Drug Testing Advisory Board (DTAB) Meeting

Open Session

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Virtual

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CASET Associates, Ltd.
caset@caset.net
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Agenda Item: Call to Order – Approval of December 2021 Meeting Minutes

MS. DAVIS: Good morning, everyone. Thank you for bearing with us through the login process.

My name is Lisa Davis, and I am the designated federal officer for the Drug Testing Advisory Board, otherwise known as DTAB. I would like to welcome everyone to the March 2022 quarterly DTAB meeting. We are conducting this meeting remotely, so please continue to bear with us through any technical issues that may occur.

I officially call this meeting to order and want to welcome the staff, the Division of Workplace Programs, federal partners, contractors, invited guests, members of the public and finally, our board members. I wish to once again, thank Faye Caldwell for accepting an extension to her term on the DTAB. We appreciate your continued support.

Today's open session is scheduled from 10 a.m. to 1 p.m. Eastern time. Just a reminder, before a board member speaks, please state your name for the benefit of the transcriptionist and all other attendees. With that, I will start the roll call.

Faye Caldwell.

MS. CALDWELL: I'm here.
MS. DAVIS: Jason Schaff.

DR. SCHAFF: Present.

MS. DAVIS: Barry Sample.

DR. SAMPLE: Here.

MS. DAVIS: Kristen Burke.

MS. BURKE: Here.

MS. DAVIS: Deborah Motika.

MS. MOTIKA: Here.

MS. DAVIS: Steven Taylor.

Alison Stockdale.

MS. STOCKDALE: Here.

MS. DAVIS: David Engelhart.

DR. ENGELHART: Here.

MS. DAVIS: Elizabeth Stuyt.

DR. STUYT: Here.

MS. DAVIS: Chair Ron Flegel.

MR. FLEGEL: Here.

MS. DAVIS: Now I'll call ex officios and federal partners.

Paul Harris.

MR. ZALESKI: This is Brian Zaleski. I'm participating in behalf of Paul Harris for the NRC for today.

MS. DAVIS: Thank you, Brian.

Joseph Kotarek.
MR. KOTAREK: I'm here.

MS. DAVIS: Bohdan Baczara.

MR. BACZARA: Good morning, everybody. I'm here.

MS. DAVIS: Erin Wilfong.

Lynn Wagner.

MS. WAGNER: Good morning. Here.

MS. DAVIS: I'll just make sure the other presenters are here. Brian Zaleski.

MR. ZALESKI: Present.

MS. DAVIS: Hyden Shen.

MR. SHEN: Present.

MS. DAVIS: Eugene Hayes.

MR. HAYES: Here.

MS. DAVIS: Svante Vikingsson.

DR. VIKINGSSON: I'm here.

MS. DAVIS: And then Steven Taylor. Are you on the line?

DR. TAYLOR: Yes, I am.

MS. DAVIS: Thank you. That's the roll call, and we do have a quorum.

First up, the DTAB members were given the opportunity to review the meeting minutes from the 2021 DTAB meeting. If the board has any changes or additions, they will be incorporated into this meeting. Do any of the board members have any requested changes?
Hearing none, may I have a motion to approve the minutes, please.

DR. SAMPLE: I so move.

MS. CALDWELL: I'll second.

MS. DAVIS: Thank you, Faye. The minutes are hereby approved. Thank you.

In today's DTAB session, we will discuss the Mandatory Guidelines for federal workplace drug-testing programs. The Department of Transportation, the Nuclear Regulatory Commission, and the Food and Drug Administration, will provide updates. Additionally, there will be presentations on the Drug-Free Workplace Program comprehensive review scheduled for May, NLCP drug testing results, and Dr. Svante Vikingsson will give a presentation on synthetic urines and adulterants.

Please mute your phones when not speaking to prevent any background noises. We have a public comment period scheduled for 12:40 p.m., following the last presentation prior to adjourning at 1 p.m. If anybody would like to provide a comment, they will be able to do so at that time. All information from today's open session meeting, including a meeting summary and meeting presentations, will be posted on the DTAB website. Any questions or public comments will also be posted.
Once again, thank you, everyone for attending. I'm now going to turn it over to Ron Flegel, the chairman of the Drug Testing Advisory Board and the director of the Division of Workplace Programs, for his opening remarks.

**Agenda Item: Welcome and Introductory Remarks**

MR. FLEGEL: I wanted to also thank Lisa for accepting the DFO position, and also thank Ana for being the acting DFO when we were in transition. So I do appreciate that a lot.

I want welcome all the board members, Ex Officios, federal partners, and industry leaders, and representatives and members of the public to this Drug Testing Advisory Board meeting. Thank you for taking time out of your schedules today to attend.

As you are aware, SAMHSA continues to improve the quality of services for forensic workplace drug testing in federally regulated testing and private sector testing by assessing the science and technology used in drug analysis, by improving the quality of related laboratory services, and systems for drug testing, and by setting standards for laboratory certification for federal workplace drug testing programs. Which again extends to many of the regulated and nonregulated drug testing sectors. We have helped to guide national policy, especially with the introduction of oral
fluid as an authorized specimen for the Federal Workplace Drug Testing Programs.

Regarding the DWP status update, the notice of proposed Mandatory Guidelines for federal workplace drug testing programs using hair was published in the Federal Register on September 10, 2020, for public comment. The public comment period closed on November 9, 2020. Again, a federal agency choosing to test a hair specimen as written in the Guidelines would be required to authorize collection and testing of at least one other specimen type that would be either urine or oral fluid that is authorized under the Mandatory Guidelines for federal workplace drug testing programs and to provide procedures whereby the alternative specimens is tested in the event that the donor is unable to provide a sufficient amount of head hair for faith-based or medical reasons or due to an insufficient amount or length of hair.

SAMHSA is currently engaged in revising the proposed Mandatory Guidelines using hair based on the public comments and review of the current scientific literature that was cited in the public comments. Once complete, the final draft of the hair Mandatory Guidelines will undergo HHS departmental clearance, and ultimately, OMB review, followed by a Federal Register publication notice.
The new proposed revisions to the Mandatory Guidelines for federal workplace drug testing programs using urine and oral fluid are currently undergoing OMB review and clearance. The goal of these proposed revisions will be to facilitate modifications to the authorized drug and cutoff as needed based on the science and emerging drug trends and to aid in the detection of donor attempts to subvert their drug test.

They are currently engaged in reviewing potential framework that incorporates the best available research and advice, including input from relevant regulated drug testing sectors. I had hoped that I would be able to present the information from the revisions for both urine and oral fluid, but unfortunately the Guidelines are currently under OMB's review.

DWP continues to focus on other special projects undertaken by the National Laboratory Certification Program in conjunction with RTI International and Johns Hopkins University, which includes Dr. Ed Cone, Dr. Ryan Vandrey, Dr. Tory Spindle, and Dr. David Kuntz of CRL.

Just to note, many of these items will be discussed in the DTAB presentations for the purpose of addressing emerging issues, and topics stated prior. I will have a follow-up presentation later in the program.
Again, I would like to thank everyone for attending the Drug Testing Advisory Board meeting today. I hope you find the presentations informative, and I do apologize for the delay. There were some technical issues, but in order to have it redundant so you could both sign in to the presentation as well as you had to sign in with your phone, so it was a little bit different than what we're used to.

With that, I will turn it back over to Lisa Davis, the DFO, to move forward. Thank you.

MS. DAVIS: Thanks, Ron. For our first presentation this morning, I'm going to turn it over to Bohdan Baczara, from the Department of Transportation.

Agenda Item: Department of Transportation (DOT) Update

MR. BACZARA: Good morning, everybody. Bohdan Baczara here.

Thank you for having us, and also the opportunity to provide an update on our programs. The things that I'll be highlighting or talking about are the COVID-19 guidance that the agencies have put out. I'll be providing the latest data from the Driver Clearinghouse Database. I'll talk a little about the oral fluids notice of proposed rulemaking that we just published in the Federal Register.
And also the availability of the MIS aggregate data for the public.

With respect to the COVID-19 guidance, still in effect, we have three DOT agencies including ODAPC, that have issued guidance related to drug and alcohol testing during COVID-19. In essence, the bottom line and the big picture is that you are to continue doing testing. If you cannot conduct tests for certain reasons, to fully document the reasons for not being able to conduct the test related to COVID-19, and that will be something that the DOT agencies would take into consideration when they're auditing that particular employer or service agent.

With respect to ODAPC guidance, there are two statements that are out there. The first one is the statement of enforcement discretion for substance abuse professionals and service agents. We just updated it -- not just, but November 29th -- and we've extended it until June 30th of 2022. In a nutshell, it basically says that for collectors, BATS, STTs, Medical Review Officers, and substance abuse professionals, if you do not have an opportunity to get requalified, your qualification status is still good, and you can continue acting as a service agent.

For the Substance Abuse Professionals, with respect to remote evaluations, that it is optional, and you
can conduct your assessments via remote video, but it must be a two-way audio and visible remote video. Again, this was extended until June 30th of 2022.

The other guidance document that we have out there, has been standing from the beginning, is that again telling service agents, that they do need to conduct testing and if testing cannot be conducted, to fully document why and obviously coordinate with the employer.

Here is the latest data from the Federal Motor Carrier Safety Administration's Driver Clearinghouse, and you'll notice there's a link at the bottom, you can access that report directly. In a nutshell, the clearinghouse became effective on January 6, 2020, and several entities are required to input information into that database. That includes employers, Medical Review Officers, and Substance Abuse Professionals.

Overall, since the beginning of the program, there have been just over 11 million queries conducted, and queries meaning that employers are looking to see the status of a particular individual to see whether or not they have a drug or alcohol violation. The number of drug violations reported as of February 1 was 115,367. The number of alcohol violations was 2,639. And with respect to the prevalence of drugs, the top three were marijuana,
cocaine, and methamphetamine, and pre-employment being the test reason with the most reported drug violations.

There are 83,283 drivers in a prohibited status. That means that they were reported as having a violation and they have not completed the mandatory return-to-duty process, and therefore an employer cannot use them in a safety-sensitive function until they complete that particular process.

With respect to the rulemaking, we were very happy, very proud, to announce the fact that we had issued our notice of proposed rulemaking for oral fluids. We issued it on February 28 in the Federal Register, and comments are due to us by March 30 of 2022. The link you see there, it takes you to the actual PDF of the Federal Register notice, and what I wanted to do was just highlight some of the times that we are asking for comments on.

We are proposing to permit oral fluid testing as an alternative drug testing method for DOT-regulated employers. That does not mean it will totally replace urine drug testing, but it will be something that we're asking for comments on whether or not to include it and whether it should be used in certain situations, certain test reasons.

We're harmonizing with the HHS Mandatory Guidelines with respect to oral fluids. Basically, we're
proposing to use the same collection procedures that HHS has outlined. And we're also proposing to allow the direct observation urine collections by any licensed or certified medical professional legally authorized to take part in a medical examination in the jurisdiction where the collection takes place.

Some of the other proposals are to allow the medical review officer staff to contact pharmacies to verify prescription medications. The other whether or not an MRO can un-cancel a test once they did cancel a particular test. Allow the use of options for official identification numbers issued by state or federal authorities, instead of Social Security numbers. That would be on the chain of custody form, as well as the alcohol testing form.

We would be proposing to have laboratories provide the DOT biannual data to us, by test reason and by specimen type. Currently, they only provide a dump of all the test results performed. The other is laboratories withdrawing from the NLCP program to continue to provide data to us for the period in which they withdrew from the program. And we're proposing for laboratories be required to keep nonnegative specimens for only 90 days.

The final slide on this is that the proposal to require that the phone number put on the federal chain of
custody form by the collector be a number that would go
directly to the collector and not to a general call center
or a supervisor. That remove provisions that are no longer
necessary, such as compliance dates, and we're proposing to
remove all the cross-reference sections found at the end of
the sub-parts of each of the sections. We're also adding
clarifying language to other provisions, such as
definitions and web links as necessary, and we're also
proposing to allow substance abuse professionals to conduct
evaluations virtually.

That kind of sums up the major points of the NPRM
that is out there. We highly recommend that everybody
involved in the DOT drug and alcohol testing industry,
employers, service agents, including SAP’s, including MROs,
including laboratories, that you all take a look at the
NPRM. Please do provide your comments, read other people's
comments and comment on those comments. This way we're
going to get a full breadth of what's out there and what's
what. Please take note of that and please do submit
comments. Thank you.

MIS aggregate data, I just wanted to highlight
the fact that we do have a set of data out there on our
website. You see the link there. Basically, what it is is
a dump of all the MIS data provided by employers by DOT
agencies, when they're required to do so by the DOT
agencies. It does not contain any personal data. It is just a dump of how many tests were conducted and what the final answer is, meaning positive or negative, and if positive, for what drug.

And we're just making it public that it's out there. If you have any questions, if you think it's of use to you, please do let us know, or if we need to modify it or present it a different way that would be helpful to the public, that would also be good. We did update that information to provide data limitation information on there as well, so that you know what is what when you're looking at the particular data.

That's it from my presentation. I just wanted to provide a couple of resources for everybody out there who's not familiar with our program or our web page. It's transportation.gov/odapc. It's a one-stop-shopping website for all the DOT agencies with respect to their regulations, their contact information, and specifically Part 40.

We do have an "Am I Covered?" decision tree on our website, so if you're not familiar with or you're not sure if you're covered by DOT regulations, you can certainly go to that application and find out if you are covered. We do have a listserv available to everybody, so if you do want to know what's going on in the DOT world related to drug and alcohol testing, you need to subscribe.
And also it is a requirement for service agents such as breath alcohol technicians, medical review officers, SAFs, and laboratories to sign up as service agents into that particular listserv.

Our regulation part 40 is on that particular page. So that's a good resource as well. And we do have a guidance page, and if you're, after looking at our wonderful website, and you still don't know what the answer is, and you want to reach out to us, certainly email us at odapcwebmail@dot.gov.

I think that's it. Thank you for the time. Appreciate the opportunity to present.

MS. DAVIS: Thank you. Our next presentation will be from Brian Zaleski with the Nuclear Regulatory Commission.

**Agenda Item: Nuclear Regulatory Commission (NRC) Update**

MR. ZALESKI: Good morning. Thank you so much for the opportunity to provide some updated information on the NRC's Part 26 Fitness for Duty program. My name is Brian Zaleski. I'm a fitness-for-duty specialist, and my colleague Paul Harris is also attending this session, although he's not speaking today.

There's entirely two people that support the fitness-for-duty program at NRC, unlike DOT, who regulates
a tremendous amount of the United States, American civilians operating safety-sensitive positions.

We just wanted to provide a brief update on a couple key elements of our program that might be of interest to the Drug Testing Advisory Board and have some updated information, at least on one element, subversion attempts, which I know that there's a presentation later today on that that might be beneficial.

Always helpful to understand the program objective of Part 26. Part 26 is a broad-based program, and we'll go through those pieces of information to help the public understand one of the key elements of fitness-for-duty at NRC licensed facilities. We're talking about operating nuclear power plants primarily.

We have a rulemaking that is in final rulemaking stage. The commission is currently voting on the package and hopefully we'll be getting some information on their decision soon. The FFD, fitness-for-duty, program performance trend that I spoke about briefly, on subversion trends, every time I make presentations to the DTAB, I talk about this because it's an ongoing issue. Especially in the nuclear industry and the way we capture the data, we have precise information, and we can share that it might be beneficial to others.
And then some laboratory performance issues that have come up this year that were unique and unusual, I would say, compared to normal operating environment. Clearly, we're dealing with COVID, clearly, we're dealing with other issues in our country, that may have resulted in some of the issues for we've seen in the past year.

The program objective of the NRC's fitness-for-duty program is that a licensee, so the way we regulate entities is we issue a license to them to have a license to operate a nuclear power plant. A licensee must implement a fitness-for-duty program to provide reasonable assurance that persons are trustworthy and reliable. When we say trustworthy and reliable, that's specifically related to an individual and making sure that they're not going to attempt to sabotage a nuclear power plant. This is to make sure you do not have bad actors inside of nuclear power plants.

The other element of that is not under the influence of any substance, legal or illegal, or mentally or physically impaired from any cause, which in any way adversely affects your ability to safely and competently perform assigned duties.

Clearly, that directive, the objective is beyond the drugs that we test for. One of the key elements of our program and any other regulated program is there's defense
in depth to make sure that we provide an adequate level of assurance that individuals are not going to harm individuals because they're impaired.

This is just a high-level schematic of the different key elements of the defense in depth strategy, although they're not all of them. So access authorization at the top of the pyramid. In order for an individual to walk around a nuclear power plant unescorted, they need to complete an access authorization process, and it's a detailed process of fingerprinting, criminal history check, reference checks, et cetera, psychological evaluations. It's quite detailed. And that's in addition to the fitness-for-duty part of this, which is the drug and alcohol testing.

As well, comparable to DOT's hours of service, we have a fatigue management program that applies to specific individuals or job categories that work inside power plants, and then behavior observation. This is the for-cause testing, reasonable assurance testing.

Rulemaking updates. There's been a Part 26 rulemaking ongoing for quite some time. We had a proposed rule that was issued back in 2019. During the proposed rule phase, we received sufficient public comment to warrant modifying the package in final rule phase. This package initially started off aligning our drug testing
panel to the substances and the cutoff levels with the 2008 HHS Guidelines, which have been in place for quite some time, since 2010. Based on comment we received during the public commenting phase, we have proposed, the staff has proposed now -- this is only a proposal to the commission. They're going to vote up or down on this and give us direction as the staff whether to proceed or not.

So what I'm speaking about here is not a done deal. It's just what the staff has proposed. And these are publicly available documents to look at. What we proposed to do, what we changed in the final rule is to align the drug testing panel with the current HHS Guidelines, urine drug testing panel, so all of the substances, cutoff levels would be aligned up to date with 2017 Guidelines.

In addition, during the public comment period, we received comment related to whether there was a viable alternative to conducting an observed urine collection, so we believe that there is. Oral fluid specimen Guidelines came out right when the Part 26 proposed rule was published, and so we have incorporated that element within the final rule that licensees and other entities would be provided the option to collect any specimen that under observed collection conditions using oral fluid specimen.
Finally, one of the core elements of our program, as I talked about, the access authorization, but also fitness for duty, is subversion. Individuals attempting to cheat the drug-testing program, both they're using impairing substances and they're also willfully acting to thwart the commission's regulations. These individuals are a threat to our safe and secure operations of power plants, and we make sure that we have very strong measures in place to identify these individuals and prevent them from working. It's a regulated space.

Data over time has demonstrated that there has been a lot of folks that we have been identifying that have attempted to subvert the process. We strengthened our provisions in Part 26. The provision that we've strengthened is to require limit of quantitation testing for any specimen that's collected under direct observation conditions. So if an individual submits a specimen, a non-observed specimen out of temperature range, that second specimen that's collected will be subjected to the limit of quantitation test, so that will be drastically lowering cutoff levels under those circumstances.

Laboratory performance. There are a couple of key elements that popped up. One was very unusual. The first was -- nuclear power plants are in outage typically every 18 months, and when they're in outage, power plant's
not generating electricity, it's a very costly situation for utility. They have a large number of individuals, 800 to 1,000 individuals, that come on site to do the refueling elements and any kind of maintenance that they need to do. These are big events for utilities, and there are a lot of individuals.

At the time of one outage, there was a severe weather event that shut down a shipping hub for a major express mail service, and there were several hundred specimens that were unable to be moved to the laboratory within the required time for testing by Part 26. So that created somewhat of a dilemma for that licensee. We ended up issuing an exemption to the requirements to give them some additional time to get those specimens tested.

The second bullet I wanted to bring up is there's been some issues with shipments of specimens either being lost in transit. These are hard to kind of glean the information on how this is occurring. In this past year, we've tested 115,000 specimens, so things may get lost in transit on occasion. We don't have uniform data collection requirements on that, but on occasion specimens do get lost. There was an uptick in this type of activity at the end of the year, so we're still evaluating it, looking at information that we've recently received. We have annual
reporting requirements that licensees submit information to us, so we're still in the process of evaluating that.

Third topic, the specimen testing delays, not meeting the five-business-day testing requirement. Our rule requires five business days, we need to turn around test results within five days. Sometimes, on occasion, this will occur if the laboratory is batching confirmatory specimens, and I know that it's an issue with 6-acetylmorphine testing. Our rule requires 6-acetylmorphine testing to only be conducted after a confirmed positive on morphine. The final rule for the commission will address that and initial 6-acetylmorphine confirmatory so hopefully it will address that issue.

Another situation, this was a new thing that came up, and I think this was related to an operational change for a limited period of time with one of the laboratory chains that has several locations, where specimens that a licensee sent to their testing laboratory were redirected to other HHS-certified labs in that organization, and the specimens were not meeting five-day testing requirements, and at that time there was not great tracking where those specimens were.

Again, this is something that occurred in the fourth quarter of 2021, and we're still evaluating that, but this impacted a number of our licensees. The nuclear
industry does not use a large number of HHS-certified laboratories, I think in total nine. And so therefore it’s something that's significant in our mind. Our licensees must use the laboratories they are under contract with. They can't redirect a specimen to another laboratory. We have annual auditing requirements, blind specimen testing requirements for the laboratories they use.

There are only two circumstances under our rule that permits a licensee to send the specimen to another laboratory. One is if it's a donor requested retest of a specimen, challenging a positive, adulterated, or substituted result. The other one is if an invalid specimen is received and the certifying scientist and the MRO believe that there is a possibility of identifying that adulterant at another laboratory, which I've never seen. But those are the two options for using a laboratory that's not under contract.

Finally, one HHS-certified laboratory ceased operations, and it impacted a number of our licensee testing programs, who had to redirect their specimens to other laboratories. So those are unique circumstances, almost exclusively, that I have yet to see in the many years of looking at these reports.

I apologize for the busyness of this slide. I always do that. But I wanted to provide enough information
on here to demonstrate that this is a substantial trend. Subversion attempts, it's a willful act or attempt to cheat on a required test, and generally, the way these play out, is an individual is wearing a synthetic urine in and they're identified because the specimen is out of temperature range or the collectors observed physical characteristics, that the specimen isn't consistent with urine odor, viscosity, it's bubbling, donor behavior, unusual or the absence of sound in the collection facilities. This trend has been going up for quite some time.

We collect individual-specific information on each event. So, for any positive result for an individual, any refusal to test situation like a subversion, there's a PDF file publicly available on our website. A licensee downloads that, they complete it, and we collect information. So, we collect really good, detailed information on subversion attempts. Primarily, the way these things are playing out, an individual us sneaking in a synthetic urine on a predictable testing event. There's a large number of them that are occurring, and they have been occurring over time. You'll see the top line there, it's between 305 and 272 individuals.

To give you sort of a little bit of context for that, I pulled the data that we had in our system since
2014 when we uniformly collected data from the individuals, and we've had 2,195 individuals that have been identified subverting attempts in Part 26, and what that basically is equivalent to is two years' worth of testing violations over that eight-year period of time were subversion attempts. So, this is a huge deal for us, and bolstering the ability to identify individuals using synthetic urines is a significant ask of ours, and I know a lot of other agencies as well.

To give you a perspective on that, that's more violations for subversion than for alcohol test results, in each of those years.

Typically, these are playing out on pre-access testing. Predictable testing event. And they're almost primarily driven by contractor-vendors, which provide a lot of limited services during outages. So, it's almost exclusively limited to contractor-vendors. And it is widespread. The last line item on there is the percentage of sites reporting at least one of those, one subversion, from 50 percent up to 70 percent. So, we're seeing more and, in many cases, numerous subversion attempts.

I do caveat this data because our data reporting closed about a week ago, so I tried to scrub this data as best as possible to present this, but these are pretty solid in terms of this trend has existed for quite some
time, it's not decreasing. Our collectors are highly trained and there's been a lot of best practice training amongst our licensee sites. They're acquiring subversion products, evaluating the types of technologies individuals are using. Occasionally these will be identified when individuals are entering the power plant. They go through a secure checkpoint where there's a metal detector, random pat-downs, where they'll often can identify these products, and then result in a for-cause test if they're in possession of them.

So that's subversion trends. Two of our asks, and to present whether DTAB or HHS is considering evaluating these. One is the acceptable temperature range on urine specimens. I know that we're getting additional tools, and this is a wonderful state of drug testing in the United States, to have not only urine, oral fluid, eventually hair, we all know that each of these have their benefits and limitations. I think DOT did a very nice job with the cutoff level table and having a proposed rule to demonstrate that there were variabilities in cutoff levels between oral fluid and urine. So, we have to be strategic about how we're using these specimens.

But urine drug testing will not go away, and so our licensees have always, many of them, have measured the urine temperature independent of the collection cup and
have a lot of data on this to demonstrate that individuals are able to be identified simply by having an accurate recording of temperature, and for instance, if somebody has 115-degree Fahrenheit urine temperature, they're not living, right? So that's pretty clear information that specimen did not come from them. So, the temperature band on that cup just isn't going to provide that level of detail. Having some information on whether we could tighten that range might benefit us in identifying additional individuals, or at least making it more difficult for people to subvert the testing process with a substitute urine.

The second one is that we've had a number of events, and our MROs have the ability to do this, where they've called subversion determinations on two specimens that were collected from the same individual, at the same collection event, so it's typically urine's out of temperature range, or there's some other indication of a possible subversion attempt. So, a second specimen is collected, and there's divergent temperatures. And while both of the specimens have come back negative, because this does happen, and I've seen this because individuals are either using drugs we're not testing for, or they stopped using long enough that it was not detectable. However, there have been such large discrepancies in the other
constituents in their urine that a subversion determination wasn't possible. And I just wanted to share one or two of these examples for consideration.

Here's an example, the out-of-temperature range specimen is 107.7 degrees, and typically the reason why we're able to report that temperature is industry in large part has been using either infrared temperature measurement devices or they're using a digital thermometer with a disposable sterile sheath that they're measuring temperature directly in a cup. So, 107 degrees, creatinine 61.6, pH 7.1. The observed collection was 97.1 degrees. So, 10 degrees difference right there. Obviously, that's not possible from a human being.

Creatinine in initial was 61, the creatinine in the cup, the second observed collection was 113. And the pH in the initial was 7.1, pH in the observed was 5.5. So, very significant differences in the other measurements that were taken of constituents or physical characteristics of specimens that could provide useful information. So, we would request or suggest that we try to establish an additional criteria to make determinations of subversion attempts from these other specimens. An individual may be able to sneak in a synthetic urine that's formulated to be consistent with a urine specimen, but they can't formulate it to be consistent with what's in their body.
So, those are the two sort of things that we think about in terms of the number of events we've seen, 2,195 over the last eight years.

And I think the last slide there is just to highlight the forms that we use to collect data. These PDF forms, they've been transformative, we've used them to support reasons for rulemaking changes. We were able to target where drugs are appearing in our testing program.

Bohdan, thank you for mentioning the DOT's data, the MIS data. We did use that data to support moving forward with expanding our testing panel to include the four semisynthetic opioids, and it was because we had timely data from DOT and a large sample that you have, to demonstrate that it was important for us to consider as a regulator. So, we appreciate that data being there.

And the last slide is contact information. Thank you for the opportunity to present some of this information to the drug testing advisory board.

MR. FLEGEŃ: Thank you. Thanks, Brian, for presenting.

MS. DAVIS: The next speaker we have giving a presentation is Joseph Kotarek with the Food and Drug Administration.
Agenda Item: Food and Drug Administration (FDA)

Update

DR. KOTAREK: Thank you. As she said, my name is Joey Kotarek. I'm from the FDA. I'm acting branch chief for toxicology in the Division of Chemistry and Toxicology Devices, and all in vitro diagnostics, drugs of abuse assays, come through our group.

I did want to go through a few bookkeeping pieces first. I don't quite know if there's been some update or what the flexibility is in the agenda. It looks like we're a bit behind time so I'll try to go through my slides efficiently.

The other point is that, again, I am happy to take questions now or later. I have the chat window open. If you have a question, I should be able to see it there, I think. However, I don't know if that is the format that you guys had in mind for this meeting. If you guys want to have questions another time, I can answer those later, which is also in conflict with my earlier statement of going through slides efficiently. But I can see your questions if you put them in the chat, and I will try to move through, go through some updates, and some other pieces about, give you some details about how we regulate oral fluid drugs of abuse tests and some of the things we look for in point of care tests.
As I said, I'd like to go through a few updates about what we look for and specifically what drugs of abuse tests we look for. There have been some updates to the regulation, so I want to go through what's provided to FDA and when we see it. I also want to talk about how we review oral fluid drugs of abuse tests, what we look for, some of the differences in what we look for when we're looking for the validation of an oral fluid test, versus, for example, a urine test. And I can cut to the chase; what we look for is obviously the differences are in the sample collection, which adds some new complications that need to be addressed, and also the cutoffs are going to be different, and we look for evidence to support that those cutoffs are valid, as well.

Finally, for point of care drugs of abuse devices, again, I want to talk a bit about the data that we look for to ensure that those devices perform, give accurate and reliable results. To cut to the chase, the differences in those tests, the evidence that we look for, evidence that it can be used by not just run in the lab or by highly qualified staff, but whoever the intended user is and in their intended use environment, that they are able to accurately collect and interpret results as appropriate.

Starting from the top-level view, most drugs of abuse tests are regulated under what we call a Class II or
moderate risk regulation. And most of them require 510(k) clearance prior to marketing. And that applies to a broad swath of devices; that's prescription devices that are everything from what would be run on a large clinical analyzer, maybe as a single assay, maybe it's part of a panel of over a dozen drugs, that you'd be screening for.

All of that would be under the same kind of classification. That also includes point of care, which would be anything done at the patient's bedside or an emergency room, where you're doing the test and interpreting it next to the patient, not taking it back to a laboratory for interpretation.

Over the counter drug tests are also under the same 510(k) clearance. We look for a little additional information to ensure again that the intended use population is able to accurately use those. I'm not going to go into many of the details about over the counter testing and what we look for there. I'm going to focus now more on the prescription use devices. But I will say that in terms of a lot of the testing for all drugs of abuse that we look for is common. Depending on where you want to use it, we might look for some additional testing, to ensure that it works well. But a lot of the testing, it's not specific as much to the drug, as much as it is specific
to the intended use environment. I'll get to that more in a bit.

I wanted to back up, because I said there was some updates to what we look at, and this was the update to which I was referring. At the end of 2019, there was an update to the Federal Register, where we exempted many drugs of abuse assays from the requirement to submit a 510(k) prior to marketing. And I'll go ahead and read this, and this is a drugs of abuse assay is not exempt if it is intended for any use other than employment or insurance testing or intended for federal drug testing programs. The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter, subject to the limitations of 862.9, which I'll get to in a moment. Provided the test system is intended for employment and insurance testing and includes a statement in the labeling that the device is intended solely for use in employment and insurance testing and does not include devices intended for federal drug testing programs. E.g., programs run by the Substance Abuse and Mental Health Services Administration, SAMHSA, the Department of Transportation, DOT, and the U.S. military.

So, what does that mean? If you go to the next slide, I'll try to sum up in less legalese. What it means is if you have a test that you want to sell for exclusively
for insurance and employment testing, and that testing, it's preemployment screening that is not related to, well, anything that's been discussed today, not for any type of government program, not DOT, DOE. Not for SAMHSA. It's just for commercial employment and insurance screening, and you do not exceed the limitations of exemption, and by that I mean, there are -- not specific to drugs of abuse, but for all medical devices, even if they would otherwise be exempt from 510(k) requirements, and I should pause -- by 510(k) requirement, I mean before you market it in the United States, you submit a package of information to the agency that demonstrates that your device is safe and reliable, and you do that before you market the device.

If your device is only going to be used for this employment and insurance testing, then you do not have to, and you don't exceed the limitations of exemption, you do not have to send that pre-submission to the agency. You can go ahead and market it without sending in that 510(k) submission with that information showing us the device works.

You do have to have, I should caution, you do have to have that information. The device is still regulated. It is still a medical device, and you would need to keep that on file. If you are under this new exemption from 510(k) requirements, you are still subject
to, for example, all post-market -- if there are problems, you can be inspected, and you would be expected to have all that information on file. But you would not have to submit that to the agency prior to marketing it.

The limitation of the exemption that is, there's a few, and if you go to the regulation, it will list them all in exhaustive detail, but in brief, if it is a new technology -- for example, if you are a first-in-class, you have a new analyte that's never been measured in oral fluid before, we would expect that that would trip the limitations of exemption, because we would consider that a new technology and it would need to have a 510(k) submission that would need to be sent to the agency before the device was marketed.

But, for example, if you have a barbiturate assay that's going to be used in oral fluid and it's going to be used only in employment and insurance screening, that is not for federal use in any way shape or form, and it is for prescription use -- it does not trip the limitations of exemption -- then there are devices that have already been 501(k)-cleared for measurement of barbiturates in oral fluid, and you could market that without coming to the agency prior to marketing it. It would need to be registered as a medical device, and if you are interested to know what devices do exist and are presently marketed,
there's a link to the registration and listing database where if you follow that link you can find every medical device that is registered with the agency, including all drugs of abuse assays that have been registered for the agency and sold in the United States.

What hasn't changed is everything else. Again, this exemption from 510(k) submission requirements, where you would need to send this package of information to the agency prior to marketing the device, if you are intended for anything beyond non-federal employment and insurance testing, if you want to be used in any federal program, if you want to be used for any type of clinical indication, then you are not 510(k)-exempt, and you would need to send in what we call a 510(k) submission package to the agency, that would be reviewed by the agency.

We'd review that data, and I'll talk about that a bit more in a second. But then you would also, in addition, register and list, so if you go to that registration and listing database, you can find all devices 510(k)-cleared or no, that are sold in the United States as medical devices.

Next, and I'll use the term 510(k) submission a lot, I want to try to unpack a bit more about what that is, and also how you or anyone is able to find more information
about any drugs of abuse assay that has a 510(k) clearance, that has been reviewed by the agency.

This is probably, the next three slides are probably, hopefully, the most useful information that I'll present today, so if you hear nothing else, please hear this. All 510(k) cleared devices, we review the information and then we post a summary of that information, the validation of those devices, publicly. You can find it if you go to this link, you can find this database, and it has every drugs of abuse assay that has been 510(k) cleared. And it also walks through all of the validation data that has been used to support the 510(k) clearance of that device, to show the device works and it works in the hands of the users who are going to actually have it and generate results.

It's admittedly not the most user-friendly database, but it is very helpful. It's definitely not the worst. I probably should sell it better than that. But I would strongly encourage anyone who has questions about what we look for in drugs of abuse devices, in terms of their validation and the information FDA is looking for, I'd strongly encourage you to go to this database. You can search by -- if there is a particular manufacturer you want to look for, you can search by applicant name. If you're
familiar with the product code for a particular device, you can search for that.

But one example I'll walk through, is if you were to go ahead and search for -- one of the nice convenient things about this database is almost all in vitro diagnostic devices have the analyte name that they measure in the device name. So, if you just search by whatever drugs of abuse you're looking for, you'll find dozens if not hundreds of examples.

So, if you were to, for example, type in amphetamine, I'll show you what you see. Here is a list of -- and you can see there's ten results per page, and there's over ten pages. We have many, many devices that have been 510(k) cleared for measurement of amphetamine. And just even on this front page here, you can see there are prescription devices, there are over-the-counter devices, there are devices that are for urine, there are devices for hair. There are devices used individually, there are devices to be used as part of a panel to detect multiple drugs of abuse, and I want to encourage you -- again, even by what could be a two-minute search, you can find all of this information, and each of these links will lead you to a summary of the information that was used to support -- and that's a great question.
I will say, unfortunately, forensic use devices, where they would be used in criminal justice, that's going to be out of the scope for this discussion, and if you have a question, please follow up with me later and I can try to address that offline.

On the next slide I can show you a bit more of what you see. If you just follow one of those links, you can get to what we call the 510(k) decision summary. This has, not just all of them, for this specific device, which is for measurement, as you can see here, amphetamine, cocaine, methamphetamine. It's just a test strip, like an immunoassay test strip, it has the 510(k) number, and this has, if you follow that link and go to this, just go the site, you'll find this page, and it'll have a summary of all the data that supported the device accuracy, supported the device precision, supported -- listed what interferents were tested and found potentially would interact with the device, any interference or other drugs might cross-react with that were tested, as well as the intended use environment, and if you also are a device manufacturer, and you're looking for what testing is the FDA looking for that I need to do to validate the device to provide to the FDA, this is a great resource to look at many of the, most of the test, it's common across almost all drugs of abuse, it is specific to a cutoff. Meaning the concentration that
you would test are more specific to the cutoff, which is specific to the analyte and the sample matrix that you're measuring.

But, again, please use this website. We've put a lot of work into trying to get this information out there for every 510(k) clearance that we grant. And we do hope it's helpful. If you have questions after looking at it or before looking at it, we're happy to talk to you, but I would really encourage you to use this resource.

That's probably the most important thing, or at least the most useful information I'll give, and I'm going to go through a lot more discussion giving a top-level view about what we look for in oral fluid and point of care devices, but as I said, if you have three slides that you take home from this today, please take these three.

I wanted to pivot a bit to talk a little more specifically about drugs of abuse, oral fluid tests. We've cleared many, we've reviewed many. We have maybe a dozen different drugs that we have reviewed the information for and are sold as medical devices that have been 510(k) cleared in the United States, both as individual assays, we see them in drug panels where multiple drugs can be tested at the same time. We've seen oral fluid tests where they're sent to a central lab for testing, versus also
we've seen point of care testing as well that's been 510(k) cleared.

The advantages are, I think most people here are familiar, the sample is easy to collect, it resolves a lot of issues around observing sample collection. There are, at least from the FDA's perspective, additional concerns that are unique to oral fluid that you wouldn't have to necessarily consider or validate when you're working with a urine or other alternative sample.

In brief, those are biocompatibility, just ensuring that the sample collection is safe for the individual you're collecting from. Also, there are some performance considerations. Is the device accurate? And that's not just is the device itself, does it, if you were run this in a lab, will it give you the correct answer, but in the hands of users and unique work instructions the user will have to execute that are specific to oral fluids versus what you might give for an alternative sample matrix, are they able to execute those in a way that gives reliable information?

And finally, there's additionally clinical validity. Because all of the concentrations for drugs in oral fluid are not necessarily, aren't usually different than what you would see in urine or in some other matrix. So we would need to make sure that the results that you're
getting have clinical meaning and that they are able to detect recent use of the drug.

So first, talking about user safety and just biocompatibility, if you have any sample collection where, for example, a sponge that the individual might hold in their mouth to collect saliva or oral fluid over a course of several minutes, that is mucosal membrane contact, that we would raise this question, just we want to make sure that it didn't create any biocompatibility issues where it would somehow harm or damage tissue or the individual.

After you recognize the standard for biocompatibility testing, and the testing we would expect based on the exposure to the individual -- and that covers everything from what you see here, from relatively brief mucosal membrane contact to an implant that you would maybe wear for months or even years. Obviously, the testing that you would do would be less robust for something that has a contact time of a few minutes, rather than, say, an implant. But there is still testing that we look at.

As noted, we have guidance on how to apply that standard that is publicly available, and also, if you're like me and your background is not in biocompatibility, we also have, we try to update the website such that there's guidance on using the guidance that will walk you through what is the duration of contact, what type of tissue does
it contact, is it skin penetrating, is it just contact with mucosal membrane, contact with just intact skin? And it'll walk through the types of testing that we're looking for.

Typically, for biocompatibility for a mucosal membrane contact like a sponge, we often see testing that validates cytotoxicity, irritation, and sensitization, to ensure -- that's the types of testing we often see to support a sponge you might hold in your mouth for, say, 5 to 15 minutes.

Again, I would encourage you, if you have questions about any specific sample collection, I would look at the guidance documents referenced here for more information about how to inspect any specific sample collections. They do vary. It can be anything from somebody who, for example, spits in a tube, to someone who holds maybe a sponge or other device in their mouth to collect samples.

Here I wanted to talk about the next aspect we look at, which is what is the performance of the test in terms of how well does the device result correlate to the clinical truth, the actual concentration of the analyte that's in the sample, or even in the individual, but does it relate to the intended use claim, does it detect recent use of the drug? It's mentioned earlier, for oral fluid, that isn't just does the device work when everything is
done perfectly, but we also look at can the sample collection be done accurately and does that sample collection have any impact on the substance device results.

Ideally, what we want to see is something more akin to that graphic on the right. We recognize no device is perfect. Users will occasionally have errors, either inadvertently or purposefully. Also, the devices may not just technically be perfect. There is no such thing as a perfect device. If you run this 1,000 times, it will not always give you the correct answer. But we want to see something where we see highly reliable results, rather than what we see in the graph on the left, where the device is telling you -- and maybe even if you send it for confirmation testing based on the error that you might have, it might even give you, like if you send it confirmation testing, that result may not be accurate, and we want to ensure that we're able to quantify that so we know how well these work and also minimize the error such that it's able to be considered a reliable and actionable clinical result.

As I referenced before, there's for oral fluid tests, one of the questions around performance is around a lot of it is around sample collection. Some that's pure usability. Can an intended user provide a sample? And that's, for example, sometimes it's sample volume to run
the actual assay, including the confirmation assay, you want to make sure that the collection device itself is capable, in the hands of the person it's going to be used on, able to provide a sample. And also that they're able to follow the instructions for providing the sample that are given to them, for example, on the package insert of the device, to ensure that they're able to follow those instructions.

If your instructions say, for example, to hold the sponge in your mouth for 5 to 10 minutes, are not just an average person able to do that, but maybe especially, as many of these are used as part of treatment or monitoring for an identified drug user, their ability to generate saliva may be very different, may be inhibited from, say, an average user. So, we would look for, in a 510(k) submission, evidence that the intended user, whoever's going to be providing the sample, and often cases that is an active drug user, is able to provide that sample following the instructions for use. And that involves obviously looking at these volumes that they're able to provide, and if there are instructions around how long to provide it, that those are actionable for the actual intended user, that they provide within that window.

The next thing we look for is accuracy. Does the amount of analyte and drug that has been collected map to
what the amount of analyte that actually was in the sample originally? Sometimes we have seen that the actual sample device itself can interfere with the -- for example, absorb some of the material or otherwise interfere. So, we want to make sure that that's validated fairly robustly.

For that, we use a combination of spiked synthetic, artificial samples, as well as native samples that have been collected by drug users. We look for validation of every step in the process, because we want to make sure that there's no step -- and that's everything from, if there's any extraction, if this is going from a sponge to some other diluent prior to measurement, if this is going to be shipped, if the instructions say it can be stored for six months -- we want to know that if the sample sits in that sample collection tube for six months, that it's going to still be representative of -- the concentration you measure after six months is still representative of the concentration when the sample was collected. So, every step in the process should be validated just to make sure the recovery is accurate and representative of when the sample was freshly collected.

Another piece that we look at is interference testing, which is looking at whether both substances that might interfere and inhibit, artificially lower device results, versus anything that might cross-react and
increase, like artificially positive device results. Obviously, in oral fluid, that's going to vary -- the substances you look at are going to be very different than what you look for in, say, urine or hair or any another matrix. And also we'd want to make sure that, for example, sometimes we'll see instructions that say make sure you have not consumed food or drunk or other, within, say, 10 or 20 minutes of collection.

We still want to know, one, what those effects, we want to make sure those substances are tested, especially if the device, if the instructions are misinterpreted, we still would at least understand what happens when that happens. Is that going to lead to an erroneous result?

The other thing is thinking about the concentrations of analytes that we test. The concentrations which you would see in saliva are going to obviously be very different than what you see in urine. So, we want to make sure that both the compounds that are being tested, as well as the concentrations they're testing at, are relevant to what maybe you'd find in an actual sample that you'd be collecting from your intended use population.

Looking at not just the sample collection itself, but once you actually have a device that's going to measure
the oral fluid after sample collection, we look for to make sure the device, the performance, we can quantify it and that it is accurate enough to ensure that we're able to get a highly reliable and actionable clinical information from the result. We look at, for precision testing, we typically look at spiked samples, where you take whatever drug substance you're attempting to measure, and you look at it around the cutoff. Because we want to ultimately make sure that, again, these are qualitative devices, and we want to make sure that if the sample is below the cutoff that it gives something negative, and above the cutoff it gives a positive result.

We want to see that not just in a lab. We want to see, for example, we -- whenever you're doing this, we would be looking for more than -- we have our own employees run this test, and they provided accurate results. We want to see the devices in the hand of the intended user and HCP out of sight, where they would typically be using it, such that the intended use environment and all the distractions that it might have are kind of taken into account when you do this testing, so that we really know what the precision, we have a good idea of what the precision of the device is going to be when you actually use it in the field.

Similarly, for accuracy testing, we look for, we want to see that you're collecting samples from intended
users, and also that they're collected by intended use operators. We want to see native intended use samples with concentrations both below and above the cutoff. And we really want to see that from the intended use population. For example, sometimes we've seen samples either that are collected from people who are probably not going to be the intended use population, especially if it's not for employment or insurance screening, if it's meant to be used as part of a treatment program, screening your own employees would not necessarily tell you as much about what you might expect a device performance to be as when you're in the intended use population, where it's a lot more likely, for example, that somebody in that intended use population, even if they don't have the drug you're testing for, may have other drugs of abuse in their systems, and you want to ensure that you have at least the opportunity to capture what impact those drugs are, or anything that that person might have ingested, what impact that may have on device accuracy.

Finally, we also look at especially at read time studies. We want to make sure that the instructions for use are followable. For example, if you say that the device is meant to be read between 10 and 15 minutes, we want to see that you're testing the device at 10 minutes, 12 minutes, and 15 minutes, in addition to that, maybe even
a bit beyond that, just to know if the user were to not quite look at their watch right or just was in a hurry or got distracted with something else that was going on, maybe had to deal with another patient, and then when they come back, what happened not just within that read time range that you claimed, but a bit beyond that, just to ensure that we know, if somebody's just briefly a minute over, or maybe a couple of minutes over, at what point does the device start to give erroneous results? Because we want to be able to account for the risk that any user does get distracted and does maybe not necessarily follow those instructions, so that we can account for that in our review.

Finally, as mentioned before, again, we want to ensure that even if the device is accurate, if it's accurately recording the analyte concentration or the concentration of drug that was in a user's system, that that concentration does map to an actionable result, and that the clinical validity of the cutoffs that we use where ultimately a concentration above a certain threshold indicates a recent use of an analyte, versus below that threshold indicates that there has not been recent use of the analyte. And as mentioned in an earlier slide, no device is perfect, and no cutoff is perfect. There are tradeoffs that you ultimately end up having to consider.
Both in terms of what is the tolerance for false positive and false negative results, but also how recent are you attempting to catch, versus something a bit more like are you looking for something like 24 hours or 48 hours. Like, what is the device able to tell you?

We look for that, the information to support all of that either comes from, for lack of a better way to describe it, the easier way to do that, in terms of the data that you would need to provide, the easier way would be to cite a previously established cutoff that has already been established as being clinically valid. For example, if you look at a device that has already been FDA cleared, already been reviewed and vetted by the agency, any given analyte with a specific concentration in that matrix, then you can leverage, we've already established the clinical meaning of that cutoff, and so you don't have to reinvent the wheel.

If you have a new cutoff that we haven't seen before, that would need to be supported by evidence, again, that it can detect recent use, and also quantify what that recent use is, and that can be either a published or unpublished study. I know there's guidelines, that for example, by SAMHSA and others, about what cutoffs make sense or are appropriate for oral fluid. But it's evidence that we would need to see, because by definition, if it's
not something that's previously been cleared, the FDA has not seen or vetted or assessed that information, previously.

So, having that information about what those cutoffs mean, what the risks of false positives or false negatives are, not just analytically, but clinically. Like, even if you get an accurate result analytically, like if you know the concentration there, how do you interpret what that concentration means? Because that's all information that we try to take into account as we review these devices.

So that is in kind of a 10,000-foot view some of the information that we look for in 510(k) clearances when we look for assessing and validating oral fluid devices and point of care devices. And thank you again for the opportunity to speak today, and with that I'll close, and I'll look forward to any questions that anyone has later in the session.

MS. DAVIS: Thank you, Joey, very much.

We're running a little behind schedule. Let's squeeze one more presentation in before the break. Next up we have Hyden Shen, who's going to talk about the Drug Free Workplace Program comprehensive review meeting coming up in May.

Hyden?
Agenda Item: Drug Free Workplace Program Summit

Meeting May 2022

MR. SHEN: Good morning and thank you very much.

The Federal Drug Free Workplace Program has been in existence for 30-plus years, and we're happy to say that it's not only seen as the gold standard within the federal sector, but also in the private sector, which have adopted our policies, procedures, and Guidelines to implement safe and drug free workplace programs for their employees.

In this 30-year-plus history of the program, it's been very stable, and we continue to base the direction of the program on medically and scientifically sound research and legally defensible decisions. In order for us to continue to ensure the integrity of the program, we are currently in the process of taking a look at the past, the present, and the future of the federal Drug Free Workplace Program, through a high-level review so that we can identify and assess critical issues and implement the proper programmatic policy and scientific updates that allow us to continue to protect and ensure the national security, public health, and public safety of our country.

Starting this year, we will be convening a number of workgroups made up of subject matter experts from the scientific, workplace, and drug-testing fields to provide
us with the insight into how best to plan and prepare for the future of the program.

In the interest of time, I'll end there. Thank you, Lisa.

MS. DAVIS: Thank you very much, Hyden.

(Break)

Agenda Item: NLCP Drug Testing Results

MS. DAVIS: Our next speaker is Eugene Hayes who will talk about NLCP drug testing results.

DR. HAYES: Good morning, everyone.

As of February 1st of this year, there were 21 certified laboratories. The largest group of laboratories was category 2. In this category, there were 6 of them. There are no category 0 laboratories currently in the program. We had six category 1 laboratories, which includes one IITF. We had six category 2 laboratories, one category 3 laboratory, and three category 4 laboratories and two category 5 laboratories. Excuse me, there is one category 6 laboratory and two laboratories that are category 7. Those categories were introduced into the program in 2018 and 2019 respectively.

During the past five-year period, there have been about ten labs that have withdrawn from the program. Those reasons for withdrawal are anything from changes in operations, mergers, inappropriate conduct regarding
forensic drug testing, and re-shifting of workload amongst laboratory corporation groups.

And on the bright side of those things, we have had one laboratory certified in the past five years in February 2019. We do have a couple more laboratories that are in the pipeline for certification.

The number of specimens tested in 2012 was 6.17 million. It rose to a high of 6.65 million in 2015. The number of specimens tested dropped to 5.75 million in 2016 but began a recovery in the following year and continued through 2019 at 6.56 million specimens in 2019.

The number of specimens tested in 2020 was 6.1 million, and that was down by 400,000 as compared to 2019. This testing significantly declined between March and April predominantly due to the onset of the global pandemic. However, testing did manage to rebound later in 2020. Monthly totals were up comparable to 2019, and in 2021 the number of specimens tested was roughly about 6.9 million.

The total number of specimens reported as drug positive, adulterated, invalid, or substituted (non-negative) increased from 136,000 in 2017 to 196,000 in 2018, a difference of roughly 59,000.

The first full year federally regulated testing for hydrocodone/hydromorphone oxycodone and oxymorphone in 2018, as mandated by the revisions to Mandatory Guidelines
for Federal Workplace Drug Testing programs for urine were effective in October 2017.

Non-negative reporting decreased year over year after that, 2018-2019, the decrease was 11,000, and even further, 2020, the decrease was 31,000 non-negative reporting increased significantly 2020 to 2021 going from 153,000 to 181,000. As a function of total specimens tested, the non-negative rate was about the same in 2020 and 2021 at 2.56 and 2.67 respectively.

However, in 2021, there were 19,432 specimens that were reported as invalid. We note that the number of specimens invalid due to pH rises in warmer months and is lower in the cooler months. This is a trend that we noted almost the beginning of the program. It's continued throughout.

As shown by this chart, the percentage of specimens reported invalid due to pH remains higher than other invalid categories. The percentage of specimens reported invalid due to pH continued to demonstrate a seasonal increase, March through October, and then decreased October through February.

In 2021, as a percent of the total tested specimens reported invalid due to inconsistent creatinine and specific gravity concentration increased by more than 90 percent as compared to 2020, while those reported
invalid due to possible oxidant activity decreased by about 33 percent.

Other invalid categories are abnormal physical characteristics, confirmity, immunoassay interference, all varied from month to month, but overall remained at the 2019 levels.

As shown by this chart, the percentage of specimens reported as invalid due to pH remains higher than other invalid categories. The percentage of specimens reported invalid due to pH continued to demonstrate a seasonal increase.

In 2015, the percent of specimens invalid due to pH rose well above levels that had normally been observed. The increase was primarily due to the number of specimens with pH greater than or equal to 9, but less than 11. The majority in the pH range of 9.0 to 9.2. This trend continued into 2016 and 2017.

The percent of invalids low pH related averaged 7.4 percent per month in 2016 and the first nine months of 2017. However, revisions to the Urine Mandatory Guidelines which included raising the lower pH cutoff from 3 to 4 for identifying specimens as adulterated resulted in a number of those specimens previously reported invalid due to the low pH, decreasing from previous years. Since the October
2017 effective date, the percent of invalids low pH related averages only 2.1 percent per month.

As a percent of invalid specimens, those reported invalid due to pH decreased in 2018 and what has been seen in years prior, this was due to the influx of specimens being reported invalid due to immunoassay interference. In 2021, we saw the percent of specimens invalid due to abnormal high pH increase, and many appeared to be reported in conjunction with the same specimens being reported invalid due to inconsistent creatine and specific gravity values.

There has been an increase in those specimens reported invalid due to pH greater than or equal to 9.5, and invalid due to inconsistent creatinine concentrations and specific gravity results, with creatinine less than 2. This increase began mid-2020 and has since continued. This could be a signal to indicate the presence of new synthetic urine or adulterant products in the market resulting in an increase in the type of invalid reporting. I'll talk about it maybe a little bit later, but we do have some adulterant studies that are going on currently.

Specimens reported invalid due to immunoassay interference during routine lab testing increased significantly in late 2017 and throughout 2018. There was a noticeable swell in the number of those specimens
reported as invalid due to immunoassay interference beginning around August 2017 and a rapid increase thereafter. The number of specimens being reported with immunoassay interference in 2017 more than tripled that what was seen in 2016.

In February 2018, two large labs notified the NLCP of the increase in invalid reports due to immunoassay interference. It was also noted that most of the specimens exhibited depressed immunoassay results with 6-acetylmorphine using CEDIA reagent and some had depressed results with amphetamine using CEDIA and amphetamine/ecstasy reagents. This data was presented during the March 2018 DTAB session.

It was suspected a substitution product containing something that interferes with the immunoassay caused a significant increase. The reports have decreased over the past three years, though are still elevated as compared to 2016 and the beginning of 2017.

Of specimens reported as invalid due to immunoassay interference, the majority occurred with the hydrocodone/hydromorphone immunoassay in 2021. Overall, the percent of specimens reported as invalid due to immunoassay interference stayed about the same in 2020 and 2021.
This slide demonstrates the decrease in specimens reported invalid due to immunoassay interference, 6-AM, since the highs reported in 2018 and 2019.

This slide demonstrates the large percentage of immunoassay invalids with interference for hydrocodone/hydromorphone in 2021. Of those specimens reported invalid due to immunoassay interference, roughly 60 percent had interference for hydrocodone/hydromorphone. At this time, all HHS-certified laboratories are using the same immunoassay kits for hydrocodone/hydromorphone.

Immunoassay invalids with interference for amphetamines and cocaine have remained consistently low over the past couple of years, as you can see. The combined positivity/non-negative rates have increased significantly in 2018, 3.27 percent. This was due to primarily to an increase in the drug positivity rate due to the inclusion of the opioids, hydrocodone/hydromorphone and oxycodone/oxymorphone.

Program projects. At any given time, the NLCP has roughly about 40 to 50 projects going on at the same time or simultaneously. I'll just give you a couple of those projects with a few highlights. Urine and Oral Fluid Mandatory Guidelines for Federal Workplace Drug Testing, some of the things that the NLCP is involved in. The routing of review, submission, to HHS, submission to OMB,
the ECCF applications and review process. The extension of
the current CCF, the Hair Testing Proficiency Program that
we're currently working on, laboratory investigations. We
have actually had 11 laboratory investigations since
August. Failure to reconfirm laboratory investigations.

And then we have a series of studies. I think we
have about 28 studies going on right now. Marijuana Smoked
and Vaporized Studies, and a whole assortment of other
studies as well.

We also worked on a Marijuana SmartBook, from a
few years ago. We do plan on revising that and updating
it.

NLCP publishes and continues a continuing
education newsletter on topics of interest to the drug
testing industry. We have published about 25 newsletters
to date. Anyone is welcome to subscribe by sending an
email to NLCP@rti.org, with subscribe-DTM as the subject
line, and back issues are also available at the same email
address. You can see some of the topics that we've
published on.

Okay, summary. The number of regulated specimens
tested by HHS-certified laboratories increased 15.4 percent
in 2021 as compared to 2017. On average, testing increased
3.8 percent per year over the same period, and the yearly
percent differences ranged from -6.6 to 12.7 percent. The
number of regulated specimens reported as positive, adulterated, invalid, substituted increased 32.7 percent for the same period.

Specimens reported as invalid due to low pH decreased from levels seen prior to revisions to the urine Mandatory Guidelines, and specimens reported as invalid due to high pH continued to increase in 2021. Specimens reported as invalid due to immunoassay interference continued to decrease from highs experienced in late 2017 and 2018.

If you do have any questions, I know I'm over my time, I do apologize, but if you have any questions, please drop them in the chat and as a group we'll answer those and get back to you. Thank you for time, your attention, and thank you for the opportunity to present.

MS. DAVIS: Thanks, Eugene. I want to remind all board members, you're welcome to ask questions. We did have a few questions for Joey. I know Barry had a few questions. We can go ahead and take those questions now for Joey, and then if anyone has questions for Eugene or any others, we can take those before the next presentation.

DR. SAMPLE: I really had two questions. First, if you look at the regulatory requirements, specifically SAMHSA Mandatory Guidelines and then ultimately DOT, which goes along with it, how do those cutoff requirements align
with the FDA's desire for sponsors to demonstrate -- I believe the word you used was clinically relevant cutoffs. So with the new E&I, employment and insurance exempt devices, those updated regulations still require 510(k) clearance for devices used in federal testing programs. So if the sponsors can't demonstrate the clinical utility of the cutoff, would that impair the ability of both manufacturers and laboratories to have access to immunoassay screening devices for drugs of abuse at the federally mandated cutoffs?

DR. KOTAREK: That's helpful. We do look for that at -- and again, information to support the clinical validity of the cutoffs. Part of that information can definitely be if there is a mandated, for example, Department of Transportation or Department of Energy cutoff that's been mandated this is the cutoff that will be used for this device and with -- I would strongly encourage any sponsor who is developing that to cite that as part of the evidence to support that cutoff. One thing that would also help is inasmuch as it is available, all of the public available discussion around that cutoff and how it was determined this is the cutoff that we will use would be really helpful to help us understand how, for example, DOT or whatever other organization determined that was the correct number, or an appropriate number to use.
So that was kind of a longwinded answer, but the short of it is, you know, I would strongly encourage sponsors to cite those requirements for various government programs and inasmuch as it is possible to also provide all the public discourse that occurred around those discussions where those cutoffs were finalized.

DR. SAMPLE: So that's helpful, because really at the end of the day, I think the cutoffs, Ron would agree the cutoff is the cutoff, without going back to the rulemaking process and it seems like there could be some difficulty getting some congruence, for both --

DR. KOTAREK: We would look to clinical data, as well as what's required by the regulations. We would definitely take in consideration if there's a federal agency that requires specific cutoff testing, we do take that into consideration when we're looking at the clinical validity of any new cutoff.

DR. SAMPLE: Thank you. My second question, I use the 510(k) searchable database tool quite regularly. So personally I'm very familiar with it. One thing that I think would be helpful for those of us who get into this really geeky stuff would be to have a search tool analogous to the 510(k) database for the E&I exempt devices. So for those of you who know the various FDA websites, it's possible to backend around it by searching the facility
database, because you know who the manufacturer is, because the E&I devices have to be registered with FDA, and its registry is the manufacturer of those devices, you can back into it. But it is somewhat of a cumbersome process. So is that something the FDA is looking to enhance at some point down the road for the E&I-labeled devices?

DR. KOTAREK: It's interesting, that's a really interesting point. I will fully admit I had not thought of that. I'll say one thing that we need to work out to do something like that would be that you don't have to -- for registration listing, I don't think you have to explicitly call it an E&I -- if it is E&I device, then you could register and list it without a 510(k). But you don't in the registration listing have to explicitly identify it as an E&I device, I don't believe. So I don't think that's a field that's captured in registration listings specifically, or at least there's no like field -- I have to go back and check to make sure that's information that's captured that there'd be a way to -- it's a really interesting idea. Admittedly I've never thought of that, but there may logistical hurdles in creating a database like that, but we could certainly look into see what, if there's a way we could get to something like that.

DR. SAMPLE: I think maybe at least in the device registration process as a manufacturer, there is something
that captures that, because as I recall, there's something that says insurance and employment exempt, or something along those lines. It would be helpful for searching purposes.

DR. KOTAREK: And I'm trying to think if you could do it by product code.

DR. SAMPLE: No, the product code is the same, unfortunately.

DR. KOTAREK: I can try to look and see what options might be available.

MS. DAVIS: Do any other board members have any additional questions at this time?

MR. FLEGEL: I'll add I think it will be very important when it comes to collection devices too, what we look at moving forward out of FDA. Thanks, Joey.

MS. DAVIS: Ron, you are next up as the next speaker.

**Agenda Item: Regulatory Program Updates and Mandatory Guidelines, Ron Flegel**

MR. FLEGEL: Again, I want to thank all the speakers for the presentations that they've had today, a lot of useful information, a lot of information. We're trying to stay on target for the DTAB meetings, it has been difficult sometimes, but we are I think on target for having all the quarterly meetings.
Ana, if you can go to slide view...

MS. DONOVAN: I'm not sure why it is not letting me. Give me one second.

MR. FLEGEL: I think I'm the only one that stands in the way of your lunch, or prior to lunch. But I'll go through this. There are some updates; relatively things have stayed relatively close to our last Drug Testing Advisory Board meeting, but I want to put -- I was really at this point now emphasizing the presentations, I was hoping to actually give some information and revisions that we've looked at or have completed for the urine and oral fluids, but that will be hopefully the public will be able to see that prior to the next Drug Testing Advisory Board meeting, and then we'll be able to talk it specifically.

Okay, since we're a little behind, I'm going to go ahead and next slide. Again, the Division of Workplace Programs. I just want to emphasize, I couldn't do any of this stuff with everybody on this list. As I commented last time, Joshua Hunt, who is a PharmD, he is now with us, and we also have a new, at least a change in title, and that would be Anastasia Donovan. She's changed to a public health advisor. With that, everybody else has pretty much remained the same.

Again, I just wanted to give a listing of the board members. I appreciate all that they have done. It's
been, for the last two years, it's been a little bit difficult, because we haven't had meetings where we're together, but hopefully in the next three months we can schedule the next meeting that will be on site. What's what we're hoping to see. So again, we still have one nominee that is still going through some of the information that we need, and then we have several extended members, which I wanted to thank the extended members for continuing to participate in DTAB.

Again, the DWP objectives, our overall goal, SAMHSA is continually assessing the science and technology. The goal currently is the implementation of the first HHS-certified oral fluid testing labs as Eugene sort of touched on that. We really have finished most of the documents at this point, and with DOT's NPRM out on oral fluids, we really hope that oral fluid laboratories will be able to submit application packages very soon now that they've seen the NPRM or the actual regulatory rule under DOT.

Presently, again, implementing the Mandatory Guidelines using oral fluid as an alternate specimen to enhance the Federal Drug Free Workplace Program, and I will say based on my opening brief, I think it's also critical that at least within federal agencies once oral fluid is implemented and we have an HHS certified laboratory, that agencies will have the ability to test a second specimen.
I think that's important for donors, because donors in themselves sometimes, let's just take an example, paruresis so that they're unable to provide a urine sample, we can go directly to an oral fluid sample or vice versa. So, I think it's important that all matrices that the agencies can go back and forth.

Under the Drug Free Workplace Program, as Hyden indicated, we're looking at a high-level review of that, and really around the existing challenges.

In the future, we refer the proposed mandatory guideline using hair as a federal register notice.

Again, just the Drug Free Workplace Program impact, you heard from all of our federal partners, I also should add Department of Defense here. There's the number of civilian employees under the Department of Defense that are federal employees, but they fall under DoD. So again, a lot of testing has really bounced back from where the COVID era was two years ago, a significant decrease in testing, to actually we're above currently where we are or where we were with the testing prior to COVID.

We continue under the Drug Free Workplace Program, there still are a number of issues not only federal laws but state laws specifically around the drug testing policies. As you heard from Faye Caldwell many times, employees' rights, et cetera, under CBD and hemp
products or specifically under the Farm Bill. We continue to wrestle with that as well as do a number of studies that we've looked at marijuana in a number of different things and also continue to look at studies around marijuana and the impact. Look at the impact of CBD on positive results. So, there's a number of things on that slide. Again, later in the presentation, that will show some of the actual programs or studies that we continue to look at.

Again, you've seen this slide before, both the legislative authority as well as main roles, the science around the forensic drug testing as well as policy for the Drug Free Workplace Program. I also will add that I was going to do a slide in here looking at emerging issues. We always have the emerging issues, around the revisions that I talk about with oral fluid and urine. I think it's going to be important to look at the different drugs, that not only are, as I mentioned before, for instance like fentanyl, but other drugs in the future that we look at whether it's the synthetic drugs or other drugs that are listed drugs being used, of how or if they will be added to the drug testing panel or removed from the drug testing panel.

Mandatory Guidelines, again the routing process, I just wanted to give an indication where we are with urine and oral fluid, as you can see around number 13. With that
also at number 14, around hair, we really are at where we're preparing the final Mandatory Guidelines, and again, there's multiple steps within that, but we are at the point where we are preparing the final Mandatory Guidelines, hopefully.

And again, under 11 or the urine and oral fluid, this would be a proposed rule that hopefully the public will see very soon.

The Urine and Oral Fluid Mandatory Guidelines, this will remain the same, whether you look at urine, oral fluid, and/or hair. As I mentioned earlier, looking at the different emerging issues, that's where we will look at the impact of other illicit drugs, as well as ones that we'll remove or add to the panel in the future.

We just updated the Mandatory Guideline update. Under urine, obviously the latest version was October 1, 2017. Oral fluid, it was an effective date of January 1, 2020. This now can be paired up with DOT's NPRM on oral fluid. So again, I think this is an important leap forward for both federal programs to have the ability hopefully in the future to be able to test oral fluid.

And then again, hair is under the proposed Mandatory Guidelines that was published on September 10th of 2020, and we're currently reviewing all public comments and looking at the scientific literature that was cited in
those comments to look at the impact on the actual regulatory rule.

Under the hair Guidelines, this is just a reiteration. The establishment of new standards and technical requirements, the inclusion of the same lists obviously of, say, analytes or drugs allowed to be tested in urine and oral fluid. Establishment of the initial and confirmatory drug test cutoffs, the analytes and the methods for hair testing, requirements for each laboratory to have procedures for decontamination, which I think is a really important part when it comes to hair testing to actually identify whether it's use or external contamination for some reason. So that's an important part of what we've looked at.

And then the revisions of the requalification requirements for individuals serving as MROs, and then the last point was also the inclusion of references to use as an alternate specimen, as I mentioned. I think it's very important to be able to have the ability to test all three. As we have seen from Eugene's presentation, there's no limit, I think, on the different adulteration products and for products that we don't necessarily know about that have invalidated samples or raise the pH, lower the pH, have immunoassay interference, et cetera. So, I think it's
important when it comes to having a comprehensive program looking at all the matrices.

Under the Mandatory Guidelines plan, we again proposed a new matrix. We proposed the Mandatory Guidelines using hair on September 10. As I mentioned, HHS requested public comment and scientific information, which we received quite a bit. HHS will publish an FRN with supplemental revisions to the proposed Mandatory Guidelines, and this would make again, it would make it the same as the proposed for urine and oral fluid that's currently under OMB review.

Publication of a final Mandatory Guidelines will be done, again, OMB review, in conclusion to publish the final FRN, and once this final FRN is published, hair would be an authorized matrix at least within the federal program.

Last bullet point was DOT may publish a separate notice for public rulemaking to also include hair.

Again, the status update is we've organized the public comments. There were over 700 individual comments, 213 commenters. We have went through and reviewed all comments, submitted information, and the scientific studies that have been referenced by commenters, and we continue to monitor the scientific literature going forward as to if
there are additional studies that we're looking for to prepare the final Guidelines.

In March of 2021, DTAB had a closed meeting. We've summarized public comments presented. In June of 2021, under DTAB we had an also closed meeting. DTAB members reviewed the draft HMG, and again, going forward, SAMHSA will be reaching out to hair testing laboratories to gather some additional information that we would like to look at under the proposed rule.

Urine and oral fluid, really the few things I can say is the goal again is to propose revisions that would facilitate modifications to the authorized drugs and cutoffs as needed based on the science and emerging drug trends that we see and to aid in the detection of donor attempts again to subvert their drug test.

We have currently engaged in reviewing potential frameworks that incorporate the best available research and advice, including input from our federal partners. As mentioned several times, the revisions are currently under OMB review.

Again, just to mention, if board members have any questions throughout, if you want to ask, please feel free to stop me and I'll try to answer the question at the time.

Just as a timeline for the revision timeline, again we published the proposed urine Mandatory Guidelines.
That was what we would do going forward in the future, a federal register notice requesting public comment. We would then publish a supplemental to the proposed hair Guidelines. We would publish then a final urine and final oral fluid Mandatory Guidelines, and then we would come to publishing a final rule for the hair Mandatory Guidelines. Starting in 2022, as indicated, we are going to look at or conduct a high-level review of the Drug Free Workplace Program to identify any existing challenges.

Again, just a current list of the National Laboratory Certification Program studies that we've worked on. As you can see, there are some that have been completed. There are a couple that are on hold and there are some that are just starting essentially for instance, JHU topical application of CBD products. That's looking at different lotions or balms or topical solutions, interesting since there's so many out there of what those actually do with the three matrices of specifically urine, oral fluid, and hair.

So again, looking at starting a THC/CBD pulse study in the presence of fentanyl and opioid-positive specimens. So, there's a number of studies, ongoing studies, studies that we've completed, as you can see. We don't lack being busy, that's for sure, and again, I also want to thank the National Laboratory Certification Program
for all that they do with all the studies that we've started and finished.

In the evolving environment that we have, which is really under legislation, we had the 2015 FAST Act which we continue to report. We just did a congressional report on hair, which is moving forward to Congress. The 2018 Farm Bill and the impact obviously on the Drug Free Workplace Program around legal and illegal sources of THC specifically. We have the 2018 Opioids Crisis Response Act. I appreciation Brian saying that. It is very important I think since we've started the program of looking at the synthetic opioids or testing for the synthetic opioids. I think that we've seen, I would say, a significant decrease in the opioids in general under the federal program.

Changes in science and technology. Drug testing and specimen collection technology are continuing to improve, and especially the Mandatory Guidelines for drug testing around oral fluid. As Joey indicated in his presentation from FDA, I think there's a number of things that we're waiting for, we're looking at. One of those being obviously the point of collection testing, or point of collection devices, collection devices in themselves, I think that's going to be very important going forward, what will be used in the federal program.
And then under the evolving environment, new and novel drug use continues to emerge, especially around the synthetic designer drugs or the CBD or the THC isomers, and that also includes CBD products and, again, it's around the workplace safety and security of our program, with all federal programs really. Again, looking at specifically what will come out from around the delta-8 THC, looking at that as either a THC isomer or is it actually a synthetic drug that's produced from THC. So, I think that still has to be evolved yet as to when or if that is one of the analytes that we look to test in the future.

And then an increased demand on the Drug Free Workplace Program, especially around the COVID and the return-to-office challenge, as we now know that we go back on March 30, as far as some of the federal employees. So, I think that's important as federal employees return to the office, especially around the drug testing portion of it.

And then ongoing challenges, again. Finalizing the hair Mandatory Guidelines, again that will be something that is definitely in the future on our radar, and the implementation and funding new programs, oral fluid and/or hair, again as we moved forward, I think that's going to be important to not only have the funding for those programs but to be able to start those at least have initially two labs for oral fluid, if not more, we looked at more, the
same with hair Mandatory Guidelines for the federal testing of that, looking at the labs.

And then again, addressing emerging issues, as I mentioned around the hemp products, the CBD, the opioids, the synthetic drugs, and federal legislation as well as state legislation on marijuana in general. Then implementing the Mandatory Guidelines. I took off not only hair, but the oral fluid is very important, because although we've completed all the documents for that, we still have to actually have an HHS-certified laboratory to conduct oral fluid testing.

This is just, again, just a rundown of the implementation, the documents that we've worked on that are now in the final status or finals. So, we have all of this documentation that we can send the laboratories that want to send in an application regarding oral fluid, and it's sort of a rundown again on the -- we've begun accepting oral fluid applications again in 2022, and then the certification process, I was just asked recently how long does it usually take for the certification process.

So usually by the time you get through three initial PT cycles and a laboratory inspection, it's usually anywhere from three to four months is what we've looked at. Maybe a little bit different because it will be a brand new matrix that we're looking at, but again, that's what we're
targeting as a three- to four-month time window once an application is submitted.

Again, the marijuana studies that I've shown earlier with the NLCP, we have many scientific peer reviewed journal articles that we continue to update on our website. I also again would like to thank Dr. Ed Cone, Dr. Ryan Vandrey, Dr. Tory Spindle, and Dr. David Kuntz from CRL for not only the studies in themselves, but the work that has gone on to actually look at the different matrices that Dave has looked at in all the analytes that we can test and look at now in the studies that we're doing, whether it's blood, oral fluid, hair, urine, et cetera.

Again, studies for CBD and data continue to be shared with other federal agencies as it becomes available. We'll continue to work on that, and as we resolve and finalize those studies, we will obviously do peer reviewed journal articles so that the public can see that.

And just the Drug Free Workplace Program resources, where you can find those. We are updating the 2013 guidance for selection of testing designated positions, also the model plan. We now have an initial new supervisor training course for supervisors for the federal agencies around the Drug Free Workplace Program, which we've never had in over 30 years of the program. So, I think that's going to be important. That right now we're
currently working on the last of those as far as revisions to get that out to supervisors.

With that, I'll ask for any questions from the board, as well as thank you for your participation in the Drug Testing Advisory Board meeting today. I think, again, some new information, some very great information regarding for instance DOT's NPRM et cetera for our program, too, and with that I will close or I'll ask for any questions and turn it back over to Lisa.

MS. DAVIS: We have one more presentation before we do close the meeting, and hopefully it will enlighten us more on some of the urine issues that we're seeing in the laboratories. Svante Vikingsson is giving an update on synthetic urines and adulterants.

**Agenda Item: NLCP Updates – Synthetic Urines and Adulterants**

DR. VIKINGSSON: Good afternoon, everyone. I'm going to talk a little bit about synthetic urines and adulterants, and I'm a part of the NLCP scientific staff at RTI. For the purpose of this presentation, a synthetic urine is a product that you submit that you replace your own urine sample with, and an adulterant is a product that you add to your urine.

We've seen some statistics on this today. Dr. Hayes and Brian Zaleski both presented some data on how we
see samples that have been subverted, and we wanted to look at this. So about just over a year ago, we did a market survey where we identified 32 different synthetic urine products that were on the market and three different adulterants. So, we purchased a bunch of those products and after some initial testing, we sent out 10 synthetic urines to five of the certified laboratories, and we also included all the adulterants. This slide is actually not quite updated. I see we have now received the results back from all laboratories.

In addition to normal sort of NLCP program testing, we also asked them to do a couple of specific assays and novel assays to look at the synthetic urines, uric acid and magnesium, a biomarker panel, and we also looked at some of the dipsticks adulteration assays that were out there.

This is what the three adulterants look like. On the left we have the Spike additive, which is a solution that you add to the urine sample, and we actually did not identify any active components in that one, or we didn't find that it had any effects.

The Urine Luck in the middle is actually a two-component solution that you mix both of these in the urine sample, and that actually behaved a lot like it contained iodate, as we will see from the testing results later.
The third one on the right there is the Klear additive, which we believe might be potassium nitrate, and I don't know if you can see it, but there's little crystals in there.

This is a little bit what the synthetic urine products look like. This is not all of them. But as you can see, most of them are premixed urines that come in these little bottles, but we also have urine concentrates and powdered urine that you dilute in just tap water. As you can see, the products are sort of similar in the look and feel as other products you buy in your local stores, which to me implies that this is business and it's a professional operation that produces these.

You can also see that a lot of them have these temperature strips, and that is used to make sure that you get within the temperature range, and one product actually even came with a little heat generating powder that you were supposed to add it.

So, if we start with adulterants, what we did was that we prepared a urine sample that was targeted around double the NLCP initial cutoff levels for these drugs. If we look at this table, what you see here are the different kind of drugs and you see what the result of the initial immunoassay screening was. You can see that it's mostly green, meaning that both the control urine and the
adulterated urines mostly gave the expected positive results. We did see interference for 6-acetylmorphine and methamphetamine in a few laboratories, and when we cross-referenced with the methods used, we see that it is the CEDIA assays that create this interference with adulterant A2. We also see a couple of negative results for THCA or THC-carboxy, and that is actually might be because those concentrations were actually lower.

And if we go to the next slide and take a look at the confirmation results, we will get to that. I apologize for the busy slide. What we're looking at here is that we sent each sample to five different laboratories. So, each bar is one result from one laboratory. You see the negative or the control urine on the left and the adulterated urines on the right.

As you can see, we didn't really see any effect on codeine or hydrocodone, and that's also true for benzoylecgonine and PCP, which are not shown here. We did see small reductions for oxycodone, morphine, hydromorphone, oxymorphone, for adulterant A2, and they're all opioids. We saw a tiny little drop in concentration for the oxymorphone also with adulterant A1. But I'm not entirely sure that that is a true effect of the adulterant.

So if we go to the next slide, here we can also see that we didn't really see any effects for the 6-
acetylmorphine, but if we look at THC carboxy down there or the THCA, which I think is the analyte that the producers and the users of these products really wants to hide from us, we do see that both adulterant A2 and A3 produce a reduction in the observed concentrations, when we get concentrations.

As you can see, there are not five bars for each of those, and that is -- the missing bars represent instances where the laboratories reported interference, which meant that they couldn't quantify it and the usual interference was a lack of internal standard recovery.

So, we see that these adulterants have a little bit of an effect. Next question is can we detect this effect. We did see with A2, we did see immunoassay interference, and we did see some interference with the confirmation assays for A3. pH, creatinine, and specific gravity were all perfectly normal, and they didn't change much from the control urine.

For A3, we did see oxidant activity which is consistent with nitrite salts, and the product actually comes with a little warning that it's not supposed to be used for U.S. workplace drug testing because it will be detected. For A2, we have one laboratory that tested specifically for iodate and got a positive result, and we also see that a couple of labs have a little bit of oxidant
activity, which is also consistent with what is expected in a specimen adulterated with iodate.

If we move to synthetic urines, because based on the products we see and the reports that we're hearing, this might be a more prevalent way to subvert drug testing than adulterants. So, we, as I said, bought 16 of these, and this is what they looked like, and to me with the possible exception of S11, which has a little bit of a green tint, they look pretty inconspicuous to me, and if you click one more time, we should be able to get some more information on this slide. There we go.

So, pH, oxidants, and creatinine all came out perfectly normal for all of these, and what we see is one with low specific gravity and one specimen with high specific gravity, but we need to remember that if creatinine is normal typically specific gravity wouldn't be tested on these specimens.

The results were pretty expected by us. We did bring in some other assays as I said, and this first one is just AdultaCheck10 dipsticks. We are really looking at the four bottom ones, because the top ones are all covered by laboratory testing, but we did test these specimens for aldehyde, chromate, peroxidase, and halogens, and they seem to come out negative both the adulterants and the synthetic urines.
We're going to get a little bit more interesting with a dipstick that's specifically designed for synthetic urines. We tested all of the ones we have, and the little squares on top of the graph there is actually cutouts of the testing pads. As you can see from the legend there, synthetic urines should turn the pad either bright red or leave it uncolored, while the different shades of yellow and brown are consistent with normal urine.

You have the reference, the control urine, which is human urine, on the far left there, and you can see that it's a little bit darker than the synthetic urine pads in the middle there, but at least to me I think these color differences are too subtle to be able for a collector or an analyst to make reliable decisions based on.

We also took the colors of these pads and converted them to a single number between red and white which is shown in the graphs here, and you can see that the synthetic urines are all lower than the control urine, and this might be important to investigate further, because these test reagents could be also be used in an analyzer where you could actually measure this.

What we don't know is how large the variability is in authentic urines, because we only have one urine source here and how much that would overlap with the range of the synthetic urines.
This slide summarizes the results from the uric acid and the magnesium tests, which is a combined assay that one of the laboratories did, and what we can see is that almost all the synthetic urines contain uric acid at normal levels, and most of them also contain magnesium, but at slightly lower concentration than what would be expected in human urine.

What gave a little bit more indication was the biomarker assay, which is an assay that contains seven different endogenous and exogenous biomarkers that are expected to be present in authentic urine specimens, and what we see is that our control urine contains all seven, while the synthetic urines typically only contains one or two of them. I think there's two urines that contain three.

Of special interest is product S14 and S15 there at the bottom, because those products are actually marketed as being authentic human urine that's been tested by GCMS to be drug free, and they charge pretty well for those. But I would say that from the looks here, it looks like that particular piece of marketing is not true.

To summarize a little bit here, we did test three out of the three adulterants that we could find. We observed, with the exception of THC, we saw only small effects on drug screening and quantification, and the two
active adulterants that actually impacted screening were also identifiable by the oxidant screen and/or by immunoassay interference. So, we believe that these would probably have been identified.

The synthetic urines, on the other hand, were not detectable by the typical SVT assays, and the uric acid test was of limited value. I think that clearly shows how quickly these products will adapt to new testing schemes, which is something we need to keep in mind. While the biomarker panel can be used for confirmation, I do see I have a question for me in the chat here from Jason, who asks for the biomarker simulated urine testing, how time in storage stable are the target biomarker compounds?

The short answer to that is the lab might have done some work on that. We have not. So, I don't know. I do think that that is where I do think that the biomarker results come in. It gives us some -- it could work as a confirmation test, but it's too involved and expensive to work as a screening test, but I do think that some of these markers that are in there could be evaluated as potential screening markers. But then of course, we would have to know what happens during -- with stability can a sample be reanalyzed and still give the same results?

With that, I think if we go to the next slide --
DR. SAMPLE: I had sort of a follow-up question to what Jason asked. Were all of these products lyophilized? Or were any of them liquid? Because I'm wondering if maybe just the lyophilization process may impact the biomarker test.

DR. VIKINGSSON: So, I would say that most of them were liquid. As for the two that were human urine were GCMS tested, one of them was supplied to us in a frozen state or it was frozen when shipped, and the other one was actually a lyophilization, a powdered product, that was supplied with deionized water to resuspend it.

I agree, the lyophilization probably is interesting, would probably affect these things, too, which probably is a good thing for us, because we probably -- and I mean, that's sort of what I'm thinking is that stability of these products or what biomarkers we use, I think the uric acid shows that we need to think about what markers we use so it's not becoming too easy to just add them, and that is going to be one of the challenges where we are going to have to do some more work.

I also would like to, before I end here, just give a brief shoutout to Dale Hart and Shannon Krauss at RTI who helped me with preparing the spiked urine sample and to evaluate the dipstick tests.
With that, I thank you for your attention, and if anyone has any more questions, I would be happy to answer those, too.

DR. SAMPLE: This is Barry Sample again. This question may actually be more for Ron than for you. A number of years ago, Congress was looking at products that were used to subvert the drug testing process. There are still a number of states today that are introducing bills or considering that, and it really is quite a patchwork as you look at that legislation. There's no model legislation. So, is HHS able to do anything to try to move that along, either at the federal level or to assist the states that are looking to restrict the sale and use, more specifically, more typically, the sale, but sometimes also the use of these products?

MR. FLEGEL: I appreciate that question. At the federal level, I don't know of anything that's moving forward currently. At the state level, there's been a few that I know have moved forward and there's been comments that came from the public really, for stakeholders and that.

But again, I see it more as a state level of how it proceeds forward. It would be nice to at a federal level, but again, I think even as the states move their bills forward on these products, they change the product
names or what it says it does. So, it's very difficult to capture all of these products at one go.

DR. SAMPLE: Yeah, although the state legislation that I've looked at doesn't really name products. It's really what its intended use is, which is why I was wondering, yeah, I understand the difficulty of federal legislation or regulation dealing with it, but is there something that can be done from a model language perspective?

If you think about what the recreational use and the medical marijuana use people do, there's model language that proponents of the users of these substances put forth. Could HHS take a page out of that book and have model language for states, and that may also help encourage states to draft legislation to restrict the sale and use or certainly the sale and perhaps the use as states are interested in looking at this issue.

MR. FLEKEL: I think that would definitely be a benefit if the states are looking at drafting a bill like that to have an example or a model of that. I think it is interesting, though, if you look closely on the back of the CCF, you're basically attesting to the fact that that is your sample. There is consequences if a person was prosecuted based on the fact that they substituted their sample with the synthetic urine.
So, it is interesting, although there's no case or cases that have moved forward in the punishment of essentially from a court standpoint of putting that forward. So, if you have any of that draft language, Barry, I would appreciate you sending me the link and I'll look at it.

DR. SAMPLE: Sure. I've commented on a number of those. So, I'll be happy to share with you the comments I've submitted.

MS. DAVIS: Are there any other questions from the board. Thank you, Svante, for your presentation and all the speakers. Any other questions from the board?

Hearing nothing, we're going to move to the public comment period. Operator, I believe you have some instructions for the public comment.

Agenda Item: Public Comment

MS. DAVIS: I'll go ahead and read it. To ask a question or make a comment, please press star-1 to unmute your phone and record your name when prompted.

OPERATOR: We do have a question over the phone. Our first question comes from Carl Shadwire. Your line is now open.

MR. SHADWIRE: I had question for Joey at the FDA. When manufacturers are developing and validating new immunoassays, one of the challenges for some of the drugs
is finding authentic patient samples that have concentrations that fall within that range of plus or minus 50 percent of the cutoff, which is really where you want samples to be to really challenge your cutoff. So, in those instances where it is difficult to find those samples, we're wondering if it would be possible or acceptable to dilute high positive patient samples with drug free urine or matrix to create those concentrations to evaluate the cutoff.

DR. KOTAREK: Yeah, and so the short answer is probably not, but maybe.

MS. DAVIS: I’m sorry, public comments and questions are just for the record. They're not actually answered during the question period.

DR. KOTAREK: My apologies.

MR. FLEGEL: That's okay. Usually it is comments that are for the record and we can follow up at a later point, unless you feel comfortable enough that you feel that you can answer the question, but usually we don't take questions from the public.

Dr. Kotarek: In this case, I can follow up offline if there is any specific questions. I'll leave that for now.

MR. FLEGEL: Okay, great. Thank you. Lisa, move back to you for any additional public comments.
MS. DAVIS: There's another question in the chat. For the record: Have any studies been performed on other than marijuana secondhand smoke? We're hearing concerns.

MR. FLEGEL: Again, we'll capture that in the transcript and look at that question.

OPERATOR: As a reminder, to make a comment over the phone, you may do so by press star then 1. One moment as we wait for any additional comments.

There are no comments over the phone at this time.

MS. DAVIS: Thank you. This now ends the public comment session. Before I adjourn, I'd like to turn it over to the chair, Ron Flegel, for any closing remarks.

MR. FLEGEL: Thank you, Lisa. Again, I just appreciate everyone's time and attendance today to listen to some important presentations. There's a lot of ongoing work that the board will be involved in going forward. Right now, we're sort of a little bit at a standstill with some of the issues, but again, we continue to do a lot of studies, we're looking at a lot of studies. We'll have a lot of data in the future, we really hope to report to the board as well as get a lot of information or comments from the board on the information we presented.
So again, thank you to all federal partners for presenting today. Hopefully the next meeting we will have an onsite meeting that we'll all be together.

With that, I will conclude and just thank everyone. Back over to Lisa.

MS. DAVIS: Thank you, Ron, and with that, I adjourn this open session of the Drug Testing Advisory Board. Thank you all for your attendance and your time. Thank you.

(Whereupon, the open session adjourned at 1 p.m.)