Drug Testing Advisory Board (DTAB)
Center for Substance Abuse Prevention (CSAP)
Substance Abuse and Mental Health Services Administration (SAMHSA)

Drug Testing Advisory Board (DTAB) Meeting

Open Session

December 5, 2023

Virtual

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P R O C E E D I N G S (10:00 a.m.)

Agenda Item: Call to Order

MS. DAVIS: Good morning, everyone. 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 December 2023 quarterly DTAB meeting. We are conducting this meeting remotely, so please bear with us through any technical issues that may occur. I officially call this meeting to order and want to welcome staff of the Division of Workplace Programs, federal partners, contractors, invited guests, members of the public, and finally our board members. I wish to welcome our newest board members, Michael Grommes, Samantha Tolliver, and Carl Christensen. Thank you, Mike, Samantha, and Carl, and all board members for your service.

Today's open session is scheduled from 10 a.m. to 4:30 Eastern time. Just as 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.

I'll start with the DTAB members and the DTAB chair. Alison Stockdale?

MS. STOCKDALE: Here.

MS. DAVIS: David Engelhart?

DR. ENGELHART: Here.

MS. DAVIS: Elizabeth Stuyt?

DR. STUYT: Here.

MS. DAVIS: David Roberts?

DR. ROBERTS: Here.

MS. DAVIS: Lindsey Everson?

MR. EVERSON: I'm here.

MS. DAVIS: Dawn Hahn?

MS. HAHN: Here.

MS. DAVIS: Bryan Ruggery?

MR. RUGGERY: Present.

MS. DAVIS: Michael Grommes?

MR. GROMMES: Present.

MS. DAVIS: Samantha Tolliver?

DR. TOLLIVER: Here.

MS. DAVIS: Carl Christensen?

DR. CHRISTENSEN: Here.

MS. DAVIS: And I'll also call ex-officios and federal partners. Joey Kotarek?

DR. KOTAREK: Here.

MS. DAVIS: Bohdan Baczara?

MR. BACZARA: Good morning. Here.

MS. DAVIS: Brian Zaleski?

Lynn Wagner?

DR. WAGNER: Here.

MS. DAVIS: And that is it for roll call, and we do have a quorum.

For the first order of business, the DTAB members were given the opportunity to review the meeting minutes from March 2023 DTAB meeting. If the board has any comments, they will be incorporated into this meeting's minutes. Do any board members have any comments?

(No response.)

MS. DAVIS: Hearing none, may I have a motion to approve the minutes, please?

DR. STUYT: I will. I move we approve the minutes.

MS. DAVIS: Thank you Libby. Second?

Mr. Everson: Second.

MS. DAVIS: Thank you. 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 Food and Drug Administration and the Department of Defense will provide updates. Additionally, there will be presentations on the Medical Review Officer Manual and lab-created cannabinoids and other contaminants in commercially available products, as well as updates to the National Laboratory Certification Program. We will also have a discussion regarding the proposed analyte table changes.

Please mute your phones and computers when not speaking to prevent any background noises. We have a public comment period scheduled at 3:35 following the analyte table discussion prior to adjourning at 4:30. If anybody would like to provide a comment, they will be able to do so at that time.

All of the information from today's open session meeting, including the 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 now turn it over to Ron Flegel, 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, Ron Flegel

MR. FLEGEL: Good morning, everyone. Thank you, Lisa, for that.

First, I would actually like to introduce the new Center Director for the Center for Substance Abuse Prevention, Captain Christopher Jones, who is online. He is a public health service officer and I invite him to share a few words with the members and ex-officios of the Drug Testing Advisory Board. Chris?

CAPT JONES: Thank you so much, Ron, and welcome everybody to this December meeting. The agenda is certainly packed with lots of opportunities for really important discussion. I want to thank our newest members who are joining the Drug Testing Advisory Board, as well as our members who continue their service and a special thanks to our federal partners, ex-officio members. I really appreciate over the last three months as I've gotten up to speed in CSAP, coming from CDC before that, just the breadth of the work that Ron and the division take on and the importance of the Drug-Free Workplace efforts and have been in many meetings around oral and urine, getting that across the finish line, partnerships with Department of Transportation and others, and I think it is often something that people don't recognize that we do this work in CSAP as a regulatory function for the agency, but it is a really critical part of our overall work in prevention, and one of my goals is to make sure that we're integrating those efforts into the broader prevention picture.

So I know this advisory board is very technically focused in helping to provide critical input into how we can best achieve our regulatory mission, and so really appreciate that. But also know that there's this bigger picture that I want to make sure we integrate these efforts into what prevention activities are happening in communities.

The other piece is that the discussions that will happen here today, the feedback that we'll get from the public, the presentations that we'll hear, are really

coming at a critical time when we're dealing with a changing policy landscape, a very dynamic drug market that people are exposed to. So it creates new questions and challenges for how we operate our Drug-Free Workplace Programs and how we make sure that we're trying to stay current with evolving science in a dynamic drug market. So please know that we greatly appreciate all the time that you're going to put into the discussions today.

Thank you for your service to the board, and I'll turn it back to Ron.

MR. FLEGEL: Thank you, Chris.

So I'd like to do some of my welcoming statement and some of the introduction to the meeting, and then I'll also go into the updates for all the Drug-Free Workplace Program as well as some of the NLCP updates, et cetera.

I would also like to welcome all board members, new board members, ex-officios, Federal partners, industry leaders, and representatives and also members of the public who have joined the Drug Testing Advisory Board meeting today to listen. Thank you for taking time out of your busy schedules today to attend this meeting. As Chris said, it is very important as to the work that we've been doing and are doing and in the future what we will be doing.

I would also like to acknowledge our three new board members to the Drug Testing Advisory Board. I would like to welcome Michael Grommes, who was approved in October, and Dr. Carl Christensen, and Dr. Samantha Tolliver who were both approved in November.

I would also like to acknowledge and thank Kristen Burke, Deborah Motika, and Dr. Stephen Taylor for all their contributions to the Drug Testing Advisory Board throughout the last four years. Again, certificates of appreciation will be sent to

each of you and I want to thank you clearly for all the work that you did in the last four years.

SAMHSA continually strives obviously to improve the quality of services under both the NLCP program and the Federal Drug-Free Workplace Program. For those who are listening today and attended the NLCP workshop, prior to the Society of Forensic Toxicology meeting, we continue to improve innovations to improve the program's performance and to bring additional laboratories, including HHS-certified oral fluid testing laboratories, into the program. We also continually look to our federal partners, forensic workplace drug testing, federally regulated drug testing, and the private sector testing by reviewing and assessing the science and also the technology used in drug analysis, regulatory oversight, and innovative ideas which benefit and help to improve the quality of all related laboratory services.

Our standards for laboratory certification for the Federal Workplace Drug Testing Program extend to many of the regulated and nonregulated drug testing sectors. Additionally, we completed as mentioned earlier, the Comprehensive Review of the Drug-Free Workplace Program, the existing practices, the policies, and emerging issues, by performing what we called a SWOT analysis. It's actually a SCOT analysis, which stands for strength, challenges, and/or weaknesses, opportunities, and threats. I will provide an update on the Comprehensive Review action plan to address these challenges and also improve the program overall.

We are in the implementation phase for some of these actions and items as well as other DWP tasks and initiatives.

Additionally in this meeting, there will be presentations as Lisa mentioned on the latest NLCP activities, lab-created cannabinoids and contaminants, and updates to

the MRO manual. I want to say thank you to all of our presenters today that will be presenting.

Some of the status updates that I want to go through regarding DWP is the notice of proposed Mandatory Guidelines for Federal Workplace Drug Testing Programs using hair was published again in the Federal Register on September 10, 2020, for public comment. The public comment period closed on November 9, 2020. We received many, many comments on that as well as many articles that were attached to those comments.

DWP has revised the proposed Hair Mandatory Guidelines which is currently again under review at the Office of Management and Budget.

The proposed revisions to the Mandatory Guidelines for Federal Workplace Drug Testing Programs using urine and oral fluid was recently published in a separate Federal Register Notice on April 7, 2022, and the public comment period closed on June 6, 2022. Of that, 22 commenters submitted 57 comments for the urine, 53 commenters submitted 204 comments for the oral fluid, and many included attachments with these comments. The final Mandatory Guidelines for Federal Workplace Drug Testing Programs using oral fluid was published on October 10, 2023, with an effective date of October 10, 2023. The final Mandatory Guidelines for Federal Workplace Drug Testing Programs using urine was published on October 12, 2023, with an effective date of February 1, 2024.

I also wanted to mention that we are currently working with our federal partners to set a revised implementation date to accommodate DOT's NPRM for these changes. So again, that February 1 date may change and probably will change to a later date at that time. But we will hopefully be able to give the public more information in the next several weeks.

I do believe that to have an effective drug testing program you need a comprehensive approach to federally regulated drug testing, including adulteration testing and substitution testing, and also utilizing multiple matrices including oral fluid and urine.

I would also like to acknowledge and thank DOT for publishing the final NPRM on oral fluid in May of this year. There's been a lot of activity since its publication, and we are currently working closely with manufacturers and laboratories to move the oral fluid testing program forward as quickly as we can to get an HHS-certified oral fluid testing laboratory. DWP continues to focus on other special projects, and I will show in my presentation shortly this morning what has been under way with the National Laboratory Certification Program in conjunction with Johns Hopkins University.

Again, I would like to thank everyone for attending the December Drug Testing Advisory Board meeting. I hope you find the presentations very informative for all the program initiatives we are working on currently.

With that, Lisa, do you want me to turn it back over, or do you want me to go right to the regulatory program updates?

MS. DAVIS: You can keep on rolling.

Agenda Item: Regulatory Program Updates and Mandatory Guidelines Updates to Proposed Urine, Oral Fluid, and Hair Guidelines

MR. FLEGEL: Okay. So again, I want to thank all the staff within the Division of Workplace Programs. It has been a busy year, busy several months over the last months, getting the urine and the oral fluid publications for the finals of those, the revisions, et cetera, but a lot of work has gone into a lot of different things, and I want to thank the staff for that.

Also, I want to thank the Drug Testing Advisory Board members. Again, we have three new members at the bottom, Michael Grommes, Carl Christensen, and Dr. Samantha Tolliver, which I thank you for your service upcoming in the future. I think you will find this board interesting of all the work that we do around the Federal Drug Testing Program.

Overall, SAMHSA is continually assessing the science and technology in the drug detection to advance national drug policy that is based on the latest scientific findings. One of the things that I'll talk about more is around the analyte table changes upcoming. I think that's important, and as we've looked at that and as we've now got the final guidelines out, this will be something as a process new in the future, which I think is very important.

Also, one of the goals is to look at the Comprehensive Review of the Federal Drug Testing Program. It's been over a year ago since we had this review. But again, a lot of action plans have come out of this review as to what we do. I have a list of action plans at the end of this presentation that hopefully you will see some of the action plans that we plan on not only initiating but also have started some of those.

Again, we examined the issues affecting the program. We looked at outlining responses to the critical issues and also looked at the initiatives to address some of the unanswered questions and still some of the unanswered questions as we go forward.

In the future, we look to identify key policy and technical issues, as well as the existing challenges for the implementation of the Mandatory Guidelines using oral fluid and/or hair. We received a number, more comments obviously, on the oral fluid, which is the brand-new program. But again, we're really hoping in the very near future

that we will have an HHS-certified lab for oral fluid to do that testing. We also wanted to look at ongoing studies around cannabis and the enhancements to the Federal Drug Testing Program overall.

The Drug-Free Workplace Program's impact is around federal agency, executive branch agencies, also Department of Transportation among the Mandatory Guidelines, Nuclear Regulatory Commission, and also Department of Defense that we work closely with. So our federal partners, one of the things that we like to look at is make sure we're inclusive of all of our federal partners when we're looking at making these changes, especially around the analyte table changes as we looked at that on an annual basis.

You've seen this slide before around the science for forensic drug testing as well as the policy around forensic drug testing, and again, what I wanted to point out was actually was in yellow below, and I'll talk about this a little bit later in the actual updates in the program, but the DWP emerging issues group, we want to address both components of the science and policy, and I put that in and we're going to actually make that a part the sections that look at the drug testing panels on an annual basis. So that is going to be a very important part is looking at emerging issues, how to address those issues, and if they rise to where we would want to either add those to the analyte panel on an annual basis or not. So, I think that's very important as we're walking through this process, it's something that I wanted to make the public aware of is this emerging issues group within the division.

I would like to say here, if any of the board members do have questions or comments, feel free to raise your hand or just chime in with anything, if there's a question

you have on some of the information I'm going over. I want to make sure that the new board members also know that.

This we updated in May of 2022. So, the total number of executive branch agencies that are subject to Executive Order 12564 are 208. Total number of executive branch agency with certified plans are 137, and again, to have a certified plan is to also once that plan is certified, you can use funds to actually test within your program or agency. So that is important to have a certified plan so that you can use these funds to test.

Total number of executive branch agencies identified without certified plans, which we are working with right now under Executive Order 12564 is 71, and this information comes from the CDM Group.

So again, a lot of plans as far as not only making new plans but also going forward when it comes to revisions of existing plans.

An update on the Mandatory Guidelines as far as the finals. For urine it was published for urine was effective date is February 1, 2024, and as I mentioned earlier, we will be working with federal partners to look at that implementation date. Oral fluid, the final was -- the effective date of October 10, 2023, I think the question arose on several occasions as to why those two had two different effective dates.

One of the reasons behind that is we do not currently have any oral fluid testing laboratories. So, we can make that effective date on October 10, 2023. Obviously, we do have HHS-certified urine. So, we had to implement that effective date a little bit later in the program. Also, around hair, again, that was published September 10, 2020, for Federal Register comment, and that is currently under OMB review.

I usually give this and show where we are in the routing process around the Mandatory Guidelines, but again, both of the proposed urine and oral fluid have been finalized. Those have been published with effective dates for implementation dates. So, they sort of go off this chart. Again, when you're looking at hair, we're really around the 13, 14 mark, if people are keeping track of this, which I know they are. So that's really about where we are in the routing process for that.

I did want to touch on some of the major revisions. Hopefully at this time everybody has a copy of the final urine and oral fluid Federal Drug Testing Programs Mandatory Guidelines. But I did want to touch on a few of them and show some of the data. I think it makes it more informative of why we made some of these changes.

So, we did revise the timeline and process for publishing the authorized drug testing panel. That, again, is not only the drugs or analytes, but also the cutoffs that are established, and also not only adding but removing analytes as we move forward. We revised to report specimens as substituted based on biomarker testing. Again, concentrations that are inconsistent with established for human specimens. One of the things that we have allowed is when an HHS-certified lab, let's just say for urine, has an established biomarker testing and validated et cetera, then on an annual basis we will review that to see if it can be added to the program so that other HHS-certified laboratories can also use that.

Establish a timeline and process for publishing an authorized biomarker testing panel. So again, on an annual basis, not only the biomarker and the analytes, but also the cutoffs established for those. We raised the morphine confirmatory test cutoff from 2,000 to 4,000, in the urine Mandatory Guidelines. The oral fluid stays the same. But again, that is a revision for specifically the morphine confirmatory test cutoff.

We also revised the Medical Review Officer Manual, the MRO verification process, for positive codeine and morphine specimens. I believe Leland, Dr. Leland McClure, will be giving a presentation on some of those revisions in the MRO guidance manual.

We also required MROs to submit a semiannual report, and this is again semiannual, every six months, to HHS or designated representative on federal agency specimens that were reported as positive for a drug or drug metabolite by a laboratory and verified as negative by the MRO. We never had this feedback loop so that we can actually close that loop as to what was reported positive and what was reported negative.

When we look at going in to inspect laboratories, all we see is the positive result as to what the laboratory reported out. Now with this mechanism, we'll also have a verification process to look at what was actually verified as negative and to close that loop whether it was prescription or whatever, we actually will have a mechanism to close that loop now.

We also revised to apply refusal to test criteria for all donors, and we removed allowances for pre-employment collection. So again, all refusal to test for all donors has been revised in the Mandatory Guidelines.

Regarding the hair Mandatory Guidelines status, you've seen this before. I've given this, but I just wanted to reiterate, again, we organized public comment by subject. There were over 700 individual comments. We also reviewed all comments, submitted information, and scientific studies referenced by commenters and in preparing the draft hair Mandatory Guidelines. We also have received subsequently information since that time, since the public comment has closed, on new studies that have come forward. So, we also did a DTAB review on March 2021 where we summarized the

public comments and presented to DTAB. In June 2021, the members reviewed the draft hair Mandatory Guidelines and provided input, and then we also did some listening sessions and, again, this was March through April, several different listening sessions with seven hair testing laboratories, and that was March and April of 2022.

The topics around that were proficiency testing requirements, quantitative agreement between labs, which I think is very important when you're looking at a new program around the agreement between laboratories testing proficiency testing samples. The reporting criteria and also future technical working groups that we're going to look at to move this forward, and again, we revised the hair Mandatory Guidelines, has been submitted, and is currently under OMB review.

This is just some of the current NLCP applied studies and in progress. Again, I don't want to run through all of those, but I think a lot of these are very important as to what we're doing. As you can see, the ones on top are the ones that have been completed. The ones that are still in pending status are some of the ones that are later in the thing. One of the synthetic urine evaluations, again biomarker testing, cannabinoids in hair, morphine cutoff PTs that will go out. So, we're looking at a number of these. One of the ones that I did want to point out is the JHU CBD chronic dosing study in 2020, finishing up that. The Johns Hopkins University delta-8 THC dosing study. So a lot of these are ongoing and we hope to complete these in I would say the next year, next several months to years, of completing a lot of these.

Hair color impact, clinical collaboration, that we're looking at and also laboratory management upgrade, which is no small feat and I want to thank RTI for that.

Under the Drug-Free Workplace Program and evolving environment, we looked at emerging issues in legislation, and again, you've seen this slide before, but I did

want to point out 2015 FAST Act required development of the scientific and technical guidelines for hair testing while issuing hair color impact and external contamination issues continue to exist, and again, these were recommendations from the Drug Testing Advisory Board in moving hair forward is to also look at hair color impact as well as external contamination.

The 2018 Farm Bill, which really changed a number of things around the legal limit for THC content within products, the 2018 Opioids Crisis Response Act, which changed a lot of the Federal Program of what we looked at. Also, changes in science and technology. Drug testing and specimen testing technology are continually improving, which is great for our program. The Mandatory Guidelines for Federal Workplace Drug Testing Programs, again using oral fluid, was effective January 2020 in the Federal Program again in 2023 in the Department of Transportation program, but now a lot of the manufacturers, stakeholders, et cetera are now being able to look at the final 49 CFR Part 40 as well as our guidelines, and hopefully we'll be submitting applications in the future for more oral fluid testing laboratories.

Around the evolving environment, again, we continually see new and novel drug use, continues to emerge, especially around synthetic designer drugs. Increased public acceptability of availability of marijuana and CBD products and a reason why we did a lot of the studies that we're doing with Johns Hopkins University and RTI.

Implications around workplace safety and security, that also would refer to delta-8 THC and other THC isomers, and also state initiatives to decriminalize marijuana as we move forward. Again, that does have increased demands on the Drug-Free Workplace Programs, especially as we go through the COVID era here and some of the --

we continue or the Federal government is actually going back into the office, so again that creates challenges around the Drug-Free Workplace Program and testing, et cetera.

I won't go over this too much, but it is the MRO guidance manual and case studies. These were updated based on the 2023 urine and oral fluid, and again, Dr. Leland McClure will be giving a presentation on some of these revisions around that and the guidance, but we have revised the MRO verification process. We've looked at the annual authorized drug testing panel as well as authorized biomarker testing panels, and again, around required nomenclature for MRO reports so that all HHS-certified labs are reporting the same nomenclature when they report, say, an amphetamine or a methamphetamine. So, it will all be the same nomenclature for all.

We also have instituted MRO semiannual reports to SAMHSA or a designated representative so that we can close that loop around what was positive or reported positive to what has been verified as negative. And we also update based on the MRO relevant information. This was around NLCP notices, draft NLCP manuals for urine and oral fluid. The guidance for using the 2023 Federal CCF and also the draft MRO case studies.

And again, I think this is important, one of the things that we've tried to accomplish is in the MRO guidance manual is when you read a section in that, we try to make sure that within that section in the MRO guidance manual, it points back exactly in the Mandatory Guidelines as to where you can find the information under regulatory programs. So I think that's also going to be part, because we get a lot of questions around MROs, where can we find this in the guidance or in the Mandatory Guidelines. So, I think that will be important going forward.

Also, the 2023 MRO guidance manual case studies will be posted on the SAMHSA website shortly when we finish up all the revisions for that, and again, without the implementation of the urine yet, again, we have a little bit of time so that we want to revise those and get those published.

Some areas that we looked at under the Comprehensive Review program, and again, I've shown most of these, is really around the state of art and the science, maintaining program integrity. This is really around drug testing validity and reliability. Is it actually a urine specimen we're testing or an oral fluid or hair, so you have to look at what is the validity of it and what is the reliability that it's actually a specimen you're testing.

Workplace safety and security, these again are in safety sensitive positions. Issues, challenges, approaches, and actions. Again, ongoing training needs that we need in the program. Not only for supervisors when they're the Federal Program, but also the staff and employees of the Federal government.

Some of the future studies, policy initiatives. Again, in the future direction of the program and desired end state of what we want to look at. And all the resources that we do need to accomplish all this.

Our roadmap and action plan is we wanted to pursue the clearance strategy, which Joey will be giving an update with FDA. So, we wanted to also look at that. We also wanted to obviously reduce the length of time required to change the testing panel. We do that on an annual basis, which we now, we have finals of both urine and oral fluid. So that will be the beginning of a new process starting with this DTAB meeting and how we get to the point of changing analytes on an annual basis.

We also wanted to develop and add pulse testing. This was around emerging drugs, specimen validity issues, and that really is to inform us to know should we be looking at an emerging drug that we want to add to the drug testing panel? And again, I don't want to make people nervous in the sense that we -- this will not on annual basis, we won't be changing the panel on an annual basis every year. Some years we may have changes and other years we will not have changes to the panel.

We also wanted to review and streamline program processes, including inspections and audits, which we've looked at closely. We also wanted to align goals and timelines for SAMHSA DWP and the regulated agency partners.

These are some of the action plans that we've developed under the Comprehensive Review, and I know this is a long list. It was just to give you a flavor of what we have actually, what the priority is, what the action was, who's the point of contact, decisionmaker in that, and then also the action steps we would have to take. Again, just to read the first one, pursue emergency clearance strategies with FDA, alternatively remove FDA clearance requirements and rely on certified laboratory validations of immunoassay kits. So, it's one of the action plans that we have in place and are currently working on.

If you look at number 3, which again is now that we're working into the process currently, is reduce the length of time required to change the testing panel with that. Again, it is a process and there's a lot of let's say moving wheels with that, not only in changing the analyte table, which could be published on an annual review, but also working with DOT, NRC, DoD when we change that panel, what impact it has in the other regulated drug testing programs.

So as you can read down through, 5, develop and add surveillance program or look at pulse testing program to know what other emerging drugs do we have out there.

This is just a continuation of some of the action plans. Again, I don't want to read them all, but for instance, number 7, review and streamline where possible, program requirements, responsible persons, audits, initial testing, SVT testing, again. A lot of the things that we're looking at in the program to streamline make it not only easier for the HHS-certified labs, but also streamline it for our inspectors and everyone that goes out and inspects certified labs.

I put this slide in here because it was in the program review of all the actions and initiatives that have happened over the years from 1986, and I won't go through these, but I think one of the currently in 2023 as I pointed out, we now have revisions of the urine and oral fluid guidelines, which will be implemented shortly here, but also the question around marijuana. I know that's on everybody's mind is actually what's going to happen with that. I can't say, but I just put this here because it does or will look at the timeline regarding that of what happens, but it will be an important part of the Federal Drug Testing Program.

Some of the unanswered questions, and again, this came out of the comprehensive review. I just put a few of these up here because it is some of the ones that we've looked at as well as trying to understand in the future. Will the Federal Drug Testing Program continue to be a deterrent program or a fitness for duty? So again, we'll have to look at that. NRC is a fitness-for-duty; DOT is sort of semi-fitness-for-duty. So it's interesting. We're a deterrent program, but in the future, that may change.

What will the future of the Federal Drug Testing Program look like if marijuana is de-scheduled or rescheduled? Again, not just again a question that came from the comprehensive review, but I just put this here.

Will the Federal Drug Testing Program continue to test for marijuana? Again, we don't know what that will be, the actual outcome of that, under the Executive Order 12564. And are unique biomarkers for drug use achievable? One of the things that we've looked at very closely are looking at these unique biomarkers for drug use, and I think that's going to be important in the program to look at the actual drug use or identify that as drug use and not for say, let's say, contamination or something like that.

With that, I will close, unless board members have any questions that I can answer, and this is some of the Drug-Free Workplace Program resources. Again, you can find all of these on our website, and you can also find when we update currently or will be updating shortly some of the other, for instance, the MRO guidance manual.

With that, I want to thank you and I also want to thank all the board members and invite any questions around the presentation. Thank you.

I'll turn it back over to Lisa.

MS. DAVIS: Thank you, Ron. Are there any questions from the board? Hearing none, I'll take this opportunity to correct an oversight on my part. I'd like to welcome two other board members: Dawn Hahn and Bryan Ruggery. My apologies for not including you both in the script at the beginning.

They were brought on board in April, and I neglected to look back at the board members that were added before the June meeting, since the June meeting was canceled. So, five new board members. So, my apologies for leaving you guys off of the lists. Welcome. Glad you're here.

We are at a point in the agenda where we're at a break time, and we are a few minutes early. So, we'll go ahead and take the full break time. We're scheduled to come back at 11 for the federal partners update. So, we get an extra five minutes for our break time. So, if you come back just a few minutes before 11 so we can start right at 11, I'd appreciate it. Thank you.

(Brief Recess)

Agenda Item: Federal Partners Updates

MS. DAVIS**:** Welcome back from our break. Up next is Joey Kotarek with the Food and Drug Administration with a presentation. Take it away, Joey.

Food and Drug Administration, Joseph Kotarek.

DR. KOTAREK: Thanks so much, Lisa. My name is Joey Kotarek. I'm the Toxicology Branch chief here at FDA, and I wanted to take a bit of time and talk about our review of drugs of abuse assays, and this isn't a large update, but I wanted to just kind of highlight some options we have to make things that the reviews that are very routine, ways we can make those more efficient, and also maybe potentially new ideas about how we can take things that are very not routine and also make those -- make going through FDA a more streamlined process.

So again, at FDA we review drugs of abuse assays, typically through the 510(k) regulatory path. We clear specific assays that are for detection of specific drugs or analytes, and we clear them around specific cutoffs. We review those submissions for those devices under least burdensome principles, which we define as the minimum amount of information necessary to adequately address a relevant regulatory question or issue through the most efficient manner at the right time.

Now, that obviously is a very high-level description, and obviously a major question is how do we define the minimum amount of information necessary. But one thing, and again speaking at a high level, that's defined it's based on the indications for use, what is the device designed to do? But I also want to say it's not just the minimum amount of information necessary. It's in the most efficient manner at the right time.

And so part of being least burdensome is also being transparent about what FDA's expectations are, what we, the information and evidence that we would be looking for in a submission and providing that guidance to device manufacturers so that they can, before thinking and design processes that, by the time they actually get to FDA for review, we can minimize the number of questions or concerns or problems that we would need to resolve.

There are several sources that we try to make publicly available, sources of information that can help guide a submission for a new drugs of abuse assay, especially if you have a device that has a suitable predicate, it's similar to a device that's already sold on the market. All of the decision summaries for 510(k)s that summarize the evidence that was collected and reviewed to support any favorable review decision summarized in the 510(k) database, I have mentioned this before, but I would suggest that if you're unfamiliar with that database and you're looking for something for your particular device, a good shortcut is often to search the database by drug name. Fortunately for in vitro diagnostics, they will frequently tie the analyte into the device name, and so if you were designing anything from a marijuana or THC to oxycodone to opiate to fentanyl drugs of abuse assay, typically searching the assay by the device name is often helpful.

I think it's mentioned previously, there are obviously some limitations. It can take longer to search things if you're looking for -- for example, a specific sample matrix, but all of those devices nevertheless are there and can serve as good examples for how you might design the testing to support your device.

We've also given a few different presentations on generally what we look for when we review drugs of abuse assay. My colleague Dr. Courtney Lias gave a presentation a couple of years ago, and I've also spoken to this group as well as a few others, and there are links to those presentations, which I would encourage you to take a look at if you, again, have questions.

Another guidance that is also helpful, especially if you're looking at, say, a new cutoff that maybe we have not previously seen is the information in SAMHSA's recommendation and guidelines. If there are obviously final rules for testing, we want to be able to support them and those guidelines can help us to support the claim that any given cutoff is suitable or is fit for purpose.

Here I want to highlight a program that we have that is able to triage -- it is to triage well characterized, well-organized submissions, for device types we're very familiar with, and many drugs of abuse assays fit well under this paradigm. Just to also clarify, this isn't something -- you're welcome to in any given 510(k) submission note in, for example, a cover letter that you were interested in consideration for the program, but there is nothing specific you need to do. It is actually we proactively look for when we get any new 510(k) at FDA, we proactively look to see if any given submission is a suitable candidate for the program, and even if you say nothing about it, we will look for it, and if it is, again, a well-organized submission, we will try to put it in this Fast Track review program.

It allows us to go through submissions very, very quickly. This slide I've updated, because I also wanted to highlight that this was a recent clearance we had. It is the first FDA clearance for an over-the-counter fentanyl screening test in urine. We're actually obviously very pleased to have that available on the market, and I also wanted to highlight that again when I talk about these reviews potentially being very fast, we received the submission on October 10 and were able to complete our review with a clearance on October 26 of this year.

So again, I feel we're very happy that we're able to -- this program has had success and we're also very excited to have this device now on the market.

I, however, wanted to talk about potential device types or submissions where there isn't as clear a path, where it may not be -- it may be a very well-organized submission, but it may be something we are actually very unfamiliar with. This is an option that has recently been made available to FDA. It was actually put together and passed as part of the Food and Drug Omnibus Reform Act of 2022, which gave FDA and CDRH the authority to review predetermined change control plans. This allows us to review not only the device as designed in any given 510(k) or premarket submission, but to also consider if that device would be modified in a way that we could prereview those changes such that we could come to an agreement as to how those changes could be made and reviewed within the scope of that 510(k).

What that means is then -- and again, trying to give a practical example, if you are a device manufacturer and you're considering a new device, and maybe as you're planning, you might consider three generations of a device that you might develop and market within five years, and you look at the differences in those three generations of

devices, and you think each of these generations is really a significant change, and I would expect to submit a 510(k) for each of those three different devices.

With this type of program, it may be that we could review a proposal to validate those, the second and third generation of the device, to where instead of needing three separate submissions to review each of those three different generations of devices, perhaps we could -- the goal is to do that in instead maybe just two 510(k), two premarket reviews, or maybe even a single premarket review where we would the first generation of the device and then come to an agreement and a plan by which the second and third maybe we could agree that there were specific criteria that would be met as part of the development and validation of those devices, and again, maybe we could do that in a single 510(k) rather than requiring new submissions for each of those different generations.

Now, as I say all this, I would love to be able to point to an example of this is what a predetermined change of control would look like, this is how we would do that for a drugs of abuse assay, and unfortunately, that is not something I am able to do. This is a relatively new authority that's been granted to CDRH. There are some similar examples as noted in the slide from other device types where this kind of thing has been done.

But we don't have a good example on how we might do this for a drugs of abuse assay. And so we really would like to hear from device manufacturers if they have proposals for how they could develop a predetermined change control plan that we could review and someday provide that as the example that I could give in a meeting like this.

But of course, that begs the question of how that -- how would we come to an agreement as to what our change control plan could look like in an efficient manner?

With that, I wanted to highlight just the next slide, an opportunity for device manufacturers to come to speak to FDA and really just come with questions they have. That is the Q-submission program. This is a program that there is no user fee associated with it, and device manufacturers can submit questions along with background material to FDA with questions about a planned premarket submission, and that can be anything as I'll say as more traditional questions about is a particular predicate device, or some details about any maybe potential lay user study.

But it could also include questions about device development and questions about if you have, again, a proposal for a change control program, that might give us an opportunity to work with you with your specific device to really work out a way that this could be successfully implemented, and again, the goal is to be least burdensome and get the -- if we can get information maybe for not just device validation of a single premarket submission, but also as you're considering changes that you're planning to make to the device, maybe there's a way to review those changes in one submission rather than break it up into two or three or more.

And again, this is new to us. We are excited about the opportunity to do it. But we really are looking to partner with device manufacturers to really work out how this could be done successfully.

We hope to hear from you soon, but with that, I will -- again, I had just a short update, and if you could go to the next slide, I will conclude. That is really all I had for the group today, but I look forward to hearing from all of you soon and hopefully we look for -- I'd love to be able to come up here in the future and have more successful examples that I could share with the group that we honestly would need to work with you to finalize.

But with that, I will conclude and just thank everyone for your time.

MS. DAVIS: Thank you very much, Joey, for that presentation. Later on in the meeting today, we're going to have a board discussion about the potential addition of fentanyl to the analyte table, and where we stand now where we'd like to be as far as fentanyl goes. So, I really appreciate your availability and willingness to talk to us and the manufacturers to streamline any possible changes that might be needed as we update the analyte table now and in the future. So, thanks again for being there. I am sure there will be some questions, if not now, later on in the meeting as we get into more specifics.

But for right now, does anybody on the board have any questions for Joey? I don't hear any, so let's move on to our next presentation.

The next presentation is going to be from Dr. Lynn Wagner with the Department of Defense.

Department of Defense, Lynn Wagner

DR. WAGNER: Good morning, everyone. My name is Lynn Wagner. I am currently the deputy director of the Office of Drug Demand Reduction for the DoD, and I'm happy to be here this morning to present on some of our overall drug testing rates and just about our program.

This is just a bit of an overview of what we call the drug demand reduction program, or the DDRP. We look at it as a three-pronged approach where we have our drug testing program. We also have a surveillance program where we look at emerging drug threats, and we also then have our prevention education and outreach. We have five drug testing labs, and we are governed by three policies, including DoD 1010.09, which is the DoD Civilian Employee Drug-Free Workplace Program, and so I'm mainly going to talk about the military program and just touch a little bit about on our

DoD civilian program, but we also -- any DoD civilian, federal civilian that is in a tested-designated position will be drug tested under SAMHSA's Drug-Free Workplace Program.

As I mentioned, we have five main drug testing labs. We have two Navy labs, one in Jacksonville, Florida, one in Great Lakes, Illinois, just north Chicago basically. Two Army labs, one at Fort Meade, Maryland, one out in Hawaii at Tripler, which is right outside of Honolulu. We also have an Air Force lab, which is at Lackland Air Force Base, Texas, just right outside San Antonio. And then we have the Armed Forces Medical Examiner System and our Special Forensic Toxicology Drug Testing Laboratory, which we affectionately call the SFTDTL. That's at Dover Air Force Base in Delaware.

This is currently our drug testing panel. We have 30 drugs on our panel. The ones that are in red, we have recently added. We added fentanyl, norfentanyl, in June 2019. We added LSD three years ago now in December 2020, and then our most recent one is delta-8 THC we added in July 2021. We also have a panel of synthetic cannabinoids that we also test for. We just recently updated that last October. So, we have new eight analytes on our synthetic cannabinoid panel as well to just try to stay as current as possible even though that's a quickly changing drug landscape. But we had an old panel that had been on since 2012 or so, and so we were really happy to be able to update it to some of the more prevalent newer synthetic cannabinoids.

These are our FY22 drug use trends. We tested a little over 3.4 million service members. We tested a little bit over 1.6 million unique service members, because a service member may be tested more than once a year. So we're more interested in unique service members. So we had a little over 1.6 million and a positivity rate of 1.3 percent, and everyone's always curious about our top drugs, most prevalent drugs that we

have. Delta-9 THC and delta-8 THC are by a landslide our most prevalent drugs, followed by cocaine, LSD, which may surprise you, because LSD is not that prevalent in the civilian population, but our service members sure seem to like it.

A little bit further down is fentanyl, which is everyone knows is concerning. It is one of our top ten drugs. So, it's definitely on the Secretary of Defense's radar and on our radar as well, especially for the prevention, education, and outreach aspect of that. Then followed by oxymorphone and MDMA.

So, we always ask, well, do we deter drug use? We're a deterrence program, and so we want to be able to try and come up with different metrics and measure, well, did we deter drug use? The drug testing program began in -- the punitive drug testing program began in the DoD in 1981, late 1981, so early 1982, and it was very -- we have 1987 here we start with, which was almost 3.5 percent positivity rate. In the early 80s, it was much higher than that. And again, in 2022, we ended up with a drug testing rate of 1.3 percent. So it is, that red line, is at 2 percent, which is our threshold that's set by the Office of National Drug Control Policy, or ONDCP, which is the White House. So that is our threshold, 2 percent. We need to run below 2 percent. We're still doing a great job running below 2 percent positivity.

So, this is just kind of a little bit of a drilldown just to look at trends. Just looking at when we added fentanyl in 2019, maybe a bit of a slight bump. LSD kind of stayed the same, but boy, when we added the delta-8 THC, it really bumped us up. So that's where we are running in the .95 percent positivity rate, and then we add delta-8 THC and it bumped us up. As said before, a couple slides before, the delta-9 and the delta-8 THCs, they are the lion's share of our drug positives.

I'm going to just switch gears just a little bit and talk about novel psychoactive substances or NPS and new and emerging drugs. I just kind of wanted to set the stage for you kind of what the modern drug epidemic, the timeline of that. We started out mainly as primarily plant-derived drugs. In the 80s we had cocaine and we had crack epidemic, and then in the 90s we went to meth and then mid-90s prescription opioids really took over until 2010-ish or so, and then we really saw the synthetically-derived drugs kick off. So, your synthetic cannabinoids and your synthetic cathinones. So, your K2s, your spices, your bath salts.

And so basically now we've moved to a polydrug era. I was just reading a paper recently where the paper cited that 80 percent of opioid overdoses involve a non-opioid drug, and a lot of our drug supply is contaminated with other drugs, cutting agents and what-have-you, like xylazine, which we'll talk about a little later.

And so these designer drugs or these emerging drugs, the substances, there is really a catchall category that includes your opioids, your benzodiazepines, cannabinoids, stimulants, and hallucinogens, and so most of it comes from Asia. Again, the top bullet I think is really important, more than 500 new drugs, and there's more and more coming on, and as the DEA continues to try to schedule these new and emerging drugs, drug manufacturers just simply change the structure slightly and then there's a new drug. It's really an evolving landscape that is a challenge for drug testing programs.

We're just going to talk some about some of the new and emerging drug threats that we see in the DoD. I know this is LSD. This is not a new drug. This is one that's been around for a very long time. It's not really seen too much in the civilian population, but interestingly it is seen in the DoD. I think it's our top four drug that we see. We had -- it was on the panel originally and then we removed it in 2006 because we

just weren't seeing it. We didn't have any positives. So, we removed it from the drug testing panel, and then we started hearing in 2018, 2019 or so, especially in the Marines, an uptick in LSD usage, and so we, due to prevalence, we did some studies and due to prevalence, we added it back in December 2020, so three years ago now.

We only do 10 percent pulse testing on it, and it is for right now and it's almost kind of a probable cause sort of test that is requested from our drug testing program managers. But we sure see it. We have a lot of ongoing concerns about LSD use. You may have read in the news in this past May, there was a suspected drug ring that involved LSD and possibly magic mushrooms on the U.S.S. Reagan. So it's been in the news and it's definitely a concern for the DoD.

So, I just wanted to talk quickly about psylocibin or psilocin, magic mushrooms. There are many, many different types of mushrooms out there that will give you a hallucinogenic effect. So, they produce effects similar to LSD. We are able to test for this at the Armed Forces Medical Examiner System for probable cause or drug-facilitated sexual assault, those kinds of cases. The Armed Forces Medical Examiner System is able to test for psilocin.

This is another one that's of concern. The U.S. Army Criminal Investigation Laboratory or USACIL, which is our crime lab, is seeing an uptick in mushroom products, whether or not it's the ground up, just the ground up mushroom and put in capsules, or there's a plethora of gummies and other edibles that contain these substances. So, this is definitely a concern for us as well.

The other is another type of mushroom, amanita mushrooms. So there are several subspecies of this type of mushroom. Not all of them have the red caps, but

they're really known for their red caps. But they come in yellow and orange caps. But they have those white dots.

And so muscarine is the active hallucinogenic agent in the mushroom, and then the muscimol and the ibotenic acid, they're really they're considered toxins, but they also have psychoactive effects as well. So, the psychoactive effects have been described as like a depressant, sedative, hypnotic, psychedelic, dissociative. So, these are considered, if you go online and you can look, you can see that they are advertised as special legal high.

Anyway, so this is another one that is of concern for us. The Armed Forces Medical Examiner System tests for muscimol. So again, probable cause, barracks sweep and find something like the yums, gummies, then there's probable cause for testing for muscimol.

Xylazine, as we've all -- everyone is pretty familiar with xylazine and heard about it on the news and it is a sedative. It is to improve your high when combined with fentanyl. We also test for xylazine through AFMES. It's also of note, President Biden declared xylazine-laced fentanyl as an official emerging drug threat for the United States. So ONDCP has asked for different agencies, federal agencies, to look at xylazine and to put preventative measures in place and come up with solutions to curb the xylazine emerging threat in the drug supply.

This is tianeptine. It's marketed as a quote/unquote dietary supplement in the United States. You can find it in gas stations. It's known as gas station heroin, hillbilly heroin. It's not approved by the FDA. There was -- although it is approved as an antidepressant in some European and Asian countries. There is a consumer alert out of the FDA that came out in February 2022 discussing overdoses and adverse effects of this

substance. Some of the adverse events that have been reported to the FDA, they're for doses that are higher than the recommended doses for countries where it is prescribed. So we're talking about really high doses and that's probably most likely due for to get high, have that psychedelic effect.

Some of the adverse effects include, well, overdose, agitation, and confusion, rapid heartbeat, high pressure, coma, and even death, and so we are able to test this one at the Armed Forces Medical Examiner as well, as a probable cause case as well. So again, this is another one that is of concern for the DoD.

And with that, I will close, and I really appreciate the opportunity to speak to you all. Thank you.

MS. DAVIS: Thank you very much, Lynn, for that presentation. Really interesting. Do any of the board members have any questions? Libby? I see you have a question.

DR. STUYT: Thank you very much. That was an excellent presentation. My question was for probable cause for the hallucinogens, like LSD and the psylocybins, what would be some clinical indications that would be for probable cause that you're seeing?

DR. WAGNER: So, unfortunately, the military services, their investigative branches, so like your OSI, your NCIS, CID, unfortunately they don't have DRE trained people. So if someone walks into an ER showing some sort of sign of overdose, you know, they go through the regular drug panel. They may also -- probably what will happen is there will be a barracks inspection, which will probably show that there is, there's some paraphernalia or packaging or what-have-you, and then that urine or blood can be sent to the Armed Forces Medical Examiner.

So, they do have some training as far as like impaired driving or driving under the influence, drugs training, but so it's kind of really it just depends on the service and the investigative unit and the investigator, and the circumstances. But AFMES does get those cases quite normally for probable cause.

DR. STUYT: Thank you.

MS. DAVIS: Dawn, you had a question?

MS. HAHN: Yes, thanks, Lynn, for the presentation. It was very good. I was wondering if you could tell us what your fentanyl cutoff is for the screen and confirm.

DR. WAGNER: Fentanyl for confirm is 1, and the confirm is 1 as well, 1 nanogram per milliliter.

MS. HAHN: For both a screen and confirm, correct?

DR. WAGNER: Yes.

MR. ZALESKI: Just a quick question. I was wondering if you could explain more about the pulse testing you were speaking about with respect to LSD. Does that mean that you're not testing all specimens for that? It's only targeted specimens or random sampling of them if I misunderstood, maybe you can clarify that point for me.

DR. WAGNER: Yeah, you're right. We don't test every single specimen for LSD. We have several drugs that we pulse test for, and LSD is one of them. So actually, we increased our pulse testing rate last fiscal year because of the demand. So we put priority on the specimens that have official requests from the drug testing program managers for LSD, and the labs have a quota, let's just say, a quota per month that they have to fulfill for LSD testing and if they don't have enough specimens that are requested for LSD testing, then, yes, it's then just a random pull specimens.

MR. ZALESKI:, : So could be probable cause but it could just be at random as well.

DR. WAGNER: Exactly, yes.

MR. ZALESKI: And you said that that was the fourth highest identified substance in the program this past year.

MR. FLEGEL: I was going to ask, Lynn, do you screen for fentanyl and norfentanyl, or just fentanyl?

DR. WAGNER: We screen for fentanyl only. We have a fentanyl kit, immunoassay kit, and then any of those present as positive, we also use rapid-fire mass spectrometry as a secondary screen and then we send them off to confirm any of those positives that come off of the rapid fire then go to confirm.

MS. DAVIS: Why do you do the second screen?

DR. WAGNER: Because the kit provides -- and I don't even want to say it this way. The screen, we do the secondary screen because the first screen isn't as specific, and so we get a lot of specimens that fail to be positive at confirm, fail to confirm. So we do the second screen to manage that and to cut out a lot of our fail to confirms. So it's less work, less resources used. So that's the reason why we do it.

MS. DAVIS: Thank you very much. Are there any other questions from the board or federal partners?

Hearing none, we are once again ahead of schedule. We're going to stick to the schedule, so you get an extra-long lunch. Please come back; we resume at 1 o'clock. So, I'd like to resume at 1 o'clock sharp, if you come back a little early, I would very much appreciate that.

Thank you very much. Enjoy your lunch.

(Recess for lunch)

AFTERNOOON SESSION

Agenda Item: Call to Order

MS. DAVIS: Welcome, everybody, back from lunch. Let's get started with the afternoon session, starting with the roll call, starting with the DTAB members and the chair.

Alison Stockdale.

MS. STOCKDALE: Present.

MS. DAVIS: David Engelhart?

DR. ENGELHART: Present.

MS. DAVIS: Elizabeth Stuyt?

DR. STUYT: Present.

MS. DAVIS: David Roberts?

DR. ROBERTS: Here.

MS. DAVIS: Lindsey Everson?

MR. EVERSON: I'm here.

MS. DAVIS: Dawn Hahn?

MS. HAHN: Here.

MS. DAVIS: Bryan Ruggery?

MR. RUGGERY: Present.

MS. DAVIS: Michael Grommes?

MR. GROMMES: Here.

MS. DAVIS: Samantha Tolliver?

DR. TOLLIVER: Here.

MS. DAVIS: Carl Christensen?

DR. CHRISTENSEN: Here.

MS. DAVIS: Ron Flegel.

MR. FLEGEL: Here.

MS. DAVIS: And now ex-officios and federal partners. Joey Kotarek?

DR. KOTAREK: Present.

MS. DAVIS: Bohdan Baczara?

MR. BACZARA: Present.

MS. DAVIS: Brian Zaleski?

MR. ZALESKI: I'm here.

MS. DAVIS: Lynn Wagner?

DR. WAGNER: Here.

MS. DAVIS: And the other presenters this afternoon. Dr. Eugene Hayes.

DR. HAYES: I'm here.

MS. DAVIS: Dr. Leland McClure?

DR. MCCLURE: Here.

MS. DAVIS: And Dr. Michelle Peace.

DR. PEACE: Here.

MS. DAVIS: That is it for roll call and we do have a quorum.

The first presentation this afternoon is Eugene Hayes with an update on the National Laboratory Certification Program activities.

Agenda Item: Update on NLCP Activities

DR. HAYES: Thank you, Lisa. Today, my goal is to provide you with two things, one being drug testing results updates, and then the second being updates on the NLCP itself.

The National Laboratory Certification Program is a government program that's run by a contract through RTI. We're currently in option year 1 of a four-year contract, and we get the luxury of maintaining the high standards within the government program. I want to express my sincere appreciation for all the efforts the NLCP, through RTI, does to support to support the division, and efforts from the Mandatory Guidelines to laboratory certification. Their efforts are invaluable to our work.

As of December 1, 2023, there were 21 certified laboratories. This is an increase. The largest group is category 1 laboratories. There are six currently. There are no category 0 laboratories, six category 1 laboratories, which includes one IITF, five category 2 laboratories, one category 3 laboratory, four category 4 laboratories, and one category 5 laboratory.

There are also two category 6 laboratories and two category 7 laboratories; both categories introduced into the program in January 2018 and 2019 respectively.

And during the past five-year period, there have been four labs to withdraw from the program. The reasons cited by the laboratories for withdrawal from the program include changes to operations due to mergers and acquisitions, loss of clients requiring HHS certification, and reshifting of the workload amongst laboratory

corporation groups. Furthermore, there have been two laboratories certified in the past five years, the most recent being this past October.

The number of specimens tested in 2014 was 6.64 million and rose to a high of 7.52 million in 2022. For this period, the number of specimens tested was at its lowest in 2016 at 5.79 million.

The total number of specimens reported as drug-positive, adulterated, invalid or substituted -- non-negative -- increased from 196,000 in 2018 to 208,000 in 2022, a difference of about 12,000. 2018 was the first full year of federally regulated testing for hydrocodone, hydromorphone, oxycodone, and oxymorphone, as mandated by the revisions to the Mandatory Guidelines for Federal Workplace Drug Testing using the urine Mandatory Guidelines effective October 2017, and this was potentially -- this was the reason.

The non-negative rate as a percent of the total tested, however, decreased from 3.1 percent to 2.8 percent from 2018 to 2022.

The percent of specimens reported as drug positive, adulterated, invalid, or substituted -- non-negative -- decreased from 3.1 percent in 2018 to 2.8 percent in 2022. 2018 was the first full year of federally regulated testing for hydrocodone, hydromorphone, oxycodone, oxymorphone, as mandated by the revisions to the Mandatory Guidelines for Federal Workplace Drug Testing using the urine Mandatory Guidelines. Non-negative reporting for January to September 2023, is 2.9 percent.

As shown in this graph, THCA remains the most often identified drug in urine. However, specimens reported positive for amphetamine and methamphetamine continues to be the second most reported drug positive.

Hydrocodone, hydromorphone, oxycodone, oxymorphone being added to the panel in 2017. Laboratory positives for the opioids have declined year-over-year since their inclusion. Specimens reported positive for benzoylecgonine has begun to rise since 2020. Specimens reported as invalid as a percent of total tested has soared over the past few years. Until this year, specimens reported substituted and adulterated only had small variations in their non-negative rate over the same period. However, substituted rates so far in 2023 are .07 percent and are up significantly as compared to previous years.

Overall, the percent of specimens reported as invalid increased by more than 16 percent in 2022 from 2021. Please note that typically the percent of specimens invalid due to pH rises in warmer months and is lower in cooler months. However, with the warm fall/winter of 2022, invalid due to pH rates didn't decrease as much as they typically would October to December.

Specimens reported invalid due to pH is primarily due to specimens with high pH greater than or equal to 9 but less than 11, though with the majority being reported in the pH range of 9.0 to 9.2. Prior to the revisions to the urine Mandatory Guidelines, which included raising the lower pH cutoff from 3 to 4 for identifying specimens as adulterated, the percent of invalids for low pH related greater than or equal to 4 but less than 4.5 averaged 7.4 percent per month in 2016 and the first nine months of 2017. Since the October 2017 effective date, the percent of invalids low pH related averaged only 1.9 percent per month.

Furthermore, invalids due to pH less than 9.5 saw a slight increase of 5 percent when comparing the last 12 months of October to September 2023 to the 12-

month period prior, while invalid due to pH greater than 9.5 increased nearly fourfold for the same period.

We have also seen an increase in those specimens reported invalid due to inconsistent creatinine and specific gravity results, with creatinine less than 2 milligrams and pH greater than or equal to 9.5. This increase began mid-2020 and peaked in early 2022. Reporting has decreased, though still elevated as compared to pre-2020 levels.

Specimens reported as invalid due to immunoassay interference during routine lab testing increased significantly from late 2017 and throughout 2018. In February 2018, two large labs notified the NLCP of the increase in invalids due to immunoassay interference. It also noted that most of these specimens exhibited depressed immunoassay results with 6-acetylmorphine using the CEDIA reagent and some had depressed results with amphetamines using the CEDIA amphetamine-ecstasy reagent. This data was presented during the March 2018 DTAB session.

It was suspected a substitution product containing something that interfered with the immunoassay caused this significant increase. Reports have subsided at this point from what was seen in 2017 and 2018, and the rate as a percent of total tested continued a downward trend through 2022 and has since plateaued a bit.

Of specimens reported invalid due to immunoassay interference, the majority occurred with the hydrocodone-hydromorphone immunoassay in 2022. As shown in the previous slide, overall the percent of specimens reported invalid due to immunoassay interference has decreased in 2022 and 2023.

There has been a marked drop in cases where 6AM caused immunoassay interference. In 2021, 30 percent of invalid immunoassay results were due to 6AM. This percentage is now in 2023 decreased to below 5 percent.

This slide presents data on the consistency in immunoassay interference caused by the hydrocodone-hydromorphone, oxycodone-oxymorphone over the past four years. The interference rates for oxycodone-oxymorphone have been stable, fluctuating between 20 and 30 percent. This indicates a persistent level of interference in immunoassay due to these substances. Hydrocodone-hydromorphone shows a higher interference rate, averaging about 60 percent, but fluctuating with higher volatility. This suggests that hydrocodone-hydromorphone is a more common cause of invalid immunoassay results compared to oxycodone-oxymorphone.

This slide particularly focuses on the rising modest trend in immunoassay interference caused by amphetamines and benzoylecgonine over the past two years.

This particular slide focuses on the rising modest trend in immunoassay interference caused by amphetamines and benzoylecgonine over the past two years.

This particular slide we can see that the specimens reported invalid due to immunoassay interference by PCP and THC. The rates are pretty consistent over the time tested.

As shown by this particular chart, the percentage of specimens reported as invalid due to pH remains higher than other invalid categories. Other invalid categories are abnormal physical characteristics, abnormal creatinine, specific gravity levels, confirmatory or immunoassay interference, and oxidant activity.

To move on to some of the activities from the National Laboratory Certification Program, the NLCP publishes a continuing education newsletter on topics of interest to the drug-testing industry. This past year, to date, 27 newsletters have been published. We have archived all the newsletters and there is a scannable tag on this

particular slide that you can use with your cellphones to gain access to the newsletter, for the future and to access the archived newsletters as well.

The summary of the drug-testing data. The number of regulated specimens tested by HHS-certified laboratories increased 17.4 percent for the period 2018 to 2022. The percent of regulated specimens reported as positive, adulterated, invalid, substituted decreased 9.3 percent for that same period.

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

The combined non-negative positivity rates increased significantly in 2018, 3.19 percent. This was primarily due to an increase in the drug positivity rate and inclusion of the opioids, hydrocodone, hydromorphone and oxycodone, oxymorphone. Since 2018, the combined non-negative positivity rates have decreased, though increasing the past few years, primarily due to the increased invalid and substituted reporting.

Now onto some of the activities that we have to update on. We've been tackling some issues over the past few years within the National Laboratory Certification Program. One is diminished junior toxicologist knowledge of the program, and we worked over the course of almost 10 years to tackle this particular problem, in hiring junior staff, in making sure we promote the program to junior toxicologists at different conferences and making sure the junior toxicologists have access to the trainings that we offer within our program.

Uniform inspector education. We actually have an emphasis on streamlining inspector education to ensure consistent knowledge transfer and application of inspection criteria across the board. The NLCP is actively working on refreshing all of its courses to stay current with the latest industry standards.

You heard Mr. Flegel talk about the agility of our drug testing panel, and efforts are currently under way to revise the Mandatory Guidelines to ensure that our drug testing panel is agile. We continue to look at challenges in identifying adulterated or substituted urine specimens. We are following up on the program launch of oral fluid and ensuring that we can collaborate with FDA on device specifications. We are eagerly awaiting and anticipating the arrival of our first two applicant lab applications, because that will be the day that we mark the launch of the program.

Mr. Flegel also mentioned that we're all anxiously awaiting what's going to happen with anything that goes on with rescheduling.

This slide talks about our applied study agenda. At the heart of every successful applied study agenda lies meticulous planning. It's the bedrock upon the entire endeavor stands, and it determines the direction and scope and feasibility. You saw earlier that we probably have about 20 or so studies going on, all simultaneously. And we have an effort ongoing to put these all into an applied study agenda, one that we can focus on identifying and address critical questions that pertain to the program and that affect public safety, that can focus on prioritizing the most pressing study questions regarding drugs of interest for the program and for the country, that provide the most innovative approaches, that collaborate and partner with civilian and Federal government bodies, that provide continuous evaluation of our program and the drugs of interest; and

that share the information that we get, and that really help broaden the ability for us to get the information that we need.

One of the things that I like to say is that we cannot do this alone. We have to find partners to be able to do this work, and our applied study agenda is one of the ways that we are going to try to reach out to civilian and federal partners to try to broaden that scope.

The applied study agenda continued. We've moved from this being a method for DWP and NLCP to just share a list of studies that will increase our ability to draft regulations based on evidence and a method for us to lead studies in understanding areas that impact the Mandatory Guidelines. We understand that we will not have the funding to complete every study that is needed, and we hope that by speaking to an agenda that we will be able to encourage studies that illuminate and allow for studies in the areas of interest to the Federal government and to the programs of interest for DWP and for our federal partners alike.

Laboratory support. In our laboratory support piece, we have two particular items that I'll speak on. One is the GAP analysis. This is kind of like a technical assistance tool that we've implemented to help laboratories who are new to the system gain some insight into being certified. This does not allow for a consultant to basically do the work for a laboratory, but it allows for a consultant to go out and tell a laboratory what things they need to look out for, what things they need to do to become certified. It's more like technical assistance than we've ever seen before.

I think we currently have two laboratories in the process right now. But we're looking at being able to build on the laboratories that are currently applying, to make sure that they can meet the requirements.

And then the second is the electronic custody and control form. We want to make sure that all of our laboratories, all 21, have access to an electronic custody and control form. What we found is that not all of the laboratories have access to the major providers, and we want to provide access, and we want to provide and ensure that access is able to be retrieved within a timely manner because it's mandated by the federal government outside of DWP.

So, we queried the laboratories to see what was going on in the field, and if they had the access or if they did not have the access. We queried the ECCF providers to see if they're providing access or if they were not providing the access, and we were able to validate that not all laboratories had the access that they needed. And then we're currently in the process of researching eCCF product solutions to see what we can do as an entity, as NLCP-DWP, to help strengthen our laboratories' ability to have access to the eCCF products that they need to move into the future.

That is all that I have for the National Laboratory Certification Program. If you have any questions from the board, I'll be happy to take them.

MS. HAHN: Dr. Hayes, I was wondering if you could provide an update on the status of the new urine and oral fluid lab manuals.

DR. HAYES: We are currently working on the urine and the oral fluid manuals.

DR. WINECKER: We are finishing up the manuals currently. We should be done with them very soon. The issue is the final piece that we'll need is the agreed-upon date for Department of Transportation.

DR. CHRISTENSEN: How do you know that a specific drug is the cause of immunoassay interference, and not just in the specimen along with another unidentified drug?

DR. WINECKER: It's not the drug that's interfering with it, it's something else. It's the drug that was named was the assay that the interference was noticed in.

MR. ZALESKI: A quick follow-up on that in terms of the immunoassay interference for those different analytes. Reading between the lines, are we assuming that there are some interfering products that individuals are using to thwart the testing process, or there's an issue with that particular assay and something else interfering with it? Or maybe you can answer this -- do you pair these specimens, so you're going to do a recollection in a lot of those situations. Do you have that data to see if the second collection turned out to be a positive or not, to get some insights on those issues?

DR. WINECKER: No, we don't have that data. But it is a combination of things, so some of it is just that particular immunoassay, that particular brand of immunoassay, maybe that particular lot of immunoassay for that brand. And some of it is definitely some kind of interferent that is being added to the urine.

MR. FLEGEL: I was going to answer Brian, too. Sometimes when the manufacturers change their products, for instance like a colored dye, all of a sudden we'll see interference with the immunoassay. So, it is dependent on what is put in those products as to what is going to interfere with what assays.

MS. DAVIS: And I'd like to add that there's a couple of immunoassays that go strongly negative when some sort of interfering product or a product used to attempt to tamper with a specimen is added to the sample. So, it may be an indication of specimen tampering going on.

Any other questions from the board or federal partners?

Thank you very much, Gene, for that update.

Presentation: Update on the Medical Review Officer Manual

MS. DAVIS: The next presentation is from Dr. Leland McClure, and he's providing an update on the Medical Review Officer (MRO) manual.

DR. MCCLURE: We're going to talk this afternoon and give you an update in terms of what the status is for the updates for the Medical Review Officer guidance manual, and this is the updates that have been performed in accordance with the newly published Mandatory Guidelines for both urine and oral fluid.

As was talked about earlier today, back in this October, October 12, the new updates for the Mandatory Guidelines were published. Urine Mandatory Guidelines go into effect on February 1, 2024, next year. And the oral fluid Mandatory Guidelines, it's a retroactive date back to October 10 of this year.

In accordance with this, some of the major changes, we've heard about this from a number of presenters today, the morphine cutoff for the confirmatory testing for urine was adjusted to 4,000 nanograms per mL. And there's a requirement now for a separate Federal Register Notification annually for the drug testing panels, the biomarker testing panels, and any required nomenclature change that's in there.

The biomarker testing changed so that it's not based on invalid, but it's going to be reported as substituted now. There's a new requirement now for medical review officers that they provide a semiannual report that goes to SAMHSA. And there's a new requirement also for federal agencies regarding the use of an MRO. This is an entirely new section that's been added on there. The MRO verification of positive

codeine and morphine specimens, the 15,000 nanograms per mL threshold to report positives, that was removed.

Mr. Flegel talked about the refusal to test criteria now, it's been normalized. So, it's the same criteria for all donors out here. And for the medical review officer review and verification, there are some additional edits also.

And these are some of the additional edits on there, and these are specifically in section 13.5 for the medical officer review and the verifications. When we look at the bullets in through here, the first one that's in through here is that a medical review officer is going to take action for an invalid result when the specimen's other results, either positive, adulterated, or substituted, are verified as negative, and that would be negative based upon a legitimate medical explanation. So that would be the only time that an invalid, in that situation, is going to be acted upon by the MROs.

Next bullet item on through here is a new item that states that when a donor admits unauthorized use of a drug that caused the positive result, the MRO is going to document that use of an unauthorized use of the drug, and the records are reported to the federal agency, and it's going to be reported as a positive.

The next bullet item on this is that for the instance where you have either ingestion of food products or passive exposure, it was in the previous version of the Mandatory Guidelines only applied to marijuana. Now this section has been revised so it applies to any positive drug test result. Not just marijuana. And again, that's for passive exposure or ingestion of food products that have caused that to occur.

Next bullet item on this is that a physician's authorization or medical recommendation for a schedule I controlled substance is not an acceptable medical explanation for a positive drug test. So, anybody that's using a schedule I drug, even if

it's with a script from a licensed physician, that's still not an acceptable medical explanation.

Last bullet item that's on this, and this is one where the invalid process has been greatly simplified on here, when the recollection of an invalid specimen, a specimen reported as invalid, is still invalid, the MRO now is going to cancel the test and they're going to recommend recollection using a different specimen type.

With the guidelines, we have oral fluid, we have urine. So, for a urine test, this alternate specimen type would be oral fluid. If an agency, however, does not authorize the recollection of another specimen type there, the MRO is going to consult with the agency, and they're going to arrange for a clinical evaluation to determine if there's a valid medical reason for the invalid result. This is much simplified from what it was before.

Oral fluid. It's similar to the urine, with the one point on here in that we have expanded information on the collection devices. So, we still have, with the top bullet, the separate Federal Register Notification for the drug panels, biomarker panels, and nomenclature.

The substituted update. Semiannual summary reports for the MROs; federal agency use of an MRO; verification for the positive codeine and morphine specimens. Now, this has been changed for oral fluid, so specimens that have less than 150 nanogram per mL are going to be reported as a negative. Again, same criteria for refusal to test for all donors.

This slide is almost identical to the other one that we looked at for urine. In most instances, when we look at the guidelines, the sections pretty much run in tandem with each other. So, for 13.5, for the MRO review and verification section in through

here, the section and the quotation in through here, about when MRO takes action for an invalid result, it's the same section, same description. So, the MRO is going to take action only when positive, adulterated, or substituted have been verified negative based upon legitimate medical explanations.

The next bullet item that was on this was, again, MRO reports a positive test result when the donor admits unauthorized use of the drug that caused the positive test result.

The next one in through here, I did highlight this in yellow, is that there's a slightly different section that's on this, but it's the same context here, in that ingestion of food products containing a drug apply to any positive test results, and it's not just positive marijuana.

There is, of course, an exception that's in through here that includes the exception for positive codeine and morphine based upon the threshold for the cutoff.

Next section through here again it's the same context on this in that it's stating a physician's authorization or medical recommendation for a schedule I controlled substance is not a legitimate explanation for a positive drug test.

And then the last one is the same context with what we're talking about with invalid, a much simpler process now so that if a recollection for an invalid is still invalid, cancel the test, recommend another type of specimen type. If the agency does not authorize another specimen type, which for oral fluid, that would be urine, the MRO is going to consult with the agency and arrange for clinical evaluation to determine if there's a valid medical reason for the invalid test result.

What's important to recognize with this medical review officer guidance manual is that it's not a standalone document. This is dependent upon all the various

documents that have been discussed today. With SAMHSA, first off, the Mandatory Guidelines for both urine and the oral fluid, they have to go through the entire process of getting updated and ready for the final publication. Federal custody and control forms, whether it's paper or the electronic, all of those have to be updated. The various handbooks out there for collection -- if it's the collection handbook, the collection site manuals, or the collection site checklists -- these all have to be completed with the updates so that we can make the corresponding changes for the MRO guidance, where it's applicable for these topics.

For the National Laboratory Certification Program, again, the checklist and urine manuals, and the oral fluid manuals, and the laboratory checklist, all of these have to be updated so that the applicable information, again, can be referenced in the medical review officer guidance manual.

Additional changes that happened with this with the updates for the medical review office guidance manual is to align the language so that it corresponds with what's in the Mandatory Guidelines for both urine and oral fluid. Sometimes the changes that have been made in the guidelines changes a little bit of the language. That needs to be aligned so that we harmonize that in the manual.

The various tables that are in there, in particular, table 4 that's there for bottle A test result and review and actions that the MRO takes, and then table 5 for the split bottle B analysis and retest and refusals to test, all of these need to be updated. When we look at the support also for case studies, to provide examples of situations that occur, the case studies may need to be created for new scenarios, or they need to be updated also to correspond with any kind of changes that are there.

Custody and control form illustrations need to be updated on there. Additional information also has been added this time to alert the MROs of additional agency-specific information; when looking at the medical review officer manual, it's written so that it's for HHS guidelines and HHS employees, and it's not specifically covering the Department of Transportation, where we look at 49 CFR Part 40. There is some language that's in there alerting MROs to look at that, but it's not giving the specifics of what's there for the DOT. But there are instances where they have to give additional alert information for MROs.

For expired custody control forms and actions taken, that needs to be updated on there. There's an update also for CBD, especially CBD transformation in gastric fluid. I'm not saying it happens, I'm saying that there is an update out there. There's a paper that was presented this last summer that the NLCP sponsored, and it indicated that it's not likely for a transformation of CBD to delta-9-THC for urine at the cutoff levels of 50. However, that's not every instance that's out there, so take a look at that information.

Something that was just recently also notified for the laboratory directors in the program is the deletion of the confirmatory requirement to have an amphetamine qualifier present in order to be able to report methamphetamine. This applies for HHS, and currently right now the DOT is evaluating this, and we don't know exactly when that will occur. But the medical review officer manual does call this out, saying this is for HHS. Updates for when this occurs will be announced with a Federal Register Notification.

Process, real quick, with what happens for the medical review officer changes. First, it starts with Mandatory Guideline changes, the proposed. And then

processing of those Mandatory Guidelines, working it through the review process and the approvals. And ultimately, SAMHSA has an FRN, Federal Register Notification, for the guidelines. Both of those feed into identifying what the edits are and the various supporting documents that have to be edited also.

SAMHSA then, and NLCP, also then edit and publish all of these supporting documents that we talked about, and then the MRO manual can start to consolidate those edits in there, and then the next step on that is going to be the review officer manual goes to SAMHSA and NLCP for a review, and ultimately gets published.

Let's go to the next slide, just an overlay on this one. The green what's been done, and where we're at right now is the last part of the MRO manual getting ready to go to SAMHSA and NLCP for review and ultimately being published.

The timeline for which all of this is taking place started with a kickoff in November of last year, and the revision is targeted for December 2023, looking at handing this off to the NLCP and SAMHSA by the end of this week, and then we can work on whatever final revisions and updates need to be done at that point.

Take-home message for this, the guidance manual. It's a supporting document that's out there. The case studies that are out there also are supporting documents that are companion documents that are based upon, but they do not replace, what the Mandatory Guidelines are and what the NLCP manuals have. It's a support resource that integrates the DTAB SME inputs for drug metabolism and results interpretation, and overall, it depends upon the completion of all of these steps in the publications that SAMHSA and NLCP work with. So, it's a very large task that takes place, multiple dimensions of what has to be done in terms of skillsets on this, to bring this all about.

And I think this is the end of it, it's a thank-you, and it's really a thank-you to everybody that's at the SAMHSA and also at the NLCP for all of the work that they've done. This helps being able to pull all the information together so that it can be integrated into the manual.

MS. DAVIS: Thank you very much, Leland. You did a great job with that. There's a lot of tiny pieces to keep track of.

Do any of the board members have any questions for Leland?

DR. CHRISTENSEN: With the elimination of the amphetamine requirement for methamphetamine, especially when dealing with oral fluid, and maybe hair testing down the road, does that remove any safety of confirming that it wouldn't be due to incidental exposure?

DR. MCCLURE: No, actually it's something that takes into account what happens with the genome that's responsible for the metabolism of methamphetamine. So it actually helps in the detection of amphetamine and methamphetamine. The genome that's responsible for the metabolism of methamp to amphetamine, it ranges from poor metabolizer to ultrarapid metabolizers, and this change that was made will help, if anything, I believe, and I'll let others from the program chime in, it'll help to avoid instances where you have a positive test that you can't report simply because of a genome issue and the individual donor was not able to excrete the required amount of amphetamine metabolite to be detected and reported positive.

DR. CHRISTENSEN: Just hypothetically speaking, if you had a hair specimen positive for methamphetamine, how would you rule out incidental exposure?

DR. MCCLURE: I am going to defer the hair testing until we get to that point, respectfully.

MR. FLEGEL: One, I want to thank Leland. A lot of work. He's done a great job doing all this, putting it all together, interpretation and everything. I did want to add, and not to step over, but there was also a section that Leland and I talked about that we're looking at adding and that is around authority, whether it's authority of an MRO, authority of a federal agency, employer, whoever that may be, but it's something I think that we probably need or needed in the MRO guidance manual, and I think it will help in the future around authority, or who has the authority, in the drug test results.

MS. DAVIS: Any other questions or comments? Next up, Dr. Michelle Peace is going to be providing a presentation on lab-created cannabinoids and other contaminants in commercially available products.

Presentation: Lab Created Cannabinoids and other Contaminants in Commercially Available Products

DR. PEACE: Thank you so much for first your time today and the ability to present some of the outcomes from my research lab.

My first talking point is just to say that I am funded by the National Institute of Justice. My lab has been funded by them since 2014. The projects really started with trying to understand the nature of electronic cigarettes and their impact on criminal justice and their impact to substance use and abuse. And I'm really thrilled to be able to announce that we will be funded by the National Institute of Justice in the coming year to evaluate THC isomers and derivatives and do some surveillance work.

I'm very passionate about the nature of how science can inform more robust policy and regulations and legislation, so what we know is that good policy and legislation supports public safety and public health, and when there are gaps in that,

particularly at the federal level, then mythology and quality assurance in products that consumers have access to really become questionable.

I do want to talk very briefly about electronic cigarettes and how we got to where we currently are. The Food and Drug Administration and the Centers for Disease Control recognize basically four different generations. These have been chronological as well as technological advancements for each of these generations.

In my lab, we have been very careful to say there are really five different types of devices. The pod mod, the device that we probably best know as the Juul, is really what we would consider the fifth generation of devices. The fourth generation are what we have been calling drippers and dab rigs. The cannabis marketplace and people who consume illicit and non-illicit drugs refer to these devices as drippers and dab rigs as well.

The generation, these actually were born out of the third generation. They came out of need. Consumers were taking the third-generation device, which is that big boxy silver device, and they were unscrewing the mouthpiece in order to put their drug of choice directly onto the hot coil. Whether it was in some kind of semisolid form or dissolved in some kind of liquid that they would drop right onto the coil. And they do that because that coil gets between 250 to 1,100 degrees Celsius, depending on an array of parameters. This is particularly messy and inconvenient, and so the industry evolved into a wider mouthpiece that drugs could be placed on top of the coils, either in the semisolid form or as a liquid. So it's a wider mouthpiece.

When we now think about the fifth generation, this is really for nicotine, right, which is best typified by the Juul device. These are pod-based products that enable clandestine drug use. With the Juul, what we believed happened was that these smaller

concealable devices came because of Juul, and in probably most of America thinks this is what the evolution was.

What we really appreciate, though, is that the Juul device was born from the cannabis industry, and so the cannabis industry wanted and needed something that facilitated clandestine drug use. And then we know that Juul did evolve from the company that invented Pax, which is one of the first e-cigarettes used to consume cannabis in an aerosolized form.

I'm going to shift gears real quick and talk about why we care about vaping, particularly inside of the cannabis industry. This is one of the projects that we did during COVID, where we decided to just poll people to find out what are you putting into your vapes.

Not surprisingly, cannabinoids were at the top of the list. This doesn't surprise anybody, but you'll also see an array of what would be considered herbal products like melatonin, kanna, skullcap, passionflower, those kinds of things. We also asked in the survey what are the contexts in which you consume those drugs? So one of the most terrifying things that we learned is that particularly for the cannabinoids they are choosing to consume cannabinoids while they are driving. And also amphetamines and herbal products as well. But clearly what we see in this table is that we have 13 respondents, a majority of our respondents, said they consumed delta-9-THC while they are driving.

On that note, I think one of the really important things to also discuss is the nature of how the concentration in cannabis products has been slowly increasing over the last couple of decades. And in the most recent decades, it has really increased. There are reports that some plant products are as much as 20 percent THC. But it's not just

plant products. We know that e-liquids and dabs and waxes can be anywhere from 40 to 95 percent THC.

So, we spent a lot of time taking a look at e-liquids, and in the early days of the cannabis and e-cigarette coming together, there was sort of this coopting of can I use the chemicals that are used for nicotine e-liquids, can I use them for cannabinoids? And at the end of the day the answer is no, and I'm going to show you the data around that.

So, then they tried to use PEG. PEG is polyethylene glycol, which is in a lot of foods that we consume. It is approved by the Food and Drug Administration to eat, and what is problematic about vaping is that the chemicals that are used in the e-liquids are approved by the Food and Drug Administration. They're on their list as generally regarded as safe. However, they're not safe to inhale.

Because PEG is hydrophilic, meaning it's water-loving, putting oily cannabinoids into PEG didn't work. So, then they went with an oil, which essentially a coconut oil, a medium-chain triglyceride, and then it evolved into why are we using anything at all? Let's just put a wax or dab into the device that is the e-cigarette, because that will work. And indeed, it does.

These are what the dabs and the waxes look like, and again we see an array; the far-right picture is an e-cigarette type device in which the device is really a stainless-steel cup.

This is some of the data that we saw as it was emerging, as the cannabis industry was trying to figure out vaping. These were products in our lab where we see that it's in propylene glycol, vegetable glycerin -- those are the constituents used by the

nicotine industry. So, 6.5 and 7.6 micrograms per milliliter of CBD is not a lot of cannabinoid in PG and VG. That's because it doesn't dissolve. It's literally oil and water.

So, in MCTs we began to see higher concentrations, and this particular product, I'll point out here, this is CBD in MCTs and nicotine in PG and VG. Again, oil and water, this is in the same pod, there was a university was hoping to use these products in a clinical study. We urged them to not carry on with that study.

So, in this product we see that the MCTs worked; 532 milligrams per milliliter, significantly more cannabinoid in e-liquid. But again, the dabs and the waxes that they're just putting in the e-liquids now are 75 to 90 percent THC.

We continue to monitor delta-9-THC e-cigarettes. One of the things that we have noted is that they are increasingly complex in their chemical structure, not just with the terpenes from the plant that they're adding back into the e-cigarettes, but also an array of flavoring chemicals and solvents as well. They are particularly concerning from a number of public health perspectives, in addition to this public safety issue where people say they like to vape delta-9-THC while they drive.

We keep an eye a lot on the lack of quality assurance in the cannabis industry generally speaking. This was actually a study conducted by somebody else, where they wanted to look at products that were hemp-derived delta-9-THC. Hemp-derived is particularly important. They are referring to the synthetic process of transforming CBD into delta-9 in these instances.

So, these companies that were manufacturing these were using labs that were ISO accredited. They were following the guidelines for accreditation, and I can't stress enough, not to say that all labs are bad, but a lot of labs are really bad. So anyway, these companies were using ISO-accredited laboratories, and you'll see here that 50

percent of the products that they analyzed, which was about 1,800 hemp delta-9 products, were mislabeled, and that for products that were purchased online, there was little-to-no age verification for those purchases.

There's this study that has been published, that's open access online, that evaluated the phytochemical diversity, to again stress that frankly the 0.3 percent THC by dry-weight basis that the 2018 Farm Bill requires is difficult-to-impossible to hit that.

I'm going to push through this data to get to the final point. The first point is that, at least according to this study, which evaluated almost 100,000 products, that there was no real difference between the strains of sativa and indica from a chemical perspective. That's what these slides are demonstrating.

Then they wanted to look at CBD-dominant plants. These are supposed to be plants that are compliant with the 2018 Farm Bill. Eighty-five percent of the plant material they looked like were above the threshold as required by the Food and Drug Administration, and this is because it's so difficult to have a controlled grow in a field.

We're aware of the Farm Bill and the 0.3 percent threshold, but what happened with that was that CBD really proliferated in the marketplace. Everybody was growing hemp for the purposes of generating CBD. That's where the profit margin is really, really large. So, what happened then, shortly thereafter, was that there was too much CBD in the marketplace, consumers were not sure if it worked, and of course, it floods the marketplace.

Then the market fell out of the bottom of it, and now you've got millions of dollars of CBD sitting in vats, and the manufacturers don't want to lose millions of dollars, so they're going to convert it. This is delta-9-THC, with acid and time and a little bit of heat, it will convert to delta-8-THC, but it is a balance of the two, and it has to be a

long conversion time, because the longer you heat it, you'll get the balance of delta-8 to delta-9 will tip over into delta-8. That means this is a particularly messy synthetic process, meaning that you're going to get delta-8-THC and delta-9-THC in the same synthesis.

If you heat it too hot, then you are going to get potentially hundreds of degradant products, which are fantastically complicated.

One of the things that we continue to monitor, and I'm going to get to probably some of the most terrifying points, is that once they figured out that the synthesis of other THC isomers and derivatives, all of these analogues, is particularly easy, there is a call within the industry to just say since we're having such a hard time with the plant, because the plant has other kinds of problems that include pesticides and heavy metals, then why don't we just convert CBD? Why don't we just make all of these other things? And there's also gaps in our regulatory framework.

So, the multistate operators, the MSOs, say embrace the hemp-derived delta-9 and some of the other analogues, even though there's no pharmacological foundation in terms of effect and safety and toxicity of these other analogues. So there are potentially hundreds at play here, from delta-8, which does occur naturally in the plant in very trace amounts, delta-10, THC-O, and THC-P. One of the things that we have been watching is that these manufacturers, when they make a new compound, they're more likely to put it into an e-liquid to test it, to see what its veracity is. Because the American public has become sort of a petri dish for these products. They don't have to do an FDA-approved clinical study. They have the American public to do it in.

So, their test products are usually e-liquids, and if they are a market success, this is usually where they then put it into other kinds of products and begin spraying on plant material.

I do want to talk about this hemp-derived delta-8, and this has become a significant speaking point for me. This is a case in which, at the beginning of the delta-8 emergence, this is a regular cannabis consumer was looking to see what the rage of delta-8 was -- this is a honey stick. It's supposed to have honey in it that is infused with delta-8; it was supposed to have 45 milligrams of delta-8-THC in it.

He consumed one of the two that he had, he had four to five hours of what he would consider the most terrifying hallucinations he has had, meaning that he believed somebody had chopped his legs off and they were on the other side of the room, his fingers were broken, he couldn't dial his phone, he lay in that state for four to five hours.

He sent us the other honey stick, and this is what was in it: 953 milligrams of CBD, 204 milligrams of delta-9-THC and 631 milligrams of delta-8. There was no honey in this stick, it was 100 percent dab.

My argument to claim that to say that being hemp-derived is a shade of -- I'm just going to say it, it's a lie to try to propagate that these products come naturally from the plant. If we assume that the plant is at best 1 percent delta-8-THC, in order to make this single honey stick with 631 milligrams of delta-8 in it, you would need 14 pounds of plant material to make that single honey stick. So, what we know then therefore is that delta-8 in this instance is manufactured. It is completely synthetic with a strong acid over time and heated to some degree will convert to delta-8.

We monitor products sold online. This was a product that somebody submitted us, said I'm a regular cannabis user and this was not THC. He sent it to us not

knowing where, how, he acquired the product. We went onto Diamond CBD. I do not mind calling these people out, we have had more Diamond CBD adverse reaction reports than we have had most other products. So we went directly to them, purchased directly off of their website, nine products, and we see here that four products contained the synthetic cannabinoid 5-fluoro-ADB, and one product contained dextromethorphan, which is the active ingredient in over-the-counter cough syrup.

This website said that there's an all-natural process and they are safe for you if you have PTSD, lower back pain, and safe for your children with epilepsy. These products, I may remind you, were randomly purchased off of their website.

This went wide and large, we published it, Philadelphia Inquirer picked it up. The CEO of Diamond CBD was really livid with us. He said that, well, no, actually my products contain melatonin, which is still not CBD. So, I don't say this to brag but I do say this from the point of after that manuscript came out, we were in popular media around the nation.

What happened was that people around the nation started sending us their products where they had had an adverse reaction. What we see here, this is just a sampling of some of the cases that we have had, is that in the early days they were the synthetic cannabinoids like Spice and K2, the fubinacas and pinacas, those kinds of things. But at some point those fell out of favor to put in the e-liquids. That pink line indicates the threshold of essentially the Farm Bill.

So after that we started receiving products that were just highly concentrated with CBD and THC, and these three people were cannabis-naive users. They wanted to consume a product that wanted to help them control their pain, and so we've got two ladies that were over the age of 70. They were found after having days of

hallucinations and what they would consider schizophrenic breaks and really horrifying scenarios. So, these people didn't know who to turn to, and they found us.

Right now, one of the most concerning things on the marketplace is the ever-evolving isomer and derivative proliferation. I'm going to orient you to this slide. These are a handful of products that were labeled to contain HHC, HHC-O, or THC-H. For this set of products, they were labeled to contain HHC, they had HHC in the label but they also had all of these other cannabinoids -- delta-8, delta-9, 6a, 10a, delta-10, CBN, and in these we also had delta-8 and delta-9-THC-O.

For these products, which were supposed to contain HHC-O, also contained HHC. These products didn't, that was what was supposed to be on the label, it contained all kinds of other things. In this scenario we have 8 out of 14 products, just from this table -- we've tested almost 100 products at this point -- and about 50 percent of them actually have the compound in it that's on the label, and this sampling, 64 percent contained more than three additional cannabinoids.

So, the industry's like, well, what do we do with this? Because they can't get any certificate of analysis to actually match what they're putting into the products. So, they're just calling them boutique experiences, with absolutely no pharmacological foundation. This is a company that says that they have rapid onset, it lasts a long time, they can do something funky in the middle of your experience.

In this package we've got, the label is supposed to be 25 percent delta-10, and 70 percent delta-8. Do not click on that QR code, it will take you to a scam. And these were the cannabinoids we actually found. So 6a, 10a, delta-9, delta-8, delta-8-CHCV. Again, don't click on this.

This is where the company is literally saying that we can't find a lab to generate a certificate of analysis, which is what we want it to say. That all of these labs said that the products were something else, but we know what we put into our own product.

In this situation we have the same product, delta-8 is on the front of the package. Delta-8-THC-O is on the back of the package. The certificate of analysis says that it's delta-9-THC-O, and we actually found exo-THC, delta-8-THC, delta-9-THC, and delta-8-THC-O, but only half of what they said they had for delta-9-THC-O.

And this one, it says delta-8-THC and THCP, is on the front of the label. And I pulled this directly off their website. The reason THCP does not show up on the blend of the certificate of analysis is that very few labs can test for THCP as it requires more expensive equipment, more advanced testing staff, and reference samples. So, they know that there's a problem with the labs, that the labs can't analyze the products adequately, but we are to trust them what's in it.

In addition to the range of cannabinoids -- we think a lot about adverse events -- so we've certainly received in our lab lots of products that are just loaded, they fail basic tests for bacteria, yeast, and mold. In this situation it's a product that looks like it should be a gummy. It wasn't, it was plant material that had been sprayed with delta-8. These two products contained significant residual solvents.

This is not plant material at all. It is paper that has been shredded and then formed into what's supposed to look like a cigarette that has significantly more delta-8 on it than what was on the package. In this situation, what some manufacturers will do is that they'll go to a big box store and buy generic cookies, lay them all out on a table, and

spray them with the oil of whatever drug that they want to put on them. So, in this situation, when we took the cookies out of the package, they were full of hairs.

This is a situation in which a young woman here in Virginia, she was in Charlottesville, she stopped in a shop in Charlottesville, drove to Richmond, which is about an hour and fifteen minutes away, to go to an outdoor concert. Her and two of her buddies consumed the other joint that was in this, and she had seizures so bad that the lead singer stopped the concert to get her medical attention. He could see her having seizures. The other two women who helped her consume the other joint had no adverse effects. You'll see there it was supposed to be 10 percent delta-8, and it was really 6.2 percent delta-9 and also the new trend -- let's just put in THCA because that'll pass and what we know is when you -- that's the precursor -- is that when you actually heat that it is going to convert to THC. So, therefore we have a product that's almost 20 percent delta-9-THC.

This is a cider that was purchased at a farmer's market that was supposed to contain THC and CBD, it had nothing in it. We still don't know what is growing on the top of that e-cigarette. And what we know here in Virginia is that we had a four-year-old actually die from consuming what the parent believed were CBD gummies.

In this situation, we have a product came to us, and I can now speak about this a little more clearly because the case has been completely adjudicated. This is a young man who committed a felony, he believed he was a player in a videogame, in which he shot at two police cars, so he was charged with attempted murder of two police officers. When they went into his home after they arrested him, they did not collect these products. In lucid moments he said he did consume three of the ten gummies that were in this package.

When we received it, I thought that said THC-zero, meaning that would comply with the Farm Bill. No, that was a new analogue called THC-O-acetate. You can click on that QR code, it takes you to the paper in which we published this. Each gummy was supposed to have 10 milligrams of THC-O-acetate in it. You can see there from his psychologist that he had fragmented and disjointed speech, depersonalization, he was paranoid and had grandiose ideations. He had a complete break with reality. He was in a facility for mental health for about a year and a half before he was able to stand trial, and he was just found not guilty by reason of insanity.

You can click on those QR codes as well, I'm happy to supply any of our manuscripts. From a drug testing perspective, we certainly have a lot of concerns, right? Particularly with these hemp-derived products where the consumers believe that when they come from the plant, therefore they must be safe and they must be legal. We're finding more and more products that have the THC acid precursor in them, and so particularly for the ones that you will heat, those will just convert to delta-8 or delta-9-THC.

In our lab's unpublished data, we have found that THC-O metabolizes to the carboxy-THC, and that there's nothing left of the original THC-O. So this is, I think, from a drug testing perspective, particularly concerning.

We also know that if consumers are taking CBD that many of their products will have delta-9-THC in them as a contaminant because they didn't clean it out, because it was coming directly from the plant, who knows? But the CBD products will have delta-9-THC in them. We also have a lot of concern with all of these analogues, the isomers and derivatives, that in confirmation analyses, that these other analogues will co-elute with the items, the analytes of interest.

So, we have done a lot of work in my lab. This is some of the early work. You can see that method there for the details. We're still working on this method now to include approximately 25 or 30 analogues, but this is just an example of some of the challenges we've had. In this situation, we have delta-10 and 6a, 10a, essentially are co-eluting. Exo-THC was co-eluting with delta-9. Our delta-8 and delta-9 acetates also co-elute. At the end of the day, we were able to resolve all of this, and now we're adding more analytes to this method and having to make some hard decisions along the way, which I'm happy to talk to you about.

We know that the industry is running the narrative, and in this situation they're also making fairly outrageous claims as to what some of the medical benefits are. It really does require a lot of education to check them on some of their wild mythology.

The other piece is how they are recommending people consume their products. We see here, this is just, these are CBD oils, and we see three completely different recommendations for how to consume those oils. We did assess, when I pulled these three examples, they were all the same -- they were the same volume, essentially the same amount of CBD in the bottle. So, depending on who you picked, you could easily take too much, have an adverse event at the end of the day, particularly if they are contaminated with other cannabinoids.

So, we know the industry is constantly evolving to elude regulations, and federal unified regulatory oversight improves transparency to consumers. Even here in Virginia, there have been conversations about the hemp industry and the regulated medical marijuana industry having two sets of regulations to follow, and I've worked really hard to advise against that, because in order to protect public health and public

safety, you need unified regulations with those goals in mind. It requires constant advocacy in those regards.

We know that the manufacturers, the industry, technically can't make their own claims. These are not FDA-approved products. So technically they're not supposed to be talking about, they're not supposed to be advertising medical benefits. However, that does not keep them from either, a, saying it, or b, blogging about it, which they are allowed to do. So when a scientist finally comes along and says this is what the reality is, the scientist is the one that is heavily criticized, as opposed to the industry itself that originally perpetuated some of those claims.

We know that the industry has also infiltrated the peer-reviewed literature, so there's definitely some industry bias in the peer-reviewed scientific literature that makes things particularly complicated. We know that urgency is needed in these situations. We know labs need rapid response tools. We know that drug testing labs need support in developing different panels, particularly as these other cannabinoids really evolve in the marketplace.

And at the end of the day, we really do need experts from all of the sectors that service stakeholders, and we have a real desperate need for collaboration so that we don't have siloed information in that certain sectors aren't privy to some information without everybody knowing that.

It does include people from inside the cannabis industry, those insiders who say they want legalized cannabis. Well, okay, if that's the case, then help us deal with the rest of the industry that doesn't want a regulated marketplace and are more profiteering.

On that note, I thank you for your time. I'm happy to answer questions. I have the National Institute of Justice and NIH to thank for funding significant parts of this research, and I have a really fabulous research team.

On that note, I'm happy to take questions, but I'm also easy to access if you have any in the future.

MS. DAVIS: Thank you so much, Michelle, for that talk and all that information. That was incredible.

We have a question from Libby Stuyt.

DR. STUYT: Thank you so much, that was an awesome presentation, and exactly what I've been experiencing clinically. It's a serious problem.

One thing I just want to point out that I don't know how to do this, but all those things that you talked about need to be in the public domain. The mainstream media does not ever report any of the problems. They seem to be pretty much in the cannabis camp where they do talk about all the positive things, in their newspapers, they allow ads from the industry about CBD. But they're never reporting the downsides. So I'm just wondering what your thoughts about that might be.

DR. PEACE: I agree, it's really very difficult to amplify this message into the public sector. We have had -- I've been interviewed by the New York Times, CNN, I try to get VCU to run stories; they do run stories. The marketing people at VCU then pitch it to the Associated Press. And sometimes it gets picked up, sometimes it doesn't. So, it is very difficult to amplify the message.

We do a lot of work, I'm probably on the road every two to three weeks, giving talks in schools and to nurses and to frankly anybody who will listen. Substance use people. Again, trying to amplify the message, and it's just incredibly difficult.

MS. DAVIS: Any other questions or comments from the board for Dr. Peace? Seeing no hands raised or hearing nothing, thank you again, Michelle, for that great talk.

We are a little bit behind schedule, so let's stick with the ten-minute break, please, and come back at 2:40 for a discussion of the proposed analyte table changes.

(Brief recess)

MS. DAVIS: The next presentation is by Ron Flegel, the Division of Workplace Programs director, and he is going to give a little talk about the proposed analyte table changes and the addition of fentanyl, and the process moving forward.

Agenda Item: Discussion of Proposed Analyte Table Changes

MR. FLEGEL: Thank you, Lisa. With that, big changes, I'll just say. This is the beginning of the process in the proposed analyte table change as far as how we will look at that. So, we have time for a discussion afterward with board members, for any questions as well as maybe constructive feedback on this.

But again, it is a newly proposed process. It's in the Mandatory Guidelines for both urine and oral fluid, and also would be for hair so it changes the tables consistently throughout all the Mandatory Guidelines.

Some of the reasons behind that is if we had to make a change, let's say in urine, you would also additionally have to make it in oral fluid and/or hair. So you would have three sets of guidelines out all the time.

If we're now just evaluating the analyte table changes or analytes, it makes them more flexible, or as Eugene said, more agile, in making those changes, we only have to change the table and that would be effective in all Mandatory Guidelines that we have currently for authorized matrices.

So, some of these slides will remain the same, but I put these in here just to emphasize certain points. In DWP objectives and goals, one is we did continually assess the science and technology. We did assess the process that we have in place as far as going out as a proposed rule receiving comments, going through the overall federal agency review, how many different times that takes depending on what it is that we're putting through as a proposed rule. Sometimes it would take, in a sense, up to four years that we had in a few cases where we actually got the analyte in the actual Mandatory Guidelines.

So, with that, we wanted to have it so that we were more agile as well as more flexible and be able to review these on an annual basis, and as I stated earlier, it doesn't mean the analyte table is going to change on annual basis, but at least we will be able to look at that on an annual basis, specifically if there is an emerging issue drug. That's what's important right there.

So again, part of the overall goal was to look and advance national drug policy and the latest scientific findings, and specifically again around emerging issues that we see, or upcoming emerging issues.

With this, we have had that approved as an analyte table change. How it's going to work, I'll share the process in a minute. Again, if there is a question from board members, please feel free to raise your hand, stop me at any point during this process, and we can hopefully answer the question now. Or what we can do is we'll have a discussion after this.

So again, the urine and oral fluid are authorized matrices to test in the federal program. Those would be what we would look at as far as the analyte table

change. We're proposing an FRN to go out sometime in the beginning of the year, is what we're looking at. I'll detail that a little more in the actual proposed changes.

I can't see the bottom of this on my screen, but as you can see, what I highlighted before is the group that will deal with this as far as the analyte changes, emerging issues, et cetera. Again, Joshua Hunt will lead this. We don't have a big division, but there will be a whole lot of information and things we'll look at around this as how we evaluate, and that process will begin internally as to how we evaluate what would be an emerging issue, what would we consider an emerging issue, and how we would respond to that if we were to make an actual table change.

This is the actual proposed change for any type of panel changes. I'm actually going to go through this rather slowly so that the board will fully understand this, because we didn't have the guidelines published, and that is one of the reasons we had to cancel the DTAB meeting in June so that we would have this published so that we could actually talk about it in a public forum if it was accepted.

So with that, I'm going to go through each of the sections, and there are going to be some nuances, I guess, between the arrows as to what we do. I'll start and if any of the Drug Testing Advisory Board has questions, please feel free to stop me.

In number one, we'll monitor for potential panel changes, this would be new analytes, removal of existing analytes, or cut off changes to those analytes, which are currently in the table. We would review the scientific and medical literature, review the drug prevalence reports such as NFLIS, Drug Testing Index or DTI, CDC's overdose data, et cetera. There is a number of self-report, there's a number of information that SAMHSA has that we collect data on, looking at is there an emerging issue drug?

We would also solicit and review information from federal agencies or federal partners, Department of Transportation, Department of Defense, DEA, HHS-certified labs, MROs, research scientists, and then manufacturers of collection devices and immunoassay kits which I think are important in this scenario because of the fact that if we did propose an analyte table change, we have to have an immunoassay that would detect that. So again, we would reach out to all of these federal agencies, federal partners, and evaluate what we thought would be an analyte that would rise to the occasion to go onto the Federally regulated Drug Testing Program.

Within that, and again, I'll try to put some dates, what we would see in number two is around the June meeting for DTAB, we would present information on the potential panel changes. We would have an FRN three weeks prior to the meeting, as we did in this meeting. DTAB would be meeting on that date and time. We would have an agenda that included the timeline or timeframe, and the method for providing public comments, which we have in this.

We would also then have the DTAB meeting. The basis for the panel changes, all the technical and scientific data that we would present, as well as discussion on related costs and benefits. Within that, in number three, so the arrow that would go from number two to number three is where we would solicit public comments. Now, on the current process, we have received public comments from this, but they're not outward-facing to the public. Those public comments would be published on the DTAB website so the public can see what those comments are. These comments will be published, we're working through that, but again, we would review the public comments for this in this analyte table change in number three.

In number four, we would go to the next DTAB meeting, which would be in the timeline of around September. We would present comments and responses to those comments to the Drug Testing Advisory Board. We would have an FRN three weeks prior to the meeting that would again, as we stated in this FRN, would establish what we're looking at as far as what we're proposing to change. We would then have a DTAB meeting set with that agenda to go through the present comments and also the responses to those comments.

In number five, we would have DTAB's response to the SAMHSA recommendation of adding or removing an additional analyte or removing an additional analyte, so that would be response from DTAB on the SAMHSA recommendation.

In number six, we would submit for federal agency review. This would be a review and respond to comments, maybe, we don't know at this point, maybe in multiple rounds of comments, depending on the federal agency. We would give a status update on the panel changes at the quarterly DTAB meetings consistent with the next meeting that we would have with DTAB.

I also want to say that one of the things that was discussed is an expedited review from OMB. It will be a Federal Register Notice that will go out to the public with a preamble, as we do now, stating what the comments would be and how we essentially look at those comments, how we answer the questions around those comments, as well as the proposed table changes that would go out. But again, an expedited review so that we can essentially, on an annual basis, review and implement those table changes.

Then in number seven, we would have a drug testing panel Federal Register Notice. This would be the basis for any panel changes, the implementation date for each change, and that may be different, but as a program, you would obviously want

to make the analyte table change the same in all matrices. So, the implementation date would be the same in urine, the same in oral fluid, and/or hair. So, with that table change, that would be consistent throughout the Mandatory Guidelines on the date.

That's sort of the whole proposed process from basically January of, let's say, this year, 2023, to January 2024. Because we delayed the process of what we thought would occur in June, we are now in the later timeframe. But again, the first table changes are always going to be the hardest because we're working out the actual process of this whole entire how we're going to actually change these, et cetera.

With that, I'm going to go to the next slide. This is just an outline that you can review and look at as far as the review process in urine and oral fluid drug testing panel changes. Again, ongoing monitoring for potential panel changes. We would then have the quarterly DTAB meeting where we present the information on the potential panel change. The FRN, the DTAB meeting, the time, the agenda would all be spelled out along with all of our other items that we usually include when we're giving presentations in the quarterly DTAB meetings, and then a review of public comments.

After the review of public comments, we would go to the next DTAB meeting. We would present the comments and responses. This is the same as what is in the diagram I just showed. I also wanted to have it in what I could spell out as far as in a timeline. Then the DTAB would respond to the SAMHSA recommendation of the analyte panel change or removal of an analyte. We would have a federal review of the process, and this would be a review and response to comments, give status updates on panel changes at the quarterly DTAB, if it ran over that annual basis, and then we would update DTAB on this.

We would also have a drug testing panel Federal Register Notice. It would be essentially the same, very similar but not the same, to what we have proposed like Mandatory Guidelines, but this will just be a table change, and it will show that, so on the implementation date for that panel or panel change, the HHS-certified laboratories would actually implement those changes on an annual basis.

So, I put this in here because it gives us the ability on an annual basis to make changes. I don't know where those changes will be made, but the flexibility or being more agile with our Federal drug testing panel, I think, will be beneficial for not only federal agencies but also for DOT and our federal partners around those panel changes.

Some of the prevalence, and you may have seen this slide before, I know Svante presented this in a couple of different meetings as well as I believe I presented it, but one of the things I wanted to point out here is we've talked a little bit about delta-8, Michelle did an excellent presentation on the delta-8 and all the other isomers of THC, but it is a very prevalent thing that we also see now in the Federal Program.

So, if you look at the delta-8 THC, it's about 2.27 percent. That really falls right in the same categories as far as analytes for cocaine, oxycodone, oxymorphone, and also the hydrocodone and hydromorphone, so it's pretty significant as a positive, and we look at this because we have to separate out the delta-8 from the delta-9 to report delta-9 in the Federal Program. So, you're seeing this in the prevalence as far as a lot of different specimens in the regulated program.

We also looked at fentanyl. That is around 0.19 percent. This data was from 2017 and 2019. I believe, at least in information I've seen very recently, like yesterday, the prevalence rate is much higher. So we see a lot more fentanyl in non-

regulated samples, let's say, of greater than 0.19 percent. So, I think it's important, and I think everyone is aware, that that is an analyte that we're looking to add from the Federal Register Notice that was posted. So, we've had numerous conversations, numerous presentations leading up to this. I don't think it's any surprise to the board that we're proposing to add fentanyl to the drug testing panel, and that that would be our recommendation.

One of the obvious items that I was discussing in the proposed table changes or in the proposed revisions to the urine was the actual morphine concentration change. That was from 2,000 nanograms to 4,000 nanograms. What I wanted to show, and you may have seen this slide before, we've shown it in a few different presentations, but I think it's very important to show this, what we've looked at is all the journal articles around poppyseed ingestion, et cetera, that are more recent than the ones we looked at early on in the poppyseed ingestion around the Federal Program, and what we can see is a pretty clear or distinct line around 4,000 as a cutoff.

As you're aware, we've changed that cutoff in the Mandatory Guidelines for morphine to 4,000. So, anything over 4,000 really has to either come from a prescription or illicit drug use. Why is that important? What we looked at is we looked at fentanyl and we looked at 6-acetylmorphine around those concentrations. When you look at the concentration of around 4,000, or 4,000 or greater, you start to see the prevalence of 6-acetylmorphine be higher as you have an increase in morphine concentration. So 6AM is a more prevalent marker of concentrations greater than 4,000 for morphine.

But when you look at fentanyl, you actually see that there is actually more fentanyl present in anything under 4,000, or what could be considered a morphine

concentration where there could be poppyseed ingestion. But if we add fentanyl to the program requirements for testing, then I think what we're going to see, in fact I think it's pretty clear from this chart, is what we will see is we'll have more prevalence of fentanyl in the lower concentrations of morphine, and higher prevalence of 6-acetylmorphine in the higher concentrations of morphine.

So, I believe that overall you're going to have a more positive rate of fentanyl 6-acetylmorphine when we'll be excluding some of the actual morphines that we would have reported from 2,000 to 4,000. So I think it's a better marker in adding fentanyl to the program as to look at illicit drug use in these lower concentrations, better than morphine, and the same with additionally continuing to test for 6-acetylmorphine, especially around the higher concentrations of morphine, and lower concentrations.

Hopefully I explained that well enough, but it is I think a very interesting chart to show, specifically around the cutoff concentration of 4,000. Again, this goes into our analyte table change of why we are recommending that we add fentanyl.

This was what was proposed in the Federal Register Notice. After this presentation, I believe that Lisa is going to look at a very much more detailed presentation, a small presentation, around this and look at this a lot closer. So I won't touch on this a whole lot right here. But what we've proposed, and as Lynn said this morning, is the initial test cutoff of 1 and a norfentanyl cutoff of 1. That may change. Again, we're still looking at comments that came in. I believe right now I can say, because it should have been for the public, we have over 100 comments that have come in right now on the analyte table change.

Confirmation cutoffs would be the same as what DoD looks at, 0.5 and 0.5. Then in oral fluid, we're looking at 1 nanogram per mL with a confirmation of

0.5. Any comments that come from this presentation or a presentation to DTAB, you can see the information, any comments can be submitted to the DFWP website below.

One of the other recommendations, which was put back out, is the removal of MDMA from the testing panel. Eugene showed a lot of information regarding the drug positivity rates across the board and SVT testing. What I wanted to do on this is show the prevalence rate of MDMA, which you can see is relatively low. Overall, in the whole Federal Drug Testing Program, that includes DoD civilian, and DOT as well as HHS for other agency testing, it really is relatively low around MDMA.

In the next slide, I'll specifically drill down into the MDMA. So we're at about a 0.002 percent. Again, not that it's not an illicit drug that's not being used, but to maintain that for HHS-certified laboratories for the relatively small amount of samples that do get tested as positive, it's very, very difficult and not really cost effective.

I want to say the other thing with this is we also have a lot of blind proficiency testing that's sent out from federal agencies. Some of those blind proficiency testing are also included in this positivity rate. So, it's even lower than the 0.002 percent. It has come down as we tested over the years. So, it's pretty significantly come down. If you look at, I believe that was in 2017 at 0.005 percent, we've cut that in half. So, we are recommending the removal of MDMA. Libby?

DR. STUYT: I just have a cautionary comment about that. Just the fact that many states are legalizing psilocybin and different hallucinogens, and MDMA is being included in those. There are ongoing studies right now looking at the benefit of MDMA in treating PTSD, depression, different things like that, which I think is appropriate in terms of the studies. But like Colorado has just legalized open door.

I think there's going to be an increase in that because it used to be, back in the early 2000s, a very popular drug in a treatment program I ran, and, yes, it fell off popularity, but it is, I think, going to start coming back up. Just a cautionary comment.

MR. FLEGEL: Totally understand that. I think we're in a gray area because when it comes to MDMA as a treatment, I think that's very well understood in a treatment setting. If an individual were to test positive for MDMA and say that was because of my treatment, then we'd have to look at that a little closer because, yes, you're right. One of the things in the Federal Program on a case-by-case basis, if the federal agency does feel there is reasonable suspicion to believe that the person is using MDMA, for instance, or amphetamine-MDMA, et cetera, they can test on a case-by-case basis. So we do a lot of that in a number of federal agencies for what they would ask for or require under a schedule I drug.

We looked at the low positivity rate also of PCP, but it's very difficult to say let's remove PCP. That really shouldn't be something as a safety issue, that should be being used in a Federal Drug Testing Program. So again, that wasn't a recommendation, but we were looking at that as far as a low positivity rate, and even from the -- but yes, thank you for that comment. I do agree. I think it makes us fall in a very gray area when they say, oh, I'm using this for a treatment program, and yet it's in a Federal Program. We definitely will take that under advisement.

Again, as far as the new process, DTAB will be much more engaged in all of this decision-making from January 1, from now on, as we roll out this first initial process. Thank you.

So, MRO guidance manual, again I want to thank Leland for that. All of these, as we change, and the only reason I put this in here, is because as we change and

analyte tables are removed, the MRO guidance manual and case studies will have to be updated. So that really could become an annual update, almost, if we were to propose making changes on an annual basis if we had that throughout. I do not foresee that happening, that we would change items or we would change analytes on an annual basis. It may be several years, it may be one year. It all depends.

But I just wanted to point out that with all the guidance manuals, we would also need to draft those and make the changes necessary before the implementation of an actual analyte. Same as with fentanyl. That will be changed, that will be in the MRO guidance manual, as to what MRO should look as the relevant information around fentanyl.

Action plans, number three was to reduce the length of time required to change the testing panel. We highlighted that because that was one of the items that we put on the list early on, over a year ago, and we've completed that. Well, we've completed some parts of that as required in an action plan. But I just wanted to point out under the Comprehensive Review, there are many action items that we have and sometimes in the regulatory process, it takes a while, but we're going to try to get to most of these, if not all of these.

The road map and action plan, the two items on here were to reduce the length of time required to change the testing panel, and what we're looking at is a testing panel change of a little over a year, and I do not want to speak for DOT's program, but we have looked at that and DOT will go out with an NPRM when we make a panel change which might try to coincide our changes right now to make it less difficult for HHS-certified labs when they make those changes for both the Federal Program under HHS as well as the Federally Regulated Program under the Department of Transportation.

So, we're trying to make it as easy -- well, not easy when it comes to IT changes and everything in the labs, but we're trying to make it as easy as we can in making the same change across the board. We also develop and add a pulse testing. This would be in non-regulated specimens as well as possibly some regulated specimens that are being discarded. That will be around emerging drugs or specimen validity issues. Sometimes we don't know exactly how many synthetic urines are going through the program because we don't, on a regular basis, test those specimens, but to go back and look at specific markers of negative specimens that did make it through, it might give us a lot of insight into how many samples are actually being substituted with synthetic urines, et cetera.

So, an update as far as the analyte table update issues, the required time to respond to changes to authorized analytes, cutoffs, and matrices, and then the required time in the Mandatory Guideline revisions which we are trying to keep at a year. And what plays into a whole lot of this is the time for the FDA clearance process of new assays and devices. That's very important, because we can't move forward as a program unless those immunoassays or new immunoassays or assays are cleared. That's important with that.

As far as the update process, again, the Drug Testing Advisory Board presentation will begin, board discussion, public comments, and review of those comments, and then review of public comments at subsequent DTAB meetings I think is going to be important. The DTAB will see that FRN and be able to comment on the FRN for the recommendations to add or remove drugs, and then a published FRN.

This was the existing FDA paradigm. Joey talked about this earlier, so I'm not going to really go through these, but I wanted these in here because I think it is

important in that in our working together as far as federal agencies, specifically around making these changes in a timely manner, that was one of the items that we wanted to look at as far as being flexible, et cetera. But we also have to have federal partners to be able to work with around these, because it really is, in our situation where we're trying, we have an emerging issue drug that we're trying to test for safety-sensitive positions, we really need to get these drugs of abuse assays approved and into the laboratories for their validation processes so we have a good timeline in the implementation.

Again, from Joey's slides before, this was from the FDA presentation in June of 2023, the FDA identifies complete submissions and then FDA review can be as short as a month, as Joey pointed out.

Make changes to a device to respond to an evolving need, changing not only the cutoff would require clearance through FDA but also obviously adding a new analyte would have a clearance for that immunoassay if that's what was being used. It's different when it falls into GCMS or LCMS when you're doing a screen, because that's a laboratory practice as far as a validation, which falls under the NLCP program. So, I think it's easier in that sense to actually change an analyte when it comes to a screening process outside of immunoassays.

And again, can use the 510(k) substantial equivalence determination language and submit with initial application, that's all again what Joey presented, but again for the 510(k). If you want to look at the presentation, Joey gave another presentation today around this, but you can go back and look at this. I just put the link here, or contact Joey regarding FDA clearances, and I know he will be able to explain this thoroughly for you.

With that, that is the proposed. I'm sure there are questions, or possible questions, around the proposed analyte table changes of what we're looking at starting essentially with this meeting. I will open it up for questions or any discussion. If there isn't a discussion right now, then I'm going to turn it over to Lisa, and let her do a presentation, if you want to, Lisa, so that we may have more discussion after her presentation.

MS. DAVIS: Thank you, Ron. If you don't mind, we'll hold questions until after these next few slides. The next portion of the agenda is the DTAB board discussion. So, I've got a few review slides and where we are now and where we're hoping to go for the basis for the board's discussion in a few moments.

This is a review of Ron's slides showing the positivity rate for MDMA is very low. Again, this 0.002 percent, it does include a blind. So, the actual positivity rate is lower than that.

These are the cutoffs that we proposed and put out for public comments. That's where we are today.

As Ron mentioned, pulse studies are part of how we identify the potential analytes that may need to be tested. This was a pulse study done on regulated specimens that were deidentified prior to disposal. These are all specimens that tested positive, that screened positive for morphine, and were going to a confirmation for opiates. These samples are rescreened using an immunoassay targeted at fentanyl at 1 nanogram per mL. So what's important to notice here is the median norfentanyl concentration is 10 times higher than fentanyl. The immunoassay for this had very little cross-reactivity to norfentanyl. So with the higher cross-reactivity rate, we may have seen more

norfentanyl-only specimens, also had the samples to begin with not been targeted from morphine-positive specimens.

So even this data is showing an abundance of multiple specimens of very, very high concentrations, the chart on the left and table on the top that show that the concentrations of fentanyl and norfentanyl are very high, and again these are deidentified regulated specimens. According to an article in 2010 by DePriest, they noted that approximately 30 percent of specimens only contain norfentanyl and not fentanyl. The study also shows a large percentage of samples of just fentanyl and not norfentanyl, but those are important things to understand and know as we move forward and try to target, decide what our target analyte is going to be and at what concentrations.

So, you saw an earlier slide about prevalence of fentanyl. Dave Kuntz at CRL was kind enough to supply us with some of their data. They run approximately 20,000 specimens a year and, as you can see, their fentanyl, this is non-regulated workplace testing, their fentanyl positivity rate is increasing steadily. Well, even more than steadily, pretty rapidly in the last quarter or two. He also supplied us with the concentrations of those samples by the confirmation rates. So you can see the concentrations of the fentanyl on the left and the number of specimens on the bottom. You can go to the desired concentration on the left and go over to the graph and see how many specimens you would have perhaps missed, the number of specimens that you would have missed or conversely the number of specimens that are positive at that concentration.

This is the same sort of graph with norfentanyl. As you can see, obviously, the higher the cutoff, the more samples you miss.

So where are we with immunoassays? There are kits out there that are targeted for fentanyl only with a cutoff concentration of 1 nanogram per mL which is very sensitive, but their cross-reactivity to norfentanyl is very poor. Then there are assays out there that are targeted at norfentanyl, but their cutoff concentration is 5, and their cross-reactivity to fentanyl is very high. So, where we want to be and where we are now are not matched very well.

As we move forward and try to decide where we want the cutoffs to be, which analyte we want to target, what do we want for the cross-reactivity requirements, how long is it going to take for an immunoassay to get there. We are inviting comments from the public as well as discussion from the board to help us further this along.

So, with that said, Ana, you can remove the slide unless we need any of these to refer to later. The board is welcome to open the floor up to discussion. Please state your name before speaking. I'd like a discussion to happen, so I don't know about raising your hand through the whole discussion, but please state your name for the transcriptionist before you speak. I'd appreciate it. Thank you.

Who would like to start us off?

Agenda Item: DTAB Board Discussion

MR. FLEGEL: Thank you for that presentation. We could have probably spent 50 minutes on the slides because I think they're so important. But one thing I did want to note is I think we've pretty much concluded that we need to confirm for fentanyl and norfentanyl both. But the detection around the immunoassay is questionable, as Lisa was showing with not only the charts and the data, but also the immunoassay kits that are currently available. I just want to add that so it puts a little bit of context that we know what the confirmation should be.

I will also say it's concerning that you look at regulated samples and there's that many fentanyls that are in the regulated samples.

MS. DAVIS: Who wants to speak up first? Should we target one analyte area over the other? What are pros and cons of going with the fentanyl assay versus the norfentanyl assay? How much time will it take for us to get an assay that potentially could be cross-reactive to both through FDA? Is that likely? Anybody know any of that information? Do labs want to screen for both, have two assays, one for fentanyl and one for norfentanyl? I know the answer is no. We've got to get that on the record, people.

(Laughter.)

DR. CHRISTENSEN: Just a quick comment. Is there any intention of requiring confirmation of norfentanyl metabolite? Or if you are fentanyl-positive or norfentanyl-negative, is that sufficient?

MR. FLEGEL: In confirmatory, because there is such a low cross-reactivity, you're going to see norfentanyl and fentanyl. So, both are reported out. If it was a fentanyl screen and only confirmed for fentanyl, then you would report out fentanyl, or vice versa, you would just report out norfentanyl. So, the reporting would be the same for both the metabolite and the parent drug.

MS. DAVIS: Well, we would require confirmation for both and if either is present, you would report what you find, if either is present above the cutoff. It wouldn't be like you would report both negative because only one was negative. If you only found one, you would report the one that's positive as positive and report the one that's negative as negative if it's below the cutoff. Joey?

DR. KOTAREK: I'm very sorry if I missed this, but on this last slide, you had the proposed cutoff for fentanyl and norfentanyl in urine, and then you had a

proposed cutoff for fentanyl in oral fluid. I was curious, I noticed you did not have a proposed cutoff for norfentanyl in oral fluid. Can you speak a little bit about the proposed cutoff for the oral fluid, like the oral fluid cutoffs and where you guys are at this point with those?

MS. DAVIS: In oral fluid, we would target the parent unless the data comes out to show that we should be also targeting the metabolite.

DR. KOTAREK: I guess that was my question. I haven't seen the data for norfentanyl in oral fluid and I didn't know if you guys had seen that or if that existed.

MS. DAVIS: That's one of the reasons why we're requesting public comment. Thank you, Joey.

(Laughter.)

MR. FLEGEL: But you are correct, Joey. We're not proposing to look at the metabolite norfentanyl, not in oral fluid. Same as, for instance, in oral fluid, looking at THC. I don't know, I haven't seen any specific studies, maybe Ruth can answer this, but specifically I don't know if there are really low concentrations of norfentanyl in oral fluid or if there's just none.

MR. GROMMES: I'd say you do see norfentanyl in oral fluids, just at lower concentrations than fentanyl. You can get some pretty high concentrations of fentanyl in oral fluid. I did also want to comment that it would be, for the laboratories, we would only want to target one drug or the other, meaning have a multitargeted immunoassay for fentanyl and norfentanyl just so that's on the record.

MS. DAVIS: Even if it means waiting a few years?

MR. GROMMES: My opinion would be yes, or can you target just fentanyl or norfentanyl and confirm for both.

MS. DAVIS: That's what we're asking for public comment exactly. Do we want to move forward with what's available knowing we miss some, because the assays aren't necessarily very cross-reactive, and what cutoffs do we use? Or do we wait on one that's cross-reactive for both?

MR. GROMMES: That's a really hard question.

MR. FLEGEL: Really, honestly, we are a deterrent program. So, knowing that we're testing for fentanyl or norfentanyl, but again, as a deterrent program, that's a little bit different than, say, a fitness-for-duty program.

MR. GROMMES: I would say if it's a deterrent program, then fentanyl only would be what you'd want to target. That's just my thought.

MR. FLEGEL: But yes, confirming for both, I think is important.

MS. HAHN: Just a comment. I don't know what all screening reagents are that are out there as far as immunoassay reagents. I know the one that we use here doesn't meet the requirements. I mean, it doesn't cross react with norfentanyl very well so what it would meet the fentanyl, but the controls are like plus and minus 50 percent. They don't meet the current requirements of the plus and minus 25 percent. So, I'm not sure what the other reagent vendors are that are out there and if there are any that would validate at that plus and minus 25 percent control target.

MR. FLEGEL: It is a very interesting question, because as you are well aware, we have the 80 percent rule in the analyte table on other analytes, codeine, oxycodone, for instance. But with that, if there was better cross-reactivity, you could probably run one immunoassay and put a control in at 80 percent, and if it was greater than 80 percent, any sample greater than 80 percent, send a confirmation for norfentanyl

or fentanyl, whichever you targeted. So interesting, yes, whether cross-reactivity is so low or whether it's fentanyl or norfentanyl on the immunoassays. It's difficult to do that.

Dawn, if I can ask, in one of the questions that we ask that I think is important is going back and looking at samples that screen positive, let's say for fentanyl, going back and rescreening those for norfentanyl just to see the difference, as Lisa showed in that graph. There seems to be a pretty significant difference in the fentanyl versus norfentanyl.

MS. DAVIS: If you need us to put any of the slides back up, we can.

MS. HAHN: Even besides the cross-reactivity part, even for fentanyl, that reagent that we use is cleared only for plus and minus 50 percent control for fentanyl. It won't meet even the plus and minus 25 percent control that's required in the manual for an immunoassay reagent just for fentanyl, regardless of norfentanyl.

MS. DAVIS: Do you know the variation or crossover between -- have you ever tried to run a control of plus or minus 25 percent to see?

MS. HAHN: It wouldn't work. It wouldn't pass validation. I can tell you that.

DR. TOLLIVER: I have a statement and a question. My statement would be no, I concur, no lab wants to do two separate screens for fentanyl and norfentanyl. But I'm wondering, and maybe I missed it in one of the slides, the fentanyl cases, are they positive for other drugs as well?

I'm wondering, I know in our laboratory, we see a lot of fentanyl being mixed with all kinds of things. We see cannabis which I know is a big issue. We've heard talks all day about cannabis. Also, it's in cocaine and a lot of other drugs. So, I'm just wondering, are the fentanyls polydrug or are they fentanyl-only cases?

MS. DAVIS: The ones we did in our pulse study were morphine positives that we just rescreened before they were being discarded. So, I would have to defer to some of the laboratories for that. How often do you see fentanyl only without any other drugs present?

MR. FLEGEL: But just to go back and answer your question, these are all discarded negative samples. So, it's not like what I showed in the presentation around looking at the morphine cutoffs of fentanyl with 6AM. These were discarded samples.

MS. DAVIS: Those were the samples from the pulse study from the morphine-positives that were rescreened for fentanyl. Then the CRL data was just fentanyl positives, but I don't know if there were other positives found in other specimens. He just was kind enough to send us the data based on the fentanyl results that he has.

DR. TOLLIVER: The reason I am asking is the other side of the argument is that if you wait however long for a screening assay that picks up both fentanyl and norfentanyl, it seems like you would still be intercepting these individuals anyway. That's what it sounds like I'm hearing. So, you would still have some information about them. It's not comprehensive and it's not what we want, necessarily, but you would have some information.

MS. DAVIS: Also, we'd have to weigh how many samples would we miss waiting for an immunoassay when we know we could get a majority of them with what we have now.

MS. HAHN: Just for the record, I want to agree with the other laboratorians that we do not want two immunoassay reagents and validations out there but would be fine with screening for fentanyl and then confirming for both. In regards to

fentanyl and oral fluid, has anyone thought about the dilution factor, the 1 cutoff when you're using a device that has the diluent in it and it's like a one to four on the diluent? That's getting pretty low out there. So that seems like an awfully low cutoff for oral fluid.

MR. FLEGEL: We are going to have to look at that with the dilution factor because you're going to target 0.25 which is pretty low. So, we're going to have to look at the dilution factor or the cutoff change of, say, four. That's something we'll have to look at. Good comment.

MS DAVIS: Please submit a comment

DR. ENGELHART: I don't have exact numbers, but I can say with our hair testing that I would probably say it's 70 percent multi-positives with fentanyl. We rarely see it alone.

MR. FLEGEL: Let me ask this since we brought that up which I think was a great comment, and Dave, you're on too, what would be -- of course, norfentanyl is a lot higher concentrations but in oral fluid, what would be a good proposed possible cutoff knowing that there is at least a dilution factor in most devices around three or four? Has anyone done any studies on that in the labs themselves around cutoffs, concentrations, with oral fluid? I'm going to take that as a no. Michael?

MR. GROMMES: I would say the problem with the low cutoffs starts to cause issues because you'll have samples in oral fluid that are thousands and so would you have a low cutoff of a quarter of a nanogram? Carryover starts to be a really big issue, and it will also be a big issue with urine, too, because of the range of concentrations that are seen in both oral fluid and urine. So, when you start to go low, that's when it becomes an issue with carryover at laboratories, for sure.

MS. DAVIS: Thank you. We would love to see that as an official comment through the email. Thank you. All right, anybody else?

Okay, we are at the point of the agenda where we are scheduling public comment. These comments are for the record. However, we are not permitted to respond to any questions asked during this comment period.

I will begin with those who registered online to request to give a public comment. Please use the raise your hand feature in the Zoom controls at the bottom of your screen. When prompted, unmute your microphone and ask your question. The first person who requested a public comment is Dr. Lance Presley.

Agenda Item: Public Comment

DR. PRESLEY: Thank you, Ms. Davis. Thank you for the opportunity to address the addition of fentanyl to the analyte table. The Laboratory Corporation of America Holdings, or LabCorp, is one of the largest occupational substance abuse testing providers in the world with multiple SAMHSA-certified laboratories throughout the United States. As a provider of Federal Workplace Drug Testing services, LabCorp would be directly affected by proposed changes to the analyte table for federally regulated testing programs such as the addition of fentanyl and the removal of MDMA or MDA.

The following comments relate to these proposed changes. The department has requested public comments on the recommendation of adding fentanyl and norfentanyl to the analyte table in the Mandatory Guidelines for Federal Workplace Drug Testing Programs. The department proposes adding fentanyl and norfentanyl as target analytes in urine with an initial test cutoff of one nanogram per milliliter and a confirmation cutoff of 0.5 nanograms per milliliter.

For oral fluid, fentanyl is proposed as a target analyte with an initial test cutoff of one nanogram per mL, and a confirmation cutoff of 0.5 nanograms per mL.

LabCorp has supported development of a process to enable the program to be more flexible and adapt Federal Drug Testing panels to changing drug use trends and also supports the addition of fentanyl to the analyte table.

We offer the following comments for consideration. Number one, the availability of analytical reagents. The department indicates that based on the 2023 survey of the SAMHSA-certified laboratories, 84 percent currently analyze non-regulated workplace specimens for fentanyl and/or norfentanyl in urine using commercially available immunoassay kits. However, we are not aware of any commercially available FDA-cleared immunoassay kit that currently meets the proposed cutoffs and cross-reactivity requirements for both fentanyl and norfentanyl.

If kit reformulation and submission to the FDA is required to meet proposed cutoffs, the timeline for addition of fentanyl and norfentanyl may present a significant barrier to the implementation. There are commercially available FDA-cleared immunoassay kits optimized to fentanyl with limited cross-reactivity to norfentanyl and at least one kit optimized to norfentanyl at a cutoff of 5 nanograms per mL. The department may want to reconsider the proposed analytes or cutoffs in the context of existing products in order to advance this initiative more quickly.

There are no FDA-cleared immunoassays for fentanyl in oral fluid at this time. The timeline for adding this analyte to the oral fluid Mandatory Guidelines will be dependent on the availability of a kit that meets the requirements. Unless the regulatory process is streamlined, timelines associated with assay development and submission or

clearance by the FDA will continue to impact the ability of the program to respond quickly to changes in drug use demographics.

Number two, cutoffs. We are interested in understanding the process used to arrive at the proposed cutoffs of 1 nanogram per mL in the initial test and 0.5 for the confirmatory test for both urine and oral fluid. We believe it is important for any changes to analytes or the cutoffs be supported by scientific studies and/or population data that document the prevalence in analyte concentration across multiple populations so that the final standards are fit for purpose. The relevant concentration ranges in a group of individuals with opiate use disorders may differ from a population of patients monitored for medication compliance purposes.

As an example, a sampling of non-regulated workplace fentanyl results in 2022 and 2023 demonstrated a frequency of fentanyl at less than 1 nanogram per mL at 1.6 percent while more than 50 percent have results greater than 100 nanograms per mL for fentanyl, and greater than 1,000 nanograms per mL for norfentanyl. The proposed cutoffs should be reviewed in the context of population-based data and revised if so supported in accordance.

An additional consideration for oral fluid is that specimens collected in buffered devices will be diluted such that the concentration of drug in the device is significantly below 1.0 nanograms per mL. There will be analytical challenges in developing and maintaining robust assays that support the cutoffs and required quality control for this matrix at the proposed cutoffs.

And lastly, the concordance of analytes and cutoffs across federal agencies. There are multiple operational and logistical challenges for laboratories. If the changes to the analyte table are not adopted across federal agencies and federally

regulated industries at the same time, from a laboratory's perspective, we urge the various stakeholders to work toward concordance.

Thank you for your consideration of our comments on the proposed changes to the analyte table. LabCorp looks forward to working with the Department to revise the panel in the most effective and efficient manner possible while avoiding unintended consequences. Thank you.

MS. DAVIS: Thank you very much for the statement and those comments. We welcome the submission of those. Ana, could you go to the next slide? We welcome the submission of those comments to the email listed on the screen here. Thank you for very thoughtfully expressed comments on multiple topics.

All right, our next person who requested a public comment is Jo McGuire.

MS. MCGUIRE: Thank you so much for allowing us to make these comments today. The National Drug and Alcohol Screening Association is a nonprofit professional association representing over 5,000 private and public sector employers and service agents who administer and manage workplace drug and alcohol testing programs covered by the Mandatory Guidelines, the Omnibus Transportation Employee Testing Act and the Department of Transportation's procedures for transportation drug and alcohol testing programs, as well as the DOT agency regulations, the Nuclear Regulatory Commission's regulations, and non-federal non-mandated Drug-Free Workplace programs.

NDASA's membership includes laboratories, employer substance abuse program administrators, compliance auditors, consortia third party administrators, specimen collection facilities, collectors, breath alcohol technicians, screening test

technicians, laboratories, device manufacturers, medical review officers, and substance abuse professionals who support employers in their Drug-Free Workplace Program initiatives.

NDASA is a member-owned organization who has led the way for industry education, training, and expertise in the Drug-free Workplace arena through NDASA university courses, industry-specific certifications, annual conferences, educational webinars, and publications that keep our industry apprised of pertinent information.

With the recent merger of the former Drug and Alcohol Testing Industry Association into NDASA, we are now the largest trade association representing employers and their drug and alcohol industry service agents in the United States. As such, we thank the Division of Workplace Programs at the Department of HHS for this opportunity to provide the public comments. These come from our members. We poll our membership, we ask them, we meet with different various agents and ask what their concerns are, so we're bringing this to you from our membership.

So today, we're primarily commenting on the proposed changes to the drug test panels. We respectfully submit these remarks in response to the Federal Register Notice proposing to amend the urine and oral fluid Mandatory Guidelines for Federal Workplace Drug Testing Programs to include fentanyl in the analyte table and remove MDA and MDMA from testing panels for urine and oral fluid specimen testing.

Conceptually, we support the addition of fentanyl and the removal of MDA and MDMA from the testing panels for both the urine Mandatory Guidelines and the oral fluid Mandatory Guidelines as long as the cutoff levels for fentanyl are supportable and the laboratories will implement on the same effective date as DOT's

amendments to include fentanyl and remove both the MDA and MDMA from its own regulation, 49 CFR Part 40. In addition, we applaud the decision of the Division of Workplace Programs to retain PCP in the testing panel because PCP remains a matter of considerable concern in the DOT-regulated industry.

Under the new procedures for amending its urine and oral fluid drug testing panels, respectively, there is inherently a balancing that we highly recommendation DWP conduct. While DWP has a strong interest in developing a nimble panel that can respond to substance-related workplace threats, there also needs to be a well-established scientific basis for setting initial and confirmatory test cutoffs. That basis needs to be clearly articulated by DWP in a Federal Register publication announcing the final decision of HHS on the testing panel changes.

In the past, DWP has changed cutoff levels to a parent drug's known metabolites in response to public comments. We encourage a continuation of such consideration of substantive public comments from those who are familiar with the effectiveness, efficiencies, and availability of research to support the final cutoffs. We're encouraged to hear today from the director that these will be a longer consideration of public comments and we're very glad to hear that. So, thank you, Director Flegel.

If there is a scientific supportability articulated in the DWP's Federal Register Notice, then those employers and their service agents who will litigate around testing and the testing cutoffs will have a firm footing to withstand those legal challenges. If there are no statements published by DWP regarding scientific sufficiency, the legal defensibility will be weak. That is a major consideration that we have.

With this concern in mind, we respectfully ask for the research to support the 1 nanogram per milliliter cutoff proposed for fentanyl to be shared publicly. Is this

the most current, efficient, or cost-efficient and programmatically effective cutoff level? Does this rule out therapeutic use? Are there other considerations supporting the 1 nanogram per mL cutoff? We're requesting a clear delineation of what choices DWP faced in deciding on the proposed 1 nanogram per mL cutoff and why this level was chosen for screening and confirmation for fentanyl and norfentanyl.

When the DWP adds one or more drugs to the testing panels, it is extremely important to NDASA that our members and their laboratories have sufficient time to implement such changes. Since the FDA has a complicated double clearance process, we ask that HHS not implement changes to require testing for fentanyl or another new drug until the oral fluid reagents are able to be cleared with the FDA.

If a urine drug test can be conducted by HHS-certified laboratories but oral fluid drug test cannot, that will cause significant problems for those who are required to test under DOT's regulations 49 CFR Part 40. In circumstances where an employee who was subject to testing begins a urine collection but then needs to have a direct observation collection, for instance if the individual is transgender or nonbinary, they must have an oral fluid test and not a urine test, per 49 Part 40.67 section g number 3. This situation would become unnecessarily complicated if urine and oral fluid testing cannot be available for the same drugs.

Also, DOT allows employers to choose whether to use oral fluid or urine drug testing for each drug test type, so preemployment, random, or post-accident, so if a DOT-regulated employer has a standing order that requires oral fluid testing in some scenarios, and urine test in others, having a different panel of drugs for urine versus oral fluid could raise constitutional equality protection concerns.

Thus, the effective date and the laboratory implementation date for a changed testing panel for oral fluid testing should be exactly the same timing as urine testing.

Respectfully, we would like to note for the record that the highly valued HHS certification process for laboratories and the proficiency testing that would need to be done before a drug test could be added to the panel will add significant time to the actual effective date that should be determined. This is justifiable and not to be rushed. During the time the NLCP will use to certify the laboratories and conduct proficiency testing, the DOT and the reagent manufacturers will have some time to prepare.

However, we ask DWP to be mindful of the need for synchronous effective dates for HHS and DOT. If effective dates are set too soon, there are likely to be shortages of reagents because suddenly a market of more than 7 million tests annually would open. We don't want to see reagent manufacturers monopolizing the market or running into shortages of the available supply of reagents that will drive up costs.

When removing drugs from the panel, the NDASA membership is very concerned about what will happen if HHS and DOT have different effective dates. If HHS were to remove a drug from the testing panel months before DOT is able to undergo full notice and comment rulemaking and publish a final rule under Administrative Procedures Act, would the NLCP continue to grant HHS certification to laboratories to test for the removed drugs?

If DOT still requires the testing for the HHS removed drugs and a transportation employee tests positive for that drug, how could that positive result be sustained if the laboratory was not HHS-certified to test for it? Such a gap between testing and HHS certification would create legal liability for the DOT-regulated employer

and its laboratory. Also, it seems that a gap between what HHS requires for its certified laboratories and what DOT requires of its regulated employers would certainly violate OTETA.

DOT must follow HHS for the science and must utilize HHS-certified laboratories. It is highly unlikely that HHS would certify a laboratory and conduct proficiency testing for a drug that HHS has removed from its panel. There would be a similar problem if DWP changes the cutoffs for an existing drug in the testing panels. So, in other words, HHS would be certifying and proficiency testing laboratories at cutoffs different from the DOT regulation and therefore leaving the DOT program unsupported.

Consequently, we respectfully request extended effective dates for any changes to add or remove a drug from testing panels and that the effective and implementation dates are fully synchronized with the DOT effective dates. We do anticipate filing a final version of these remarks as comments later in the month. Once again, we appreciate the opportunity to make these comments.

MS. DAVIS: Thank you very much for those comments and yes, we do welcome those at the email address listed on the screen. Thank you again for very important comments.

The third person who has requested to provide public comment for this meeting is Lane Kidd.

MR. KIDD: I am Lane Kidd. I'm the managing director of the Trucking Alliance which is a coalition of major U.S. fleets in the United States and also all proponents of hair testing in addition to the DOT-required urinalysis. I wanted to make the DTAB aware that there is soon to be a peer reviewed study published by Penn State

in its next issue of the Transportation Journal. So, I contacted Penn State to see if they would let me release it early for your review and they said yes. So, I have submitted that to Lisa Davis and Director Flegel. They will have it for you to do. I would encourage you to look at it.

We began aggregating data on hair testing and urine testing in 2015 when Congress directed DOT to recognize hair testing. We have accumulated a really large population, a huge dataset, of about 300,000 drug test results, hair and urine, of truck drivers. This particular study compares those results from trucking line carriers with the 2020 results in the drug and alcohol clearinghouse that DOT manages. It will be the first direct comparison of the two datasets.

I'll just leave you with two things. The hair testing in this study detected drugs 8.45 times more frequently than the urine test. Hair detected more cocaine, opioids, and ecstasy. Urine detected more marijuana, methamphetamines, and PCP. I think you'll find the drug test research extremely pertinent to what you're doing, Director Flegel, in advancing hair testing and hopefully it will be worthwhile.

MS. DAVIS: Thank you very much for those comments.

MR. FLEGEL: Lane, can I ask you a quick question first before you go off? Am I able to share that with the Drug Testing Advisory Board members? I don't want to get ahead of a journal article.

MR. KIDD: Yes, you can. In fact, they said they historically run late on their publication and they felt that if we needed to get it out, go ahead. Feel free to distribute that to whomever you want.

MR. FLEGEL: Okay, we will share it with the Drug Testing Advisory Board members.

MS. DAVIS: That concludes the list of the people who requested in advance to make a public comment. Is there anyone else whose name wasn't called who would like to make a public comment? We still have some time left on our meeting if others would care to make a public comment. Please use the raise your hand feature and we will call your name and elevate you to speaker or presenter mode.

DR. HARWANI: Hi, this is Suhash Harwani with Quest Diagnostics. Thank you, it's great to be here today and we appreciate the opportunity to openly comment. I won't bring up all the items that we have in our written comments or that we will be submitting for written comments, just to keep it more high-level today. Just for informational purposes, Quest Diagnostics annually performs more than 10 million urine, oral fluid, and hair workforce drug tests. Of these drug tests, 2 million or more are federally mandated to be tested through SAMHSA-certified laboratories.

At a high level, for studying the cutoffs, I think first and foremost understanding the populations of the specimens that we're trying to set a cutoff for is important. Utilizing data from prescription drug monitoring and clinical testing populations, as others have already mentioned, may not provide the insight and the information that we need to help guide our industry. This also goes into positivity percentages as well that have been reported earlier this year with the Quest Diagnostics Drug Testing Index we reported on fentanyl positivity in workforce drug testing specimens for the first time.

It was hovering between 0.1 to 0.2 percent, and we did do a percentage of the 3-year lookback, 2020, 2021, and 2022. So, it did give some minor trend information, but not very much. It was relatively stable between 0.1 to 0.2 percent. It looks like it was likely in line with what Ron had shared earlier today as well. But other

data has indicated higher percentages. Understanding the actual population that you're studying and making sure that there's exclusions for certain populations that could bias your dataset, our dataset could also be very well skewed, but we purposefully exclude datasets that aren't representative of workforce drug testing specimens. That could include medication, medical professional monitoring panels, things like that that are performed in certain industries that may have higher potential positivity percentages, so keeping that in mind when looking at positivity overall and reporting on it.

The other thing I'd like to mention, as others have already mentioned, without a commercially available screening reagent for oral fluid today, that creates potentially two issues. The separation of urine and oral fluid panels, you create a difference between a urine panel versus an oral fluid panel, one with fentanyl and one without, potentially, if that includes norfentanyl or not. Obviously, that remains to be seen and something that we will comment on as well.

But with that bifurcation also potentially causes a slower adoption of oral fluid which could occur at that same time.

The only other thing I'll mention is for ecstasy. Obviously, we've seen the low positivity percentages at 0.003, 0.002, whatever small number that is. The Quest Diagnostics Drug Testing Index has been relatively stable. If you do a 5-year lookback on that, it is relatively low. So, we do agree with that; positivity is low.

But with the foundation of safety that the industry is built on, what positivity besides 0 does that make sense to allow even 1 specimen to go positive for, or one donor to be positive for, in the industry when you're talking about safety? So I'll just leave it at that, but we appreciate the opportunity to comment on the proposals.

MS. DAVIS: Thank you very much for those comments. We really appreciate it. Again, we welcome your submission in writing to the email so that we can respond to those comments. Yes, Ron?

MR. FLEGEL: I did want to make one comment for the public. I don't want it to be a misconception in the program that we would implement fentanyl testing in urine and not implement fentanyl testing in oral fluid. As a program treating donors equally across the board, that would have to be implemented simultaneously. So, I just want to make sure there's not a misconception that we would implement separately. It would have to be implemented together. You just wouldn't treat donors differently using oral fluid versus urine. I just wanted to make aware of that.

MS. DAVIS: Is there anybody else who would like to make a public comment? We still have some time left. I'd like to remind everybody that written comments regarding the addition of fentanyl to the analyte table or the removal of MDA and MDMA from the analyte table will be accepted for review for an additional 30 days following this meeting, or no later than January 4, 2024.

Are there any other comments? All right, hearing none, this now ends the public comment section of this meeting. I'll turn it over to Ron. Do you have any closing remarks?

MR. FLEGEL: I do. One, I want to thank everyone in DWP for putting this together. It's always a lot of work. I also want to thank the public, not only in listening to the presentations, but also commenting. I think those are very important comments that we can take.

Again, this is a new process. I thought it worked very well. Right now, I think going forward, we hope to streamline this even more so that everyone will understand the process.

I also want to thank the board members, the new board members, as you can see it's always interesting, a lot of questions and conversations. I appreciate the discussion around the fentanyl and norfentanyl because it does help us. We are also scientists, laboratory people in the same sense. So, it is important that we get this right, not only around the implementation, the cutoffs, but also around the actual dates and how the federal partners work together. So, I want to thank you for that.

With that, I'll turn it back over to Lisa for any of her closing remarks and to close the meeting.

MS. DAVIS: Thank you, Ron. With that, I adjourn this open session of the Drug Testing Advisory Board. The time is 4:05 p.m. Eastern time. Thank you all very much.

(Whereupon, at 4:05 p.m., the meeting was adjourned.)