzyme. On a standard dose of codeine, the mother rapidly metabolized the drug to morphine. The morphine metabolite was delivered through the breast milk to the baby, who received a morphine overdose and ultimately died. This case was publicized and brought to the attention of physicians, alerting them to be careful in prescribing drugs such as codeine to breast-feeding mothers who may be undetected ultra-rapid metabolizers.

(Slide 13) Drug-drug interactions can mimic pharmacogenetic effects, creating a poor metabolizer effect in an extensive metabolizer.

One example of an enzyme inhibitor is Paxil. If a patient is prescribed codeine for pain management and also Paxil, he/she will not be able to metabolize codeine into morphine very effectively because Paxil itself is a potent CYP2D6 inhibitor, creating the phenomenon of a poor metabolizer phenotype in those patients. Doctors really need to be aware of drug-drug interactions. If known, a warning is provided on the drug label about these effects. The Paxil CYP 2D6 inhibition is understood well enough that most doctors who prescribe it know to look for that particular interaction.

Since there are 57 genes, several families, and a lot of different drugs, many potential drug interactions are unknown. The interactions of drugs that are metabolized by the same genes are not well characterized. That creates a problem for physicians who use pharmacogenetics information to treat their patients.

(Slide 14) How does what I've just talked about impact addiction and drug testing? Three things are the most obvious. The first one is that the metabolizer status can affect drug clearance rate. If you're doing drug testing on an individual, perhaps in treatment, and if he/she is a poor metabolizer, he/she may have taken the same dose at the same time as an extensive metabolizer but have more drug in the body for a longer time because he/she is not metabolizing that drug. Thus, it is very hard to make an

evaluation of a person's user status when you're dealing with different metabolizers.

Second, for the same “effective dose” of a clinically prescribed drug like codeine, more codeine must be prescribed to a poor metabolizer and less codeine to an ultra-rapid metabolizer. In addiction, the effective dose might determine how much drug is needed to cause addiction or create the desired effect by the user.

In terms of the implications of pharmacogenetics for drug testing, because you may shunt metabolism from the major pathway into other minor pathways when genes are defective, the major metabolites present may differ in different people. If you expect a certain metabolite profile in users, in users with genetic variations, you may get bizarre or different metabolite patterns that may be hard to interpret.

Why do we want to do pharmacogenetics in the first place? We've heard this morning about poison control, the control of adverse effects, regulatory policy, prescribing policies, and practices for trying to reduce adverse events. We are trying to do the same thing with personalized medicine. We use pharmacogenetics and a person’s individualized genetic profile to personalize dosage administration and patient monitoring.

(Slide 15) In a nutshell, personalized medicine is choosing the right drug at the right dose for the right person at the right time.

(Slide 16) Why would we want to do that? This is to predict who might benefit from a certain drug or how efficacious that certain drug will be for them. Codeine would not be a good choice to administer to a poor metabolizer. Personalized medicine would help determine how much of a dose to give. For instance, much less codeine is given to a breast-feeding mother who is an ultra-rapid metabolizer.

In those instances where two different drugs are clinically equal, knowing the metabolizer status of the patient will determine the best drug of the two to administer.

More commonly now, personalized medicine is utilized to identify those patients at risk for adverse events, to minimize overdose or sub-therapeutic events.

(Slide 17) Warfarin is given as an example. Warfarin is not a heavily abused drug, but it is a widely prescribed drug with a high rate of unwanted adverse events, thus making it a particularly good example of personalized medicine and pharmacogenetics. It's also a drug that is very difficult to dose because it has a very narrow therapeutic range that is dependent on many different clinical factors, including the age of the person, weight, and also genotype. If the dose is wrong, adverse events occur on either side. If the dose is too low, there is the risk of clotting or ineffective treatment. If the dose is too high, there is the risk of initiating a bleeding event. Getting the dose right is extremely important for warfarin, and much attention has devoted to warfarin lately.

Many studies have been done for the drug metabolizing enzyme cytochrome P450 2C9, which is the major metabolizing enzyme for warfarin. What we've noted is that CYP 2C9 poor metabolizers require lower initiating doses. If the genotype of the patient for whom you are prescribing warfarin is that of a poor metabolizer, instead of starting the patient at the standard five milligrams per day, initial dosing may begin at two with careful monitoring of the warfarin effect. Studies are being done to predict upfront the dosing strategy for a patient based on his/her CYP 2C9 genotype and his/her genotype for other relevant genes, in addition to the clinical factors of age, race, diet, and so forth.

The idea of personalized medicine and the hope of everybody involved in this field is that, in addition to warfarin, we'll be able to initiate this for other drugs, including pain management drugs and other drugs that have high rates of adverse events associated with them.

(Slide 18) For those of you who are interested in pharmacogenetics and pharmacogenomics, we do have some resources on the types of tests we regulate and what we look for in these tests. I've included the links to these specific items. We have a general guidance on pharmacogenetics tests and genetic tests for heritable markers, what we look for, and how these tests should work. We also have a test that is guidance-specific to drug metabolizing enzyme genotyping systems. I talked about the tests themselves for looking for poor metabolizers, extensive metabolizers, et cetera.

I'd be happy to answer any questions now or later from anyone. I have my contact information up here, and you can contact us at any time. Thank you for your attention.

MR. STEPHENSON: Thank you. Any questions from members of the Board? This might be one of those opportunities to look at adding some additional data points to your emergency department studies and to look at the retrospective data and to see whether or not individuals at a certain dose might have a different metabolizer status. I know a lot of other people in the medical field who are prescribing medications. It isn't necessarily true that a unit is a unit of drug. Thank you very much for bringing that message to us. We really appreciate your sharing this. Anybody else have any questions?

(Off microphone comment)

MR. STEPHENSON: Yes, write your questions down, and we will have an opportunity later to address questions.

DR. BUSH: Dr. Harper, will you be staying for the comment period and discussion with the DTAB?

DR. HARPER: Yes.

DR. BUSH: Okay. It looks like there are questions from the audience. If we can

harness them on paper, we can funnel them back.

(Break)

DR. BUSH: I'd like to reconvene. We had great deal of presentation material this afternoon, providing us with so much to think and talk about, but we must move along.

I'd like to introduce Dr. Yale Caplan, the Director of National Scientific Services, who will be giving a presentation titled Laboratory Testing in Pain Management: Approaches and Issues. Dr. Caplan.

Laboratory Testing in Pain Management: Approaches and Issues

DR. CAPLAN: (Slide 1) The slide has two names on it, mine and Dr. Cone's, since we are collaborators. If you have anything very positive to say, you can say that to me. If you have any questions or if you don't like what you heard, you can address those to Dr. Cone.

(Slide 2) Pain management testing is relatively new, even though it is using all the well-known technologies. First, I will lay the groundwork, emphasizing the familiar aspects and relating how they might be applied in pain management testing. My presentation outline includes point of collection testing, laboratory, what specimens might be used, specifics about a laboratory, and what kind of panels there are.

(Slide 3) Most importantly is how these drug test results are interpreted. Questions regarding opioid management that may be addressed to laboratories and to physicians include: Is the patient compliant? Are they taking the medications they're prescribed? Is the patient using medications that are not prescribed or not authorized? Is the patient diverting these? Are they taking licit and illicit drugs? Are they becoming addicted? Can the risk of toxicity from overdose or drug interactions be reduced or avoided by doing drug testing?

Overdose and drug interactions are a concern for physician liability. Physicians are being sued for their prescribing practices. A number of these combined pain treatment regimens have resulted in some deaths, probably not unexpected, but they have all been litigated. Tomorrow, Dr. Cone will present data from a large pain management database to illustrate the drugs that are detected and how interpretations are made.

(Slide 4) Drug testing comes in many forms, from on-site testing to laboratory-based testing.

(Slide 5) Forensic drugs of abuse testing, specifically HHS-regulated panels, is confined to urine only specimens and limited to five drug classes. In addition, it is limited by technology to immunoassay and gas chromatography mass spectrometry (GC-MS), limited to certain workplace cutoffs, and characterized by a relatively low positive rate.

In the pain management population, these are clinical-type tests. They are not regulated, which means that any test that is commercially available can be sold to and used by to physicians or individuals. Whether they understand the test or not is what we're here to discuss. In pain management testing, urine or other specimen types are used. Testing platforms for drugs range from point of collection tests to the typical ones that we are familiar with in forensic laboratories. Much lower cutoffs, near the limit of detection (LOD) or limit of quantitation (LOQ), are set. The reason for these low cutoffs will become apparent when we look at metabolites. In pain management testing, some very unique metabolites that were not expected or suspected are being found, and their presence does impact which drug was taken and whether it came from that source. The pain population is expected to be positive for some medication. With the exception of new patients who might be checked for acceptability prior to entry into a program, all patients should have positive drug test results.

(Slide 6) Thus, a whole different paradigm must be applied. These are the typical paradigms that you've seen before: onsite collection and testing which reports screening results only and laboratory testing which reports screening results only or confirmed results only.

Drug panels are different for pain management testing. Four different panels are presented here.

(Slide 7) Point of collection tests (POCT) provide instant results, are generally used for screening only, and are immunoassay-based. They have an advantage of being performed quickly in an office setting. POCT test results may serve the treatment physician by telling him the drugs that a patient was on before and thus the POCT functions as a deterrent. When a patient visiting a pain management doctor is confronted with urine drug testing cup, even though the cup will not test for all the appropriate drugs, if the patient is abusing, he/she usually leaves. Thus, the POCT does have a deterrent value.

Laboratory tests for screening and confirmation take longer to perform, but the laboratory can generally test for more drugs than can be tested at the collection site.

(Slide 8) Point of collection testing has advantages as I have mentioned. They're relatively inexpensive because a laboratory is not involved. They give instantaneous results, which have positive impacts.

The technology is limited. The training is often not done as thorough as it should be. Generally, quality control is not practiced with POCT. We usually utilize workplace cutoffs. Concentration information is not obtained from any of the point of collection tests. The test panels are limited. Mostly, it is the SAMHSA five with maybe another five, six, or seven other drugs. There may be misinterpretations from using screening only results. Education for physicians about what these tests are, what they can do, and

particularly what they can't do is really paramount.

(Slide 9) Laboratory testing is reliable technology. These drug tests have been performed for many years with specific cutoffs and drug identification. Results are quantitative. There are concerns about specimen handling, shipping, turnaround times, et cetera. It's relatively expensive, though, compared to onsite testing.

(Slide 10) Regarding selecting the best specimen type to test, urine is the most common. There are other specimen types, particularly those used for clinical therapeutic drug monitoring tests, including plasma, serum, and whole blood. Oral fluid drug testing is rapidly growing and will become a factor in pain management testing because of its ease of use, its comprehensive testing panel, and other factors. Hair testing is available, but it probably won't have any applications here.

(Slide 11) For certain specimen types, such as oral fluid and blood, a greater preponderance of the parent drug compared to the metabolite is detected. The specimen choice may dictate which type of analyte we detect.

(Slide 12) In summary, the profiles and timelines of the drugs that will be identified in a specimen are determined by the specimen source. Blood has a detection time frame of generally less than a day. Oral fluid generally parallels the blood and, for that reason, a properly collected oral fluid specimen may parallel blood for the detection window of that drug. Drugs are generally present in urine for a longer period of time, but urine is not as homogeneous or uniform specimen from person to person or time to time as are blood and oral fluid. Hair testing represents a longer period of time for detection of drugs. What question you ask - whether a drug was used, the time of use, drugs versus metabolites, and the choice of specimen - may affect the testing profile.

(Slide 13) Urine is the most standardized and widely used specimen. For blood, oral fluid, and hair testing greater analytical sensitivity is needed, which is generally

achieved with the use of liquid chromatography (LC)-MS-MS. LC-MS-MS is a fundamental tool in pain management testing because of the need for higher sensitivity, particularly for some of the other specimen types.

We already talked about the differences in the various specimen types. Unfortunately, there is the perception that test results from different specimen types have to agree, and they don't. Different amounts of drugs or metabolites in different specimens at different times may be found, and they don't necessarily have to agree. That's a difficult concept for many clinical people to understand because they believe that every specimen taken from the body ought to tell you essentially the same thing.

(Slide 14) In choosing a laboratory, there are a number of issues in laboratory testing to consider, including broad drug panels, screening, confirmation, and adulteration. For pain management testing, clinical cutoffs are a must. Cutoffs are lower for most of the drugs. The testing menu is typically expanded from the typical 5 or 10 drugs to probably 20 or 30 substances.

Normalization of drug concentration is not something that's done in the forensic or workplace laboratories but is done in sports testing and by a number of laboratories doing pain management testing. Normalization allows for better interpretation of drug compliance. The pain management laboratory reports must be fairly simplified. Reports can be complex because testing is performed for so many analytes, but the laboratory report should tell the physician exactly what was tested for and provide the best information that is supported by details.

The most important thing is how are these results interpreted? The laboratories can do the test and perform the analyses. What we can't do easily and what takes the greatest effort is explaining how these test results should be used or how they should be interpreted. Misinterpretation of laboratory results is a huge phenomenon. The

knowledge base of the average clinician, particularly the people that are prescribing pain medication such as many family practice doctors, is limited; they have no idea of how to correctly use these drug test results. They expect drug results to be positive that aren't positive or negative that aren't negative. Since they don't generally understand about sensitivity, it must be transmitted in the reports from the laboratories.

(Slide 15) My favorite expression is a test is not a test is not a test. Whenever we perform drug testing in these types of specimens, we have to define the parameters, and there's no such thing, with the exception of the HHS SAMHSA five. The only question you can ask when someone calls you and says, “I have a drug test I want to ask you about it” is “Was that a SAMHSA HHS test?” If they say yes, you can answer because you know what the caller talking about; it was a urine drug test for the five classes of drugs of abuse, done under strict screening and confirmation laboratory-testing requirements. If they say no, I say, “Wait a minute.” I have 10 questions I need to ask before I can tell you anything. Was it screening only? Was it confirmed? Was it quantitated? Generally, the caller must investigate further because people don't understand the important details about drug tests.

(Slide 16) As an example, let's group drug panels in four types and look examine the differences. The group one drug panel is the HHS five. Group two are drugs that are analyzed by homogeneous immunoassays. Group three is a homogeneous immunoassay result that is confirmed after screening by GC-MS or another technology. Group four involves comprehensive mixed testing technologies initially, using ELISA and/or other immunoassays and followed by confirmation using GC-MS or LC-MS.

(Slide 17) If group one only tests for the National Institute on Drug Abuse (NIDA) or HHS five drugs - amphetamines, cannabinoids, cocaine, PCP, and opiates – it involves only drugs of abuse or illicit-type drugs, and that’s of limited value. (Slide 18) If

those tests that are available as homogeneous immunoassays are added, other possibilities include barbiturates, benzodiazepines, methadone, propoxyphene, buprenorphine, and oxycodone.

(Slide 19) If all the drugs in group two are analyzed through confirmatory testing, the result is the list of drugs and metabolites that you see there. What remain unknown are those drugs that never screened positive. That's a very important point, with regard to pain management testing, because there are some drugs, no matter whether testing is performed for group one, two, or three, will never be identified, such as meperidine, Fentanyl, and other opioid-type drugs. (Slide 20) To test for all those drugs and add the drugs, which are less common but still very important in the pain management arena, such as oxycodone, oxymorphone, Fentanyl, meperidine, carisoprodol, and benzodiazepines, more specific confirmatory testing, in addition to general screening testing, is required. Comprehensive drug testing is important in pain management. In the data that Dr. Cone will present tomorrow, you will see the distribution patterns resulting from comprehensive drug testing for pain management.

(Slide 21) What does the lab report tell you? For pain management testing arena, it is important to know whether the person is compliant or noncompliant. Are they taking the prescription that they're given? Are they taking something else, which might be another narcotic analgesic that they were not prescribed, whether from an illegal source or another doctor? Are they taking illicit drugs? Are they taking the prescriptions as prescribed?

Whether a prescription is taken as prescribed is a difficult question. Sometimes, the normalized quantitative values are useful to determine if the results are within the ballpark of what might be expected. Therapeutic drug monitoring cannot be done. Dosage can't be adjustment based on the urine drug test result, but whether or not the

number is relatively high, relatively low, or consistent with the dose can be determined. For example, if a patient is taking 5 or 10 mg of morphine, two to three times a day, and has a test result of 200,000 nanograms per milliliter of morphine, you know that he/she is probably not taking that dose.

This type of drug testing alerts physicians to question and confront their patients and reassess what's going on. That is important information if the dose is too high. A clinician can go back and talk to the patient, ask them questions, and see whether or not there’s an inconsistency.

The cause of the anomalies that we see here has yet to be determined but I believe it is related to pharmacogenetics and anomalies in drug metabolism. The day will surely come when genetic or genomic testing will follow pain management testing. In addition, adulteration and substitution are assessed by looking at the routine analytes.

(Slide 22) In the interpretation of drug test results, the collection and the analysis must be performed correctly. Though a forensic collection is not being performed, physicians should be astute in collecting these specimens, know how it is done in their offices, and make certain what's going on during the specimen collection.

There is a practice, which is generally becoming accepted in the pain management community, of developing a contract with the patient and looking at what they call universal precautions. There have been a number of very good publications on these universal precautions from Dr. Gorley and others regarding protocols with a pain management patient, including pill counts, other systematic procedures, as well as drug testing. When these universal precautions are followed, the physician can be assured of patient compliance.

In drug test result interpretation, the drug, its concentration, the administered

dose, the route of administration, how long is the pattern of use, and whether or not they might be impaired are important considerations.

Impairment does get to be a really big question in this area, but we're not going to have time to discuss that now. Are these people impaired or not? Usually, individuals who are well adjusted with pain medications are not impaired. While their dose is being adjusted, they might be impaired. Whether or not they are a risk for DOT, HHS, or anybody else is a very, very complex question.

The one underlying issue is that the interpretation or the role of an MRO in this is going to be grossly expanded if drug testing for prescription drugs was to become a part of a Federal program. Rules can be made for the easy things. If you have a particular prescription and you're not supposed to have that one, you can call that a violation. Whether or not the person's impaired or whether or not he/she is taking more than his/her regular medication is going to be very, very difficult for an MRO or a clinical individual to evaluate. All the prescriptions must be verified and the prescribing physician contacted. A clinical workup is needed to answer that impairment question.

Factors that affect these interpretations include metabolism and other genetic issues. What biomarkers are present? In the pain management arena, drugs are being administered in mega doses that we didn't see before. Because of mega dosing, minor metabolites are being detected as routine identified compounds. Laboratories must be alert to this. For example, morphine is being metabolized to hydromorphone. Before we were able to publish our findings, I received about a dozen inquiries, such as, "I got this patient, and they got a very small amount of hydromorphone and this huge amount of morphine in their urine specimen. Do I kick them out of the practice? Did he/she violate the agreement?" Many patients have been violated only to learn later that small amounts of hydromorphone can come from the mega doses of morphine administered

for pain management. Attention to metabolism and drug interaction behavior is important.

(Slide 23) An example of a pain management drug test report from one laboratory is presented. The medications that the individual is taking are listed. A variety of specimen validity tests are performed, and the all results are listed. This report states that Percocet was prescribed, and oxycodone was found. So therefore, the patient is compliant. The concentration is here for relative use and, therefore, the person’s test would be consistent with the medication prescribed, since the other drugs are absent. More importantly, what drugs, which are on the profile, are actually included in this testing so you can look at it for a comparison?

(Slide 24) What laboratory tests cannot tell is the time of drug use or the amount of drug exactly used. These are always the questions, no matter whether you do forensic work or even clinical work. The first question always is “I got this number. Can you tell me how much they used and when they used it?” That's the most useful question and one of the only ones we never answer. We can't tell, although it is most desirable, the frequency of drug use.

Based on some of the numbers, frequency of use may be discussed. The concentrations and metabolite ratios may help establish these boundaries. We can say whether they've been using for days, weeks, or months, but not specifically whether it's in a range of factors of 10 or 100, a milligram, 10 milligrams, or 1,000 milligrams. With some drugs and some specimen types, more information is available than others, which is why eventually look at some other specimen types for assistance in making these kinds of interpretations in the future.

(Slide 25) Laboratory tests reveal the drug or drug class, but not always what was administered because of metabolism. Sometimes this is easy to do, and sometimes

it is complicated depending upon the drug. It does take a professional interpretation, either from the laboratory or from clinicians with a higher level of training, to properly use these test results. The laboratory report will list what metabolites are there; the apparent ratios; concentration quantities; sometimes the stereochemical isomerization, which might be more important for amphetamines in this arena than in others; and information about the specimen, including creatinine, specific gravity, et cetera.

(Slide 26) Regarding some interpretation problems and pitfalls, did the metabolism of other drugs cause this test result? Should dilute specimen results be normalized? The laboratories that are engaged in pain management testing will normalize; the World Anti-Doping Agency (WADA) Group involved with the Olympics normalize so that they provide a better cutoff for the drugs they test for.

Years ago DTAB discussed this idea of normalizing results, and probably for administrative and governmental reasons, we decided not to do it. Normalization will change the number of people that are potentially positive and will likely detect more individuals as having used a drug. How to interpret normalized drug test results is the important thing.

(Slide 27) One example of metabolism, which is of concern, is that morphine can come from a variety of sources. Here's the metabolism of hydrocodone to hydromorphone and also morphine to hydromorphone. (Slide 28) With a positive test for morphine, the source could be any of these compounds, including heroin, codeine, morphine, or poppy seed ingestion. Some of the additional test results will help differentiate the source. 6-Acetyl morphine (6-AM) has had success as a heroin biomarker; there may be other heroin biomarkers also. The codeine to morphine ratio may be of some use and possibly the small amounts of hydromorphone being identified in specimens containing very high concentrations of morphine. All these would help in

differentiating the source of the morphine.

(Slide 29) Here's a case where benzodiazepines are positive for oxazepam and temazepam, and here are the specific numbers. The combined numbers totaled about 1,000 nanograms per milliliter. In the case of opiates, morphine was positive at 22,000, and hydromorphone was positive at 442 nanograms per milliliter. Because in this case we're pretty sure that the hydromorphone came from the morphine, in this interpretation, the sum is probably useful. These are some of the things that laboratories need to routinely perform to more effectively interpret these pain management drug test results for clinicians.

(Slide 30) Illustrated is the metabolism of hydrocodone to hydromorphone and oxycodone to oxymorphone. Oxymorphone was recently marketed as the drug Opana about a year ago; it was previously only present in a drug test specimen as a metabolite of oxycodone. This is something the pharmaceutical industry does often when a patent expires; they then patent a metabolite, particularly if the metabolite is the pharmacologically active moiety. Many of the drugs that we looked at, like codeine and heroin, are prodrugs; these are not the pharmacologically active drugs, but are metabolized to the active drug. The pharmacologically active moiety may not be the main one detected in a drug test.

(Slide 31) In the pain management arena, many drugs and metabolites must be considered before any assessments are made. Hydromorphone could originate from the ingestion of drug hydromorphone itself, from the metabolism of the drug hydrocodone, or from chronic morphine use. How do you determine that? The interpretations and what other analytes are present in the specimen, such as hydrocodone or very high concentrations of morphine, help elucidate the source. (Slide 32) Is the concentration consistent with the dose? 10 milligrams of morphine is not likely to produce 190,000

nanograms per milliliter in urine, so ballpark assessments are helpful.

How do you deal with a dilute specimen? Assessments need to be made whether to use lower cutoffs or whether to normalize to specific gravity or creatinine concentration.

Why might a test be negative that was expected to be positive? Is the patient an ultra-rapid metabolizer? The answer lies in laboratory testing and making a clinical assessment in an area that is relatively new, relatively complex, and not something that most of us are ready for. Many of the laboratories, especially the larger ones, are doing increased testing for an increased number of drugs. The clinician really is still stuck with trying to figure out what that all means unless it's put together in some systematic way.

Even though this is “not a forensic test”, in many respects, it really is forensic. Pain patients are signing agreements to be treated, and they may be evicted from a program or called liars possibly because of an anomaly in their metabolism. We are only scratching the surface in this area of drug test interpretation. The day will come when all things are litigated and this might become a litigious issue.

(Slide 33) Finally, we always have to ask, ”What’s the question that we are asking?” We have to define or redefine the question for laboratory drug testing and put it in context because the questions are different in pain management testing from all the other areas that we might have done drug testing in before. The technology is similar and the drugs are similar, but the question is different and the interpretation is different. We have these technologies, but which one is used depends upon the circumstances. The test panels consist of broad panels, lower-cutoffs, and broader concentration ranges. Finally, the interpretation can be very challenging when minor metabolites emerge and normalization becomes more common. Then, a variety of new clinical entities are there.

Thank you.

MR. STEPHENSON: Before we move on, one of the things that we've done is a background work this morning. There was logic and a flow that was established in our approach this. We built in background data from other perspectives to get to this point.

I think with Yale starting the introduction to some of the testing components and complexities, we have just blasted off. We are no longer on the ramp taxiing anywhere; we are in the air and we're beginning to move. This is our forte, but it doesn't mean it's any more important than the parts that have already been presented earlier today. We needed to understand those background issues to help us put this into perspective. As regulatory individuals, we went down a forked branch in the road 20 years ago and deliberately looked at the illicit substances of abuse and deliberately stayed away in large part from medications that were prescribed to patients with real disease problems. That was then, this is now.

This does not necessarily imply any pending regulatory change that's going to come out of this or work product that we're going to engage in. To say that we aren't going to be energized and perhaps internally motivated to do more than we have would be a mistake, too.

I think we need to look at all of the information with a very open mind and receive it in a way that we will be able to digest, but not necessarily at this meeting. You've got to go through this process and absorb what you can, think about what you've heard, and analyze the issues that you see from your own particular perspective and your own environment. See what has been shared at this meeting and how it can help inform you.

We hope at the end of the second day that this will have generated enough cross pollination and interest from folks about areas they didn't know about so that we'll have a starting point for further dialogue in the future.

Professional Health Monitoring Programs

DR. SMITH: (Slide 1) What I'm presenting today is data from Professional Health Monitoring (PHM) Programs that our company administers and manages for approximately 110 different state programs throughout the US. The data that I'm presenting and the conclusions and questions that I'll leave you with are based on data from approximately 10,000 to 12,000 health monitoring tests that are done monthly and are processed through our various administration programs.

All of the testing that is done in these programs and the data that I am going to present is from urine testing. It is laboratory-based testing exclusively. I will present a review, piggybacking on what Yale has done with some of the various drug panels, and other considerations.

(Slide 2) Less than half of all of the Professional Health Monitoring Programs use a third-party administrator or even a medical review officer as a service agent for administering their programs. Many, many programs do this on their own with case managers who may or may not have any toxicology, pharmacology, medical, or other backgrounds or through a variety of other types of in-house administration.

(Slide 3) These are programs for a variety of healthcare paraprofessionals, as well as social workers, attorneys, psychologists, et cetera; it does run the gamut.

(Slide 4) Most of the program participants, meaning the individuals who are being monitored for compliance with a state licensing agreement or a state recovery program, had their licenses to practice revoked or suspended by the state. They may be working in their profession on a provisional, restricted, or probationary license. They may have already had their license reinstated, but a condition of that reinstatement was to continue in a monitoring program, sometimes extensively, meaning for five, six, seven, or even eight years, which I have seen in some state programs.

One thing that is unique here, and does need to be discussed, is cost. It's an

important distinction. In all health monitoring or professional monitoring programs that I know of, it is the participant that pays all costs. It's not the state board, it’s not the Lawyers Assistance Program, it is not the recovery network, but it is each individual participant. It will be significant, as eventually with any public policy, that the costs and who pays them become factors in how you determine the efficacy and or the cost-effectiveness of the program.

The frequency, the duration, and the drug testing panels, as well as the program compliance standards, are all determined by the case manager, and everything is customized to the individual participant. There is no one broad-brush approach, no one-size-fits-all, even in terms of the compliance contracts that these individuals sign.

(Slide 5) Here's the information base upon which these data that I'm presenting are based. Here are some data that are important because, remember, all of these individuals now are in a program because they have been identified, either through “self referral”; arm-twisting; administrative or in some cases criminal action for diverting drugs; abusing drugs or being chemically dependant on drugs; or other association with drugs and/or alcohol. (Slide 6) This is a population that is at extraordinarily high risk and extraordinarily relapse prone. In many instances, over 80 percent of them have access to pharmaceuticals and other drugs on a regular basis, and yet the positive rate, and this, by the way is a laboratory-positive rate, is less than 12 percent. Almost half of that is positive for alcohol, specifically ethyl glucuronide (EtG) or ethyl sulfate (EtS). When factored out, the positivity rate in this high-risk population for opiates, benzodiazepines, antihistamines, et cetera, is significantly lower than expected for this type of program.

The frequency of testing of the individuals ranges from as often as three times per week to monthly tests. The frequency that a person is monitored through chemical testing is determined by the case manager. There are statistics about the type of

specimen that was used. The test panels used in the 110 programs that our company administers or manages range from a standard HHS five-drug panel to panels that include up to 32 drugs and/or metabolites. There's even one now that has 36 drug or drug metabolite identifications.

(Slide 7) The program participants are required to enroll by their monitoring agency, be that a state board, a state medical society, et cetera. Once they are in a chemical monitoring program or health and testing monitoring program, they are required to call or log in with a PIN and password every single day of the week, Monday through Sunday, seven days a week. They must do so generally by an assigned cutoff time, such as 12 noon or 1:00 p.m. They are then informed, either by the login or by the voice system, whether or not they have to report for a drug test that day; it’s either a test day or a no test day. Based on the program particulars, they are given X amount of time to report for the test once they've been notified.

The system is also designed so that the case manager gets immediate feedback for people that did not call in or login on a given day; secondly, a no-show report is generated if they did not appear at their designated collection sites within the assigned time on a test day.

(Slide 8) The military has some history with pulse testing. In the professional health-monitoring arena, the term often used is flex panel testing. To some extent, there is some similarity to what you heard from Colonel Shippee this morning in the DoD program. Here, though, flex testing is individually prescribed. Take Donna Smith, a social worker with a drug problem, as a participant. My case manager would identify at the very beginning of my monitoring program a variety of panels, selected by the computer or by the case manager, that I would undergo on any given test date. I never know whether I'm going to get just a five-drug panel on the day that I have to go to give

a test or whether I'm going to get the 32-drug panel. The deterrent factor in the relapse prevention program is that I am at risk at all times to be tested for the gamut of everything that is available to obviously deter movement from one drug class to another.

Now, will I eventually know that I have had X number for option three, which may be the 28-drug panel, versus option two, which may be the 12-drug panel? Yes, because guess who pays the cost of the testing? I do. I will know after the fact when I am charged $110 on my account for a particular test panel versus another amount. The flex panel system helps control costs and yet maximizes the deterrence for the full range of potential drug use. This is not unlike what the military has done in its pulse testing program as a way to control costs and yet to serve as a deterrent.

(Slide 9) Participants already have custody and control forms, a forensic document that will track their drug test in their possession. They've already been assigned various places that they are to go for their drug collection and they have some alternative sites. But let's say, for example, that I am a program participant, I had to call in by noon today, and it was a test day for me. Well, I'm not in Tampa Bay, Florida where I normally have my assigned collection site, so I would then immediately have to opt out to number two. I would be asked then where I am. Well, I am in Rockville. They would identify for me and tell me where I need to go to have my specimen collected within the two or three hours that is allotted. Even with travel, vacation, or whatever, not being available geographically does not excuse the participant from meeting the compliance standard for having the test done on a test day.

The other thing that is important, and we've heard other speakers mention this in some ways, is that these programs all require upfront notification of any medications that a person is on. The case manager always knows what the person has been prescribed, including any controlled substance or other substances that are identified on

any of the drug panels that may have been used in medical treatments, et cetera. There is that kind of control up front in terms of expectation for what the testing will discover.

(Slide 10) One of the disadvantages of the urine drug test is the ability to beat it at the collection site or to manipulate the test outcome in some way. The laboratories have extensive specimen validity testing measures that are in place and, in many instances, are even more stringent than what is under the forensic standard for Federal testing identified by HHS SAMHSA.

For example, for most of the programs, any specimen with a creatinine less than 20, regardless of what the specific gravity value is or what the pH is, is considered to be an abnormal specimen. In many programs that alone will qualify as a program failure. It's a different mindset from a standpoint of what is accomplished with the testing. Any specimen that meets the SAMHSA invalid criteria, for the vast majority of the programs, is considered again a failed test or a violation of the program contract.

(Slide 11) Our company works with and uses a total of six laboratories, five of whom are SAMHSA-certified and one of which is not. The laboratories specialize in the area of therapeutic drug monitoring as well as MedPro or Medical Health Professional Panels. Those laboratories offer up to 15 different health monitoring or MedPro, as they're often called, panels, as well as custom panels for some specific clients.

The minimal health-monitoring panel that is used is a 10-drug panel with specimen validity testing. The exception to that is some attorneys' programs use only a five-drug panel. Any panel in the healthcare field does use a minimum of a 10-drug panel, which you see listed here.

It is also of interest that, unlike what has been the standard in workplace testing, whether it be under DOT or under the Federal agency programs, in almost all instances,

regardless of what the drug of choice was for the person being brought into the program, alcohol is a drug that is tested for. Even if alcohol was not their drug of choice or they did not have an abuse or a dependency diagnosis, they are still, in most instances, required to be totally abstinent from alcohol and undergo, on a flex-testing basis, testing for alcohol. The cutoff level is either 0.01 or 0.02 for all of the panels that do urine alcohol testing.

(Slide 12) The most comprehensive panel is a 19-drug panel. Listed here are the additional drugs that are typically part of that particular panel. Many drug panels also include routine reflex testing to EtG and/or EtS. If an alcohol test result of 0.01 or greater is obtained, testing is by either GC assay or on another laboratory test.

(Slide 13) There’s a lot of crossover to what is used in these professional monitoring panels. The amphetamines class almost routinely includes confirmation for D-amphetamine, methamphetamine, MDMA, et cetera. The barbiturates class, in terms of the panels that are used in the programs that our company is affiliated with, typically confirms five to seven different barbiturates. For benzodiazepines, the range of confirmation for numbers of analytes or their metabolites is between 6 and 15.

(Slide 14) Narcotics, opiates, and the opioid class typically can confirm up to 20 different metabolites or analytes. It interesting that rarely is 6-acetylmorphine (6-AM) confirmation included in the PHM panels. I don't know if it's because they were borrowed from clinical panels or that's how the programs were initially set up. Antidepressant, antihistamine, and stimulant classes, when they are added to the more comprehensive panels, do confirm for between five and eight analytes per class.

(Slide 15) This slide presents an example of screening technology, screening cutoff levels, confirmation technology, and confirmation cutoff levels that are a part of the many panels that we use. There is huge variability considering we’re only using six

different laboratories.

Now, lab A, B, and C may offer the same panel in terms of the drugs, drug classes, and/or drug metabolites, but rarely do they have the same cutoffs for screen or confirmation and rarely do they even use the same methodology for either screening or confirmation. Why, I don't know. Standardization in these programs is as far from Colonel Shippee's reference to DoD laboratory standardization as you can get; it does not exist, at least in our experience in these programs.

(Slides 15-19) I have taken some of the drug classes, from different laboratories, to show you what typically a particular laboratory may do in terms of the screening and confirmation. (Slide 17) Here's one of the more extensive benzodiazepine panels with screening is done by immunoassay. Take a look at the confirmation cutoffs on the right-hand side; note how much tremendous variability there is. (Slide 18) Here is a laboratory panel for expanded opiate and narcotics classes with screening information. Some screening is done using ELISA (Enzyme-Linked ImmunoSorbent Assay), and you see that picograms are often used as the screening cutoff concentration. Confirmation is at the nanogram level, in most cases, for quantitation.

(Slide 19) Antidepressants, antihistamines, and stimulants are also available in custom and expanded panels, typically used in the flex panel circumstance. Here are one laboratory's cutoffs and methodology that are used for those particular classes of drugs.

(Slide 20) What do I have to contribute in terms of looking at this data as it may apply down the road to either Federal public policy or to workplace testing in these arenas? Well, one of the things that is significantly different here, and we hope will not occur in the workplace setting, is that the laboratory data goes directly to the PHM program case managers. In many instances, this creates tremendous variability in how

that data are used, how they are interpreted, and what ultimately results in the outcome for the specimen donor.

The MRO interviews the participant with a positive laboratory test result in all the programs that we have except for one. For that one, it is by request only, meaning that the participant has the right to have an interview, it must be formally requested, and he/she must pay for the privilege of having a medical review officer review the drug test result, discuss it with him/her, et cetera. The majority of the PHM programs, as I mentioned, have no MRO component at all. It is the case worker who is looking at a list of medications that he/she may have received from the program participant and then determining whether the laboratory report, in his or her opinion, is consistent with that or, if not, it's a program failure.

(Slide 21) Eighty-five percent of all laboratory-positive PHM drug tests, which are reviewed by our MRO staff, are verified as authorized medical or legitimate use. There is a very, very small instance of laboratory positive results that we find are not due to authorized medical use, even in this type of a program.

What is interesting to me are these participant contracts in which the person is required to sign in order to be in the monitoring program. They cannot eat anything with poppy seeds in it. They cannot use any over-the-counter medications that contain antihistamines, alcohol, or sympathomimetics. Likewise, they sign that they cannot be anywhere where illicit drugs are found, to avoid passive inhalation and absorption through other routes. That's why most of the panels that test for things like marijuana will have a confirmation cutoff level of up five nanograms per milliliter. For them, passive inhalation is not an issue because the participant signed a contract that he/she would not be around where marijuana is being used.

(Slide 22) What are the significant test results and interpretation issues? As

much as we try to tell them that a single urine drug test result with its quantitative level cannot be related to the person's dosage, it is asked every single day. I've taken three phone calls today from case managers who say, "Your MRO refuses to tell us whether this person was taking more of their medication than they should have or refuses to tell us whether nurse Suzie should be able to work if she's taking 20 milligrams of OxyContin." There is a definite continuing belief that there is a dose response relationship to urine drug test quantitation levels.

One of the hardest things that we fight in these programs is the inappropriate use of specimen validity testing measures, especially low creatinine values. With the whole issue of a dilute specimen, some of these contracts say that once a person is notified that today is their test day, they agree that they will not consume any more than 8 ounces of liquid for the rest of the day until the specimen is taken. It is extraordinarily draconian.

Of course, there is the issue, which is probably not germane to this particular session, of comprehensive testing panels. There is the use of extremely low cutoff values for analytes like urine EtG, as low as 100 nanograms per milliliter, and for urine alcohol at 0.01 grams per deciliter. Most of this Board and audience is familiar with the CSAT Advisory concerning the role of biomarkers for ethyl alcohol. Certainly in health monitoring programs, this has been the biggest area of contention with regard to their use.

(Slide 23) Opiate GC-MS cutoff levels for morphine, codeine, and synthetic opiates are often very low at 100 nanograms per milliliter. There is the issue concerning food products or other drugs that cross react.

The belief is that benzodiazepine testing is good, it's accurate, and it's precise. The interpretation of benzodiazepine results, the understanding the various metabolic

pathways, and drug interactions cause an extremely complex situation. If you think that medical review officers, let alone non-medical case managers, have a good grasp on that with just a couple of hours of training or time on the Internet, I think we're sadly mistaken.

(Slide 24) I did present some cost data because I was specifically asked to do that. This is range data in terms of what exists today. For laboratory analysis of the various panels, program participants typically pay per test, and this fee does not include the cost of urine specimen collection, which ranges from $15 to $35, or if they elect to have an MRO interview for a report from the laboratory.

(Slide 25) There are some significant differences in the restrictions that are placed on the program participants and would not be appropriate in a workplace setting, even in a workplace setting for follow-up or post-rehabilitation testing. These are much more stringent.

My concern from a scientific standpoint is the lack of standardization in cutoff levels, screening methodology, and laboratory reporting practices. If we ever decided to go anywhere with this outside of this very narrow custom use, it is going to need greater attention.

DTAB Panel Discussion

MR. STEPHENSON: This is wonderful. Any questions from the members of the Board? I know there has got to be experience in testing capabilities from some of the members of the Board and others in the audience that would probably echo and can amplify what you said. Hopefully, we'll have an opportunity to explore this in a more interactive environment, maybe yet today, but hopefully tomorrow.

Some of the homework assignments will be for members of the Board and for

those of the audience who want to come back reinvigorated tomorrow to approach this whole subject and to think about some of the probing questions, to discover some of the issues that you want to bring out or amplify, to think through some of the presentation elements that were here today, and to see how you'd like to contribute to the knowledge base or questions that you have that maybe we need to go further with in our own exploration of finding other resources to come back to later on.

I know there are some people in the audience that have received an overwhelming amount of what must appear to be a blizzard of new information. It doesn't get easier. There will be a set of resource documents that will be made available as soon as we can post them on our Internet. It will include the presentations and a cleaned up version of the transcript. That is the legacy of this meeting. That is its intended purpose, to satisfy different potential uses in the future.

I can't say enough how much I appreciate the quality of your ability to sit and have speaker after speaker talk to you. This has been one of those times when I don't know how else we could have gotten the information out to you.

There will be opportunities for us to engage in some of this more interactively, and I really want that. I want us to be able to do this in as open and flexible and mutually respectable way possible. Anything else, Donna?

DR. BUSH: We do have time budgeted until about 4:30 for any DTAB discussion. I understand if you're not ready yet. We have a lot more speakers. This is just half of the material and half of the facets presented on the subject matter.

Many of us sitting around the table understand the complexities. It's our responsibility to bring the best people with the best experience to put the information out there, and eventually we're all going to have to discuss it. I already got input from one of the Board members about what she wants to share tomorrow.

Do you want to call it a day in terms of questions? Do you want to start some discussion? We do have a couple of people in the audience who wish to make public comments. We will honor that. I want to make sure that you have your time here now should you wish to.

DR. COLLINS: I have a question for Donna Smith. From a laboratory perspective, we quite often get a panel presented to us with cutoffs that are already being used by a group, and you're right, there's a great deal of discrepancy from group to group with regard to the panels, the cutoffs, et cetera. As an experienced third-party administrator, do you have the opportunity or try to have any discussion about what are the appropriate cutoffs from a clinical perspective to use for these groups? Or, do they come to you with a panel and say, “This is what we've always used and we want to continue to use that.” Some of these things we look at from a laboratory perspective and say, “Why on earth are you looking at drugs at that level in a urine sample? It doesn't make any sense.”

DR. SMITH: Exactly, yes. I do find it is the latter. In the majority of cases, the monitoring program has already identified, sometimes they've even voted on these things that are set by their state organization or whatever, what we are going to do, and they're very reluctant to change.

We have probably, of late, 10 states that have just begun programs for recovering pharmacists. Those are new programs. They’re much more willing to consider what we are presenting them, the pros and the cons, here's what this will accomplish, and here's what that would accomplish. Much depends on what your objective is.

But it is extraordinarily difficult. Let me just give you an example. After the CSAT advisory on ethyl alcohol biomarkers came out on EtG and EtS, trying to get our

programs to move from a 100 nanogram cutoff level to something that would be more reasonable, such as 1,000 or to 1,500, even in the context of case management was almost impossible.

There is really a very, very set mentality in these programs. While the basis of the program is deterrence, lurking behind these programs is that we cannot afford for any physician, nurse, or whomever to be found using drugs once they have their license reinstated. The detection mentality is that we must detect every single person that may be using drugs again, which overrides the deterrent nature of the program.

MR. STEPHENSON: Let me just follow up just for a second on what you had said. The EtG testing component that you had indicated has marketing preceding the science, with people selling a test that they had and convincing someone that you have a specimen of convenience that's already been collected for a urine drug test, so we might as well just perform the EtG test, which we can do it in our lab at a reasonable cost. People bought into it.

The problem with every public policy issue is once you buy into that mindset and you start something that is not supportable by the science, for those individuals in which it happened on their watch are fearful for making change because then they, perhaps, feel that they would be opening themselves up to groups of people who would be dissatisfied and who had already been eliminated because they had not complied with that earlier, lower cutoff level.

On the other hand, even when informed by reasonable documentation from multiple Federal sources and good background analysis, the program operators were not willing to make changes. That speaks volumes about voluntary compliance and standards that can be easily interpreted and implemented by folks who aren't in a rigorous environment to begin with.

The third thing we have to be very cautious about and guard against is that every person needs to be equal in protection and concerns of privacy. If you write some people off, and we often try to do this in criminal justice areas, and when we allow for a person who's an impaired professional or recovering professional, we've made them into a second-class citizen, not entitled to the rights and protections of even good science.

That's not going to ever happen in this environment. I'm sorry that it happened by using a urine specimen for other purposes that you have described. There's still work to be done. Sometime it will become a class action lawsuit that will be dealt with appropriately in the courts, and that may change peoples' perspective based on liability.

We don't have direct oversight over that. Other than supporting the concerns that have been raised by our sister center and by our staff when this earlier advisory came out, there is little that we can add to this except shame on the folks who weren't able to be convinced they needed to do better

DR. TURK: Donna, I have a question for you. You said you have six labs doing this for you? Do they have any kind of certification, any kind of performance testing (PT) program, or any kind of quality assurance? How do you know that they're giving you good results?

DR. SMITH: Five of the laboratories that we use are SAMHSA certified and have College of American Pathologists (CAP) certification, but it's under the urine drug testing screening (UDS) program. Of course, you are exactly right. For many of the classes of drugs that are offered in the more comprehensive panels, to the best of my knowledge, they do not have participation in external certification or PT programs.

MR. STEPHENSON: That's a great question, and it's very appropriate for the settings that we are in. The variability that you talked about, Donna, is another issue

that is not of concern but of awareness. How do you standardize across these different experience bases and product offerings and services?

It's never easy, but this is the role that we have been asked to play for about the last 20 years with a group of people who stretches the spectrum of professionalism and Federal responsibility, whether it's DOT, DoD, or otherwise. We don't do this by ourselves. We do it in a group environment where we try to make sense out of what is being said, and then try to derive a common benefit for all parties that would be subject to a testing environment.

Your experience in this was greatly appreciated. It's not something we could have ever obtained ourselves based on the path that we have walked for the last 20 years. It was a valuable contribution.

DR. BUSH: We are about done with the Board's comments and any discussion items for tonight. If that's the case, then we have individuals with public comments. Ms. Varlotta, you may approach the microphone, please.

MR. STEPHENSON: First, consistent with the notes from the Federal Register Notice, try to keep your comments focused on the purpose of the meeting today in a broad and general way. This isn't a caution to you because you have always been courteous and polite in what you do.

Second, your comments will be heard, but we won't respond to them. This is just an opportunity for you to speak. If you can do this in 10 minutes or less, it would be appreciated. If you can provide us with a written copy of your statement, then we can consider it for a record. Thank you.

Public Comment

MS. VARLOTTA: Mr. Stephenson and all members of the Drug Testing Advisory Board, allow me to introduce myself again. My name is N. B. Varlotta. I'm a career flight

attendant with an excellent employment history. In March of 1999, my employer terminated me one month shy of my providing 20 years of faithful service. I was falsely accused of substituting a drug screen sample under the standards established by this Board. I continue to take my time and time away from my family to travel cross-country in order to attend these meetings because I am fervent about the Board's attachment to validity testing.

After continued research, I have found there is still not an avenue in place for protecting and safeguarding an employee from being falsely accused when submitting to a DOT drug test collection. The purposes of this Board are to assess the science and technology used in drug analyses and to improve the quality of related laboratory services and systems for drug testing. Unfortunately, the assessment of the science, specifically in relationship to validity testing, has been overshadowed by collection procedures.

The ongoing concerns for the workers of America are as follows: primarily, similar to blood pressure, the BUN (blood urea nitrogen) counts, other blood chemistry functions, creatinine, and specific gravity are in a natural, continuous change in the human body. To expect a person to reproduce a specimen outside of the circumstances of the original specimen is biased and not sufficient evidence to make an accusation that a sample is not valid, for instance, flying on back side of the clock, fluid intakes, circadian clock disruptions, hours in the air, pressurization, gender, eating habits, physical body makeup, et cetera.

The amended rulings are insufficient and have not been set to protect future workers from a false accusation or to provide for the individuals that were falsely accused in the past with a remedy. Additionally, although the amended rules allow for the donor to provide "evidence" that a two or less than creatinine can be produced, what

HHS or DOT approved laboratory will perform the test? To the best of my knowledge and experience, to obtain a personal individual test certified by HHS and DOT is beyond reason and caters only to the companies and corporations. Essentially, this provision is simply published status print with the worker having no defined procedural possibility for personal testing to be obtained for their body.

Furthermore, the production of low creatinine levels can be a statistical anomaly, as Dr. Vina Spiehler has pointed out in the past. Although there has been some discussion and alerts sent out to medical review officers, no protection or avenue or procedure is in place to clear an employee of a false accusation short of the MRO simply choosing on their own personal accord or caprice to cancel a test.

I am again asking this Board to discontinue the so-called validity testing immediately until the science is foolproof. Failing such action, since careers continue to be threatened and since the science continues to be questionable and since human error can never be removed from the equation, I shall persist to advocate that it is incumbent on this board to adopt specific step-by-step procedures acceptable to all employees, employers, and workers which would allow any employee to clear their name with a remedy in the event of a false accusation.

Mr. Stephenson, members of the Drug Testing Advisory Board, I implore you to reconsider the provisions of the final rule and the suspend implementation.

Thank you for the prompt attention to a public concern.

DR. BUSH: Thank you. Mr. Drake, do you have prepared public comments?

MR. DRAKE: Yes. My name is Richard Drake. The first part of my presentation deals with the very subject that we have here today about the prescription drug program and the very interesting pie chart that was produced on the screen that indicated that 55.7 percent of the illicit drug use came from family or friends, effectively the family

medicine cabinet.

I myself have half a bottle of Percocet in my medicine cabinet for the very reason that Dr. Clark laid out; I am loathe to throw it away because I paid for it and I work in an industry where I get hurt and injured probably once every six months and I get prescribed Percocet. I don't fill the prescription because I just use what I have left.

Every single person in this room, I'm sure, has something in their medicine cabinet that they shouldn't, that they've kept or whatever, even though it's past the time of its use because they know it's going to happen again or because, oh, I'll just keep it, maybe my sister will need it.

There is a way, a very simple way, however, to remedy the program, which would decrease by 50 percent, and according to the pie chart five million illicit drug users would be eliminated, if they couldn't get it from the casual access to the family medicine chest. To have a program by regulation, law, legislation, or whatever it would take, that if you have a prescription medicine left, such as the 28 capsules of Percocet that I have left, just return them to the pharmacy and get a refund.

Although you have produced literature which I got when I got mine, that said, if you don't use it all and throw it out, well, that’s a little micro expense to me. Why not make it a macro expense to the pharmacy that would return it back to the drug company that actually produced it and receive a refund to the pharmacy?

It's such a simple, simple solution and it would work. You are giving me literature as a general consumer to throw it away; it is not going to happen. If you said, take it back, I'd be looking through my medicine chest right now and find all the things I could possibly bring back to get the refund. That's where it's going to happen. You'll eliminate 50 percent or five million casual access people or casual points of access to what would become illicit drugs. It would also eliminate the potential for a person who’s not a drug

abuser, just a child, a person who looks at Percocet and says, “Geez, I think I'll try it because it’s there, easily accessed, and free.”

Eliminate the problem, and that is the problem. People would take it back for a refund, just like they turned in their guns and just like they return bottles for refunds. This is a solution, it is so simple, but, of course, it involves making a rule against the drug companies. Oh, no, they, of course, cannot recycle them, but they can destroy them, just like you're asking me to destroy them. Thank you.

MR. STEPHENSON: Thank you very much. Any other last comments from members of the Board? Thank you all very much for being here.

DR. BUSH: We will close now today's session of the Drug Testing Advisory Board.

Tomorrow’s agenda is already photocopied. Mr. Edmeade, can you put the agenda out in the back of the room? The agenda will be available now and again tomorrow morning.

We hope to see you all back here for tomorrow’s presentations. Thank you. Meeting adjourned.

(Whereupon, at 4:35 p.m. the open session adjourned, to reconvene in open session the following day.)