Welcome to the Drug Testing for Pain Workshop. We will be starting in a few minutes.

Hello, welcome, everyone. I will give it another minute and we will start. Just one more minute. Please make sure that your microphone is on mute.

Hello and welcome to Drug Testing for Pain Workshop for the 2020 Pain Skills 20. We have it does today LTC Tiffany N. Heady and LTC Marisol S. Castaneto. We would like to inform you this session is being recorded. If you have not done so please be sure that your microphone is on mute. For any questions during the presentation during Q&A portion please use the text box on your screen. We have this recorded and posted them on the training website, along with a sign in sheet and questions that must be completed, and [Indiscernible] for CME credit. In the pod you will see the workshop agenda, the speaker's bio, self-assessment, handout in case you have not submitted it to LTC Tiffany N. Heady. Remember to download, sign and return the sign-in sheet if you would like to visit the CME credit. Please [Indiscernible] Troy Spencer bike close of business September 9, 2020. I will also put his address in the chat box so you can send it to him. In addition, [Indiscernible] attendance in this workshop as a documentation for CME and CNE. If your logged in and not using your full name, please sign out and sign back in with your first and last name. Following the training you will receive an e-mail survey evaluation. Your answers are invaluable to future planning for the training. In addition to the training evaluation there will be [Indiscernible] survey to complete within the CME [Indiscernible] website. This is from our program and CME is two completely different items. For CME and CNE it can take anywhere two to four weeks to receive credit. Once your credit has been assigned you will receive an e-mail from the system to complete the CME survey. You will need to complete the survey in the Navy [Indiscernible] to receive your certificate. Please make sure that you do this. Lastly, you're having trouble viewing the slide presentation please exit out and come back in or download the presentation from the file pod and follow along. Now without further ado I would like to turn it over to one of the speakers, LTC Tiffany N. Heady.

Good afternoon, everybody. Welcome to the Drug Testing for Pain Workshop. As you adult I am top LTC Tiffany N. Heady and I will be conducting the first part of the workshop followed by, LTC Marisol S. Castaneto. This workshop is going to be a little light on case studies and instead focus on developing a solid foundation on which to evaluate any clinical lab for testing you may use or come across to detect drugs. My background is as a clinical chemist and LTC Marisol S. Castaneto is a toxicologist, a nice mix of experiences. Thank you to all of those who completed the survey. We're certainly going to discuss the survey and of the survey results at the end of the workshop so, stay tuned. Lastly, the Learning Objective is sprinkled through the presentation and do your best to identify those and hit on those specifically. Let's get started. For the Disclosures I am who I said I am and I have no financial ties or relationship of any kind. The disclaimer, all is expressed here in the first part of these are my view and not those of the Army, Navy, Air Force or U.S. government. Here is the agenda. It looks pretty detailed

impact. We're going to start with discussing the primary source for this initial part of the workshop. These constitute the first primary source or [Indiscernible] for lack of a better way to put a. Often laboratories perspective [Indiscernible] just yet because the intent of these practice guidelines is to deliver a UDT that improves the patient outcome, but not necessarily [Indiscernible] but includes the patient outcome for pain management patient. We will talk about referrals in pain management, how that happens or how does that not happen. In the welcome does we welcome feedback from the audience because you guys are the experts. One of the things that interest me is when referrals happen, and as a function of the referral how many different types of health care providers may you have to actually -- during drug texting and try to interpret them. If you have a spectrum of tests and conceivably if there is [Indiscernible] capability capacity, true for patients. You may have to have a spectrum of providers which makes interpreting UDTs more challenging.

Next, we are going to discuss the actual lab medicine guidelines. On the use of UDTs pain management, these are laboratory medicine practice guidelines vary [Indiscernible] to your Clinical Practice Guidelines. Again, the intent for these is to improve the outcome for the patients. We're going to touch on the concept of [Indiscernible] testing to make you aware of philosophy. Some parts of it you may want to adopt. Some part you may not have even seen the next will talk about the basic principles of the UDTs and lay that foundation. Wire UDTs so pervasive? When to use a UDT? Next, we will talk about the types of urine drug tests. Three broad baskets you can put UDTs in. The reason you may want to adopt this is because it can help you maneuver how you are going to interpret the data that you get back from your urine drug test. We are going to have to touch on cut off, cut off concentration because they can be absolutely key to the ability to accurately interpret your UDTs. Once we have a good [Indiscernible] with types of UDTs and understand the cut off we're going to talk about the cost-effectiveness of the different types of urine drug tests. Again, that is not meant to push you off or put you off, it's the cost-effectiveness in terms of the outcome. We will be more specific in terms of the outcome, but it's not to save money necessarily. That's an interesting discussion. And pretty interesting from the laboratory folks. We will get the three types of cutoffs, which is important. Also, the baskets I talked about where we well [Indiscernible] UDTs but also touch on other confounders for the UDT that can make accurate interpretation more difficult. There will be a brief covering of that. It's important you are aware of those confounders because one of the things that runs through this type of guideline is that one of the biggest risks is misinterpretation of the UDT, and we want to do everything we can to reduce that risk Rick and then, lastly, will almost lastly but there are improving ways to reduce -- proven ways to reduce that risk. Thankfully for the health care providers a lot of these ways to reduce misinterpretation of UDT falls on those clinical lab community and not on [Indiscernible] providers. Lastly some good ideas that can go bad. Again, we need to make you aware of those.

Let's get started with the primary source for this presentation. The document called the laboratory medicine practice guidelines was published in 2018, and it's analogous to your Clinical Practice Guidelines. Practice guidelines for the lab are not novel. These actually exist for a

variety of clinical dose clinical lab testing. A particular diabetes has its own type of guidelines, [Indiscernible] markers and other guidelines, and so forth. [Indiscernible] urine drug screen but it also has Clinical Practice Guidelines. This is a pretty hefty document, and it is extremely methodical. It covers a lot of literature, but it uses the POCT system, a format that seeks to determine the efficacy of a given treatment. The treatment we are talking about here is the urine drug screen. Let's go to this in detail, the PICO(TS). The P is the patient population. For this guideline the patient population was exclusively acute and chronic pain management patient, very relevant for this audience. The I stands for intervention. So, the intervention for the population being studied. The intervention is the lab test. And C stands for comparator and we will compare to other tools pick up going to be talking to the choir here but the other tools that were compared to the urine drug screens the physician's interview and survey. The review of the electronic health record, [Indiscernible] County got the prescription monitoring databases, the screener and opioid assessment tool. These were all the peer orders to the urine drug screen for this practice guideline. So O, the outcome. The outcome that drove these affected guidelines for the clinical lab is adherence to pain management plan, ability to detect true diversion top and a degree -- decrease in ED visits. The time frame for the literature was from January 2000 to February 2015, 15 years' worth of literature.

The setting which can be very important outpatient pain management folks, and patient, and community patient population. Very lastly there were exclusion and inclusion criteria if you want to see those for all of the literature, they reviewed in order to come up with these practice guidelines.

The bottom-line is that primary source for the first part of your workshop is exhaustive, methodical, and it looks at what current research can tell us about the use of UDTs to monitor drug therapy in the pain management program. Focus initially here before we get started on some repeat grouping and definitions, so we are all on the same page when I say things like top drugs, and a sort of UDT test. The first thing is when this group looked at drugs of interest they were concentrating on over-the-counter drugs, prescribed drugs, non-prescribed drugs, and illicit drugs. So, those are the drugs that the UDTs need to be able to detect, of those are the ones we will discuss pick the type of UDT test, generally speaking, were divided into three baskets, qualitative call yes or no, positive/negative test, and a quantitative. And something called [Indiscernible]. Quantitative tuned to becomes confirmatory and it all means the same thing. The operational definitions get interchanged depending on who you are talking too. The quantitative definitive confirmatory are all the same. The last piece that we are not going to focus a lot on because it's a little bit preachy is the difference between laboratory perform test and point-of-care tests, went up there be in the tests performed by the bedside. But usually by someone who is [Indiscernible] laboratory. This is going to come up a couple of times in my presentation. There is a difference, and you should be aware that they can have different performances. With repeated groupings we also have repeated themes. Throughout the practice guidelines.

The first one is about a general statement you can get. They have to start somewhere and it's testing by specimen for drugs and drug metabolites, detecting the -- use of relevant drugs over-the-counter, prescription, non-prescription, illicit substances, and Pay Management patients, so everyone agrees on this point. Eventually I hope to convince you that urine is the [Indiscernible - muffled] we will talk about.

The second repeating theme is sort of a warning. I have alluded to it already before is after interpretation of that urine drug test can be difficult given the wide diversity of tests. We'll talk about that later in the three baskets. There is a wide diversity of tests and depending on who is treating the pain patient it can be a wide variety of health care providers using UDTs. It's a great recipe for misinterpretation. Doesn't like the cartoon here represents, at the text misinterpretation of what seems to be a simple routine question about parking validation. How do patients get into a pain management program? I am not a pain management position. I do not know. I went looking. I did not immediately find anything, so if you are keeping count this is one of the objectives, number one. It became clear to me there was one standard on consensus about who gets referred, what do they look like? Who do they get referred too? I looked at CDC 2000 guidelines that seemed too mostly talk about how [Indiscernible] prescribed and [Indiscernible] direct information on who gets referred. I asked Dr. Google and landed on practicable pain management which is good information. Again, I welcome input here. There seem to be three Common Scenarios for when a patient is going to get referred to a pain management group. That is when they've got this high morphine equivalent dosing from 82 [Indiscernible - muffled] to the second case scenario. Pain with co-existing conditions. Where those conditions affect multiple systems for that patient. And then, three, sort of that touch all of complex cases. A little more about complex cases, and so, this started to lend itself to the UDT more, where you can see more applications for UDT.

For example, complex cases included Pain medication, also on board we're set it is for the patient, or a patient on pain meds who continually needed more opioids, in particular. The use of unauthorized substances. Those can be unauthorized subscription meds, non-prescription meds, and a refusal to use or consider non- opioid measures, or to decrease your opioid does pick all of these things for the practicable pain management website were indicators of a complex case, which may require referral to a pain management group. I look a little closer to home because it's Google. I looked at the DoD, VA and D/HH Guidance is. For the 2007 VA and DAB Clinical Practice Guidelines I [Indiscernible] no guidance in terms of a referral criteria. Again, I'm happy to be challenged on this. I looked at the [Indiscernible], 6025.04. The closest thing I could find is almost most clinical and/or complex patients who do not improve to be referred. If you dig a little more with the help of Colonel Whitney, if you look at the Stepped Care model does a little more detail about how you might get referred. The DHA Stepped Care model has referrals to the IBHC, Internal Behavioral Health Consultant a referral if you have a patient for whom all pain is catastrophic. I'm not -- I'm try not to say [Indiscernible] word. A patient who is very emotional and catastrophic about their pain, a patient that exhibits. Avoidance, beliefs and

behaviors, a patient that exhibits depressive symptoms, or one that has concerning psychological behavior.

So, this seems to be some guidance about who gets moved from a primary care setting, probably, maybe internal medicine, to a formal Pay Management but it is not clear. There may not be any resources available either. Depending on the resources available for this workshop, important UDT may be used by a wide variety of health care providers who are understandably vastly different experiences with UDTs. For us that kind of increases the risk of interpretation. There may be no consensus on how to get a patient to a formal pain management program. They're certainly is consensus on whether you should provide the order in healthcare provider when they are trying to take care of their patients, especially if opioids are part of the pain management strategy. They are needed absolutely to treat paying, especially when prescribing opioids. There was consensus as will that UDT should be giving got a UDT should be given before you start and opioid therapy plan. It will be interesting to see what this audience things about that and see if that is a [Indiscernible] practice. That was the consensus of this LMPG group. Additionally, UDTs at bare minimum have to be able to detect positive substance -- polysubstance abuse, abuse, addiction got the possible diversion. No lab test is going to come back it's a positive for abuse or positive for addiction. For the lab community this is your ability to distinguish controlled substance from an addictive substance.

One can jump to -- I want to jump to this idea of tiered testing. This is also brought up in the Executive Summary for this practice guideline, and it made be something you are familiar with. It may pique your curiosity, because, again, the tiered testing was based on achieving those outcomes we talked about decreased ED visits, more adherence to pain programs, and to be able to detect diversions. It may actually assist you in ordering a test for most appropriate for what drug. Let's walk through this. A number of Risk Assessment surveys remember those old tools that the UDT was being compared against, those surveys that your providers use help you to determine the risk for your patients. The risk to the patient would miss use the opioid, abused opioids, or have an opioid-related adverse effect. When I saw the survey, it was in three categories, the risk associated with long-term therapy, likelihood of misuse, some [Indiscernible] commencement of there be a non- opioid general substance abuse. This tiered strategy depends on a provider understanding the risk associated for that patient.

Let's look at Tier 1. Tier-1 would be your routine, normal risk patient. The practice guideline suggests that for Tier-1 testing low-risk patients what include a stimulant, the amphetamine class, sedative, which is barbiturates, depressants such as benzodiazepine, psychoactive drugs, Benoit's, also a stimulant, cocaine, and pain or conducts opioids -- opiates and opioids. The idea behind Tier-1 is [Indiscernible] family of drugs would not necessarily be for a specific drug. This is a theme we are going to revisit later. What if you are assessing patient, give them a survey, or talking to them and they are not [Indiscernible] high-risk patient, and have a known history of abuse from medication? Or a prevalence of drug use in the local region? That was a really interesting concept here in terms of looking at Tier 2. Or they are at a risk of

Polypharmacy or have multiple providers. You may not be able to see what the other person is doing. The idea behind here to is that you had Tier-1 top which remember is kind of drug classes, not necessarily a specific drug. You had Tier-1 that tiered too. Tier-2 is going to include alcohol, [Indiscernible] can be tested in urine for the use of alcohol can include anticonvulsants, [Indiscernible], antidepressants, which is [Indiscernible] or [Indiscernible], synthetic cannabinoids also known as [Indiscernible], and that does have, a dissociative anesthetic such as ketamine, hallucinogens like LSD and CBP, and then muscle relaxants, and other narcotic pain relievers. These can be added to Tier-2 for higher risk patients. Then there is an extra dear. These are reserved for cases clinically indicated per generally that's more detail. They include what I thought was interesting options. You are going to add a DC analgesic such as Acetaminophen and antihistamine such as [Indiscernible] top antipsychotic, which is [Indiscernible]. And then synthetic [Indiscernible]. Usually, the two referred to by their initials.

For example, a synthetic cannot does come Benoit is [Indiscernible]. You could add this to your testing. Again, tiered testing is a familiarization. The recommendation from the practice from the [Indiscernible] medicine practice guideline is to consider it. There is good evidence to support at least considering this for some patient populations. It certainly would be a nice collaborative project for you pain management programs and your clinical labs, and to tailor the tiered testing to fit your particular patient population. We're going to take a quick step back and take a look at the basic principles of the UDT to understand how and why they are useful. These again were agreed upon by the practice guidelines. The first is frequency of testing. We alluded to this before and it would be really interesting to see what you, the SME's Guide the providers actually do. Frequency of you to ED testing, initial testing before therapy started was agreed upon to be important and useful. And then testing once a year for low-risk group, possibly from Tier-1 was also agreed upon. But after that there was no consensus in terms of you get that higher risk group, how often you test them. Do you test them randomly? There is just a no evidence there to support random testing versus scheduled testing and of those high-risk populations. That doesn't mean that it's not useful. It's just [Indiscernible] did not find the evidence for consensus recommendation. But they did actually add in there that some folks will test relative to the schedule of the Pain medication that your patient is on. They said they looked and there is [Indiscernible] evidence to support tailored testing where testing is tailored to the schedule to whatever drug your patient is on.

The next foundation principle is the use of other tools in conjunction with the urine drug testing screen. Really did have an effect on the outcome. If used alone the urine drug screens are more effective at detecting use of drugs, those prescribed, illicit, then using the other tool alone. So, it was more effective than the self-report, the survey, the interview, review of the electronic health record. Taken together they are highly effective, so using, again, using the UDT really are the tools appear to improve the outcome for patients for these practice guidelines.

Let's talk about large body of data for drugs in urine. This is where the best of both worlds. There's just a large body of data for drugs in urine, and that makes developing an assay easy. The data just outcompete many of the other tools used to assess compliance, because drugs just show up in urine and they are fairly consistently there. They are there in a useful way. So, that certainly boats for the validity of drugs in Europe. Urine is a specimen of choice. Lots of reasons urine is biological choice. And LTC Marisol S. Castaneto will discuss in detail the perils of fake urine or synthetic urine. But that is a side. [Indiscernible] blood, urine has a larger window detection where blood can be a minute to hours. Detection for urine can be minutes to months, which is very useful. Spot urines can provide 30 mills or more of specimen. The volume of your biological [Indiscernible] urine is sufficient. Certainly, it's less invasive unless you are in the military doing a forensic reflection. Providing a spot urine is less invasive. The Chief disadvantage is that -- it can be adulterated, and we will certainly talk more about that later. I do want to talk briefly about oral fluid because oral fluid is certainly less invasive than the urine correction, and it's pretty good compared to urine for a lot of drugs. We will go into that but where it tells is some drugs simply do not show up, unlike in the urine they don't show up in the saliva. And so, it's early stages to be able to provide the breadth of urine tacic of the breadth of drug testing you can do. You certainly me see it pop-up and be more useful.

UDTs can be placed in three general buckets we were talking about initially. Here they are with the practice guideline recommendation which speaks specifically to Learning Objective number 10. The first one is the qualitative and semiquantitative test. They're recommendation is that these tests have firm clinical utility to detect the use of drugs as you define them in the pain management patients. The second bucket of tests for these quantitative/definitive/confirmatory, remember that's all the same thing, test. These can be the first line definitive testing. First line definitive testing is recommended for detecting the use of relevant drugs in pain management population. It is recommended for any IA assay result but is it does is inconsistent with the clinical expectation. You will see that a lot toxicology labs to run a lot of specimens for pain management, is the unexpected results, the one that doesn't make sense. Confirmatory/ definitive, -- quantitative definitive test is on the next step for those results that are not matching your clinical test. Lastly in this bizarre bucket are the qualitative definitive test. It will make sense later. This is the one the practice guidelines above the most. It should be over an assay to identify the drugs that we are interested in, and it certainly should be used over an immunoassay too monitor compliance due to increase in sensitivity and specificity. We will explain in a few slides how you can actually have a qualitative definitive were qualitative and quantitative test. You may be asking yourself, okay, just explaining the buckets and it's a qualitative, it's quantitative, this doesn't really help me understand why the UDT, it doesn't know me understand how to avoid misinterpreting my UDT. We have a way to categorize them. If you [Indiscernible] significant, how do I use this information to help me better interpret my UDT data? That's an excellent point.

Let's get to it. Let's talk about qualitative tests. These are the Yes/No. These measure the presence of a substance and can suggest the absence of a substance pick I am alluding to cut off there. The results are reported descriptively and not numerically. Yes/No, present, not present. They constitute a spectrum of tests. Most of them into being a [Indiscernible] flow test which are cassettes or cartridges pick you can include dipsticks and cups, know the Cubs that have the different indicators on the side, change colors, and this may surprise you. Qualitative tests can even include an immunoassay, particularly, if your immunoassay only has a one-point toleration pick that could indicate for your point of care in your essay. It could also be the case in the large, automated core lab for the patient that it doesn't have maybe one or two calibration points, and why does that matter to you? Let's talk about that. Let's try to better understand this testing recommendation from the lab community for these qualitative UDTs. It really did not seem to convey a lot of [Indiscernible]. What we have here in the upper left-hand corner is a signal concentration curve, and this one is depicting lateral flow technology. To orient yourself, because it's better if you understand it and follow it. As your drug increases your signal assay increases. That usually a reverse of how we see these but this particular example [Indiscernible] increases and [Indiscernible] decreases. Drug in urine is competing for [Indiscernible] on the antibody that as a signal flag attached to it. The drug in the urine displaces [Indiscernible] the signal goes down. Drug increases goes down. But if the shape of this curve gives it the qualitative nature.

The more we understand that the more we can understand how useful it may be to the pain community. For a given patient at a given time. The shape of the curve demonstrates why it's qualitative. It has a very small dynamic range for the qualitative test such as these are based on usually [Indiscernible] are cassettes that can be on the cuff. The [Indiscernible] changes on the cuff. They are usually best indicators for drug classes. Again, not specific drugs. They lack that dynamic range, they lack the analytical sensitivity and specificity that you need to do targeted drug testing. You may be asking yourself, what on earth are they used for? What good would these tests be?

I can offer you an example that we had at UVA we would use of this drug of abuse lateral [Indiscernible] cards to transfer a patient you would see in the ED who seem to be having a psychotic episode, and we needed to find them space and the Behavioral Health bed, or transfer them to a safe place pick a lot of times to do that you had to show they were clean. That was a very common use for these qualitative lateral flow tests. This can also be true as I alluded to for the immunoassay test in large clinical lab and a lighter, probably those in core lab. The IA analyzer does the same is true despite the fact those tests are physically challenging. It's hard when the cuffs are not calibrated. The IA assays our calibrated. Periodically, so and just to remind you that a calibration is an assessment of an instrument's ability to deliver an accurate signal response to a nonstandard. The most IA assays or [Indiscernible] in the number of performances are calibrated to help determine how precise and accurate the assay can be. What does that mean for you? The provider who just ordered this. It helps you get a more accurate result. In fact, those immunoassays, the immunoassay test

setting on the large instruments in the core lab are probably [Indiscernible] quantitative urine drug tests, and a semiquantitative because they actually have a calibrator, maybe even two calibrators. Instead of that little, short, I don't know where my pointer is, but I am pointing at this little type sCurve here. Unlike what we see here which is a very sort of tight sCurve for your pull up instrument your immunoassay there is going to be spread out. What they give you is more sensitivity. That gives you more sensitivity. It gives you a little more accuracy. That speaks to some of the positive we see on the right inside by the green arrow. The qualitative assays have a fast turnaround time. You're just waiting for a positive and negative. Fast turnaround time, lower cost the bear to quantitative tests. I cannot prove that to you now, but you will see later. It's easier to use than a quantitative test. I was show that again later.

Yet, right, the recommendation is still tested even for the semiquantitative for using these UDTs in your pain management population. Why is that? Why is that? Many IA drugs of interest have all of the things [Indiscernible]. This is where the [Indiscernible] response come from. Separate from cross-reactivity, or sensitivity, depending on your essay and what drug or drug class you're looking for you can have increased false-positive, increased false-negative. False-positive, my goodness, is my person doing something they shouldn't? False-negative, are they diversion? Let's discuss this one example here. Urine opiate immunoassay can detect morphing quite well and [Indiscernible] Codeine. Most well not detect some specific opioids. For example, some well detect fentanyl at all or [Indiscernible]. For those drugs you had to have a completely separate immunoassay, and you may or may not have that on board in your core lab. We beg the question again and we beg for the cassette and the card, what use is it? Who uses this? If it's likely to confuse me as a pain management provider. Further on in the practice guidelines they say for initial testing, for the low-risk folks these IA assays and possibly lateral flow cassette and cuff may have a place. They may fill a void in your pain management practice for that section of folks. But the other destiny for these immunoassay drug tests is for forensic drug testing. And we are going to go there. It may help you. We're going to take a sharp left-hand turn a very briefly we are going to cover the two-step testing algorithm practiced by most large forensic drug testing laboratories. For health care providers, usually UDTs Historical Perspective can be helpful, and for this presentation it's truthfully helpful because it helps to introduce the concept, quantitative testing, and what purpose it serves for the [Indiscernible] folks. The forensic testing evolved before UDTs and pain management. Some Pay Management programs just draw from this algorithm, but they probably shouldn't because their clinical and forensic missions are fundamentally different, and if you had to put it into a nutshell it comes down to the cut off. Usually don't support each other's mission. Stepone is all specimens get screened by these immunoassay's, the ones we were just talking about and these large analyzers, and we take advantage of the forensic realm, would take advantage of the cross-reactivity, the lack of specificity, sensitivity doesn't matter to us right now because we have a solution. And we want to cast the widest possible net as efficiently as we can.

Remember, it's pretty key, right. In the forensic world false positives, false negatives our fine for these drug screens, particularly for opioids and diazepam and amphetamines. You may be asking, how do you mitigate that risk? How do you get the quality testing if you're getting a bunch of stuff from your eye a screen that may not be true? Incomes chromatography. This is the definitive quantitative confirmatory test that we alluded to at the beginning of the presentation. This forensic model adheres to the two-step method because the laptop unlike in your core lab downstairs and in your pain practice, forensic are like thousands and thousands of specimens a day. They are using those IA and use in that quantitative definitive chromatography spectrometry testing to actually get the right drug at a certain concentration. Quantitative UDTs are performed by chromatography Apollo by spectrometry. Chromatography, Colonel Meadow will go into detail about this so we will just give you an overview here, but chromatography/Mass spectrometry is the gold standard today. The chromatography separates the compound so that the Mass spectrometry can come back and analyze each compound. That is not happening in IA or in your lateral flow. It is considered the gold standard because it's highly sensitive and highly specific. It has a high clinical sensitivity and analytical sensitivity and a high clinical analytical specificity. How and why? This technology, chromatography/Mass spectrometry is taking advantage of the actual structure of the compound. Write down to the isomers. Amphetamines, you have [Indiscernible] of those are [Indiscernible]. These are in tumors. They are not super implausible mirror images. Mirror images can't superimpose of them. IA has a real hard time with that. Mass spectrometry, chromatography not so much that they can figure that out. That's important because the is illegal or bad. D usually has some of the really D strong stimulant properties. The you can find in [Indiscernible] Linhaler to compare and contrast for the Mass spectrometry, chromatography/Mass spectrometry resolves all of that. A little more about the quantitative test because, again, my argument is if you can put these tests and their buckets it can help you immediately help you in terms of accurate interpretation of whatever result comes out of that test. Quantitative because the Mass spectrometry detector has a large dynamic range with very little noise. These long line -- this long line --

Put your cursor on top of it.

You can see that now?

Can you try to move it?

I've got it, okay. Yea. Unlike remember what we were looking at qualitative test, like a little sharp sCurve to look at that. That makes laboratory giddy. I understand it may be too much but [Indiscernible] laboratory is giddy. It's good for you as a provider because this dutiful flow, long beautiful flow means I can offer you more accuracy in much more specificity. We get to talk about what opioid? Are we talking morphing? Are we talking coding? Are we talking tramadol? As opposed to just opiates. This is what allows me to give you better information. We'll start talking about things like limit of detection. What do I care about that? You may care about limit of detection because they can help you if you are worried about the version. That will become clear when we

talk about cut off. With this makes this possible. This beautiful technology makes that discussion about limited detection possible.

As you can see, we don't have one or two we've got lots and lots of [Indiscernible] which makes for a beautiful measure. With this technology you are going to get a number with certainty because you can actually measure your error in this. I can give you a CD and confidence interval for the drug concentration that I provide you. And I know exactly what drug you are detecting a measurement. You may be saying to yourself, this is perfect. Problem-solve. I can distinguish and Oxymorphone from Hydroxycut on. I can distinguish heroin use for morphine use. I can even distinguish [Indiscernible use for marijuana. You can do that. There is no free chicken in life, unfortunately. This is super expensive, particularly compared to the cup and is particularly slow. It will not be 5-minute code change and certainly not easy to do. Now what? Let's just take a few minutes before I have to talk to you about cut off concentrations before we talk about the other bucket, the qualitative quantitative bucket. The values of the drug concentrations above which the presence of a drug will be reported. It can be numerical, maybe not. Below the cut off concentration drug will be reported. It doesn't necessarily mean that it's not there. Mitchell Jun things, -- to do things. What you are measuring hugely important in terms of what you are determining correctly. Let's look at this but the first one here the SAMHSA cut off. [Indiscernible - muffled] not really much. This is concerned mostly with [Indiscernible] drug testing. What I want to draw your attention to is the two-model testing algorithm we talked about briefly with forensic testing, they both have cutoffs. You can see that for marijuana at initial screen which was, you guessed it, IA has its own cut off. And then the confirmation cut off which is the useful technology, that nice, long line has a different cut off. SAMHSA is more forensically geared for cut off are probably not be clinically useful, but you can see them right here. This is the example of the importance of cut off. These cutoffs are set by regulation. There is no clinical basis, necessarily. These are mostly set by [Indiscernible]. We had transparent and contrast this by [Indiscernible - muffled].

This is just one of many. We talked about how there are just tons of UDTs, well, there really are all different types of flavors and UDTs. From Italy not so much with a core lab but when you go to send out the world is your oyster. There is a broad diversity. This is offered by QUEST. A notice the cut off his lower than these that are more workplace drug testing. The confirmation cost more. This is a two-step process. The due in IA screen followed by chromatography and spectrometry. Some questions you may want to ask if looking into this is always concerned about a particular opiate. I actually want to get that. It says I'm going to detect opiates below the cutoff 100 per. They will tell me ml and I don't know. Also notice that this confirmation, the second step is going to cost you extra. The last thing I want to point out is most of the chromatography/Mass spectrometry confirmation quantitative test are not [Indiscernible]. These are called lab developed test. It doesn't mean they are poor quality and not safe. Quite the opposite. This lab is accredited. This method past and so it's perfectly safe and appropriate to use.

Some question you passed may have about cut off values, here is an example of a manufactured insert for an immunoassay test for Oxycodone to extend our discussion about cutoff. I like this because particularly if you have your own pain clinic using a point of care technology right there in the clinic with your patient top you absolutely should have these manufactured inserts. You said that them right there and easy to pull up and take a look at because they are a wealth of information. They can really help you get the most use out of your UDT. You are sending it out then it is the laboratory's responsibility. The sense as a couple of budget. Who determines the cutoff value? It depends on what you were using it for. If it's forensic it's probably going to be set by an Agency or a policy, something like that. The laboratory itself can set that tend to devalue. Here is why can't remember I said it wasn't FDA-approved, the lab developed that test, well, depending on their [Indiscernible], the whole nine yards that will affect the cut off, what cut off they can reliably provide you. Laboratories will develop their own cut off based on their methodology, and then you can have officials like medical professionals set that 1020. That might be useful for a given patient population. Do cut off values change? Absolutely.

They are trying to get the best performance out of the methodology that they can, but it can change and so, yes, the cutoff values can change.

What is the main factor? In determining a cutoff value come in the clinical setting this is really only relative to the clinical setting is the methodology and so is it a lateral flow where the sharp S-curve and we know what the cutoff is or is it a little more flat like an essay on the core lab instruments or is it the beautiful long slope that is helping us set the cutoff value and lastly can it affect the sensitivity of the assay and absolutely and this is a real manufacturing and it says that you can the lab can use you in the 100 or 300 calibrator cut off. To calibrate your instrument and what they did, they came down here and they use the lower, and this is probably the clinical situation so using the lower cutoff and what it actually gave me was one false positive and if you look down here you have one false positive by the DRI which is the amino acid we're talking about relative to the reference standard and in this case, gas pumped out of the [Indiscernible] and this is the gold standard. And this is by any assay he falls positive and if they were not supposed to be on OxyContin you would have to be an unexpected result and you probably have to go to [Indiscernible]. Or some other mass spectrometry method I'm ATRI. >>Method 1 tree.

Now we have talked about the qualitative test and they have an endorsement, but it does have [Indiscernible] and the qualitative basket can include amino assays and not just the cartridges and cups and then we have the semi quantitative which is really all about the calibrator and then we have a definitive confirmatory quantitative testing and what in the world is this. They put the two into the spectrum together sort of and what we do is we take the quantitative testing and don't let that go and use the quantitative testing with that beautiful flow and I can give you probably two decimal places but what I tell you is the amino [Indiscernible] are absent and they are not there. This has the advantage remember we're talking about a whole spectrum of providers it has the advantage of making really quantitative data for a substance and

not a family very easy to interpret and I got it and can go on about treating my patient and it is just easy to interpret and who does this? Lots of folks to this and to give you related example Immunosuppressants can often be, well not a mucin, amino depressants but drug testing is a better example but they will actually instead there cutoff will be, remember, the limit of quantitation we were talking about earlier and that will be the cut off so they can look as low in the weeds as they can possibly reliably and accurately look and to tell you if the drug is there are not without giving you a whole bunch of numbers. That is one example.

Let's talk about in the real world, in the real world time is money and money is limited. The idea is it is to give complete care within an allotted time and so everything is pulling for your time and there is conceivably a use for easy to read fast point-of-care UDTs and they are commonly located in pain clinic the maybe physician officers that labs will have them but beware, know what you're getting and particularly if you get an unexpected result. From one of the point-of-care UDTs. They have a decreased sensitivity and specificity and that is particularly for amphetamines and benzodiazepines and opiates so beware.

The recommendation again from this group is point-of-care UDT may in fact have a place as front-line testing but know the limitations and know if it is telling you about a drug family or it tells about drug family what compound but you be interested in or drugs that are not included. And know the cutoffs super important.

Okay you actually get what you pay for with the UDT does that mean if I pay $600 a test woohoo, $600 a test for a beautiful line to know exactly what drug and have a really good idea of the concentration in this again is, it speaks to [Indiscernible] and does it make a difference in the outcome and again the latest practice guideline is it is really relevant for us all it was focused on the outcome for the patient and so to the recommendations that came out or the qualitative immunoassay drug testing again prior to starting the pain management program with the controlled substance is very useful and can decrease adverse outcomes and it says there's no evidence that necessarily get you a better outcome so there's no evidence that suggests the qualitative and quantitative urine screening assay is more cost-effective than the beautiful chromatography mass spectrometry assay detecting the pain management so they just need better studies to assess that but that is a huge difference in cost and that we can all agree on.

So I thought I may give you examples because it helps to sort of give your bearings and understand what each bucket can offer you and what the limitations for each bucket can be in the first example here is a comparison done by [Indiscernible] in 2010 and it compares LC MS/MS and this is for spectrometry versus IA for pain management and patients and it's a relevant population and they look at 4200 specimens and they were focused on 18 discrete drugs and what you see at the side is the drug for which the immunoassay gave a false negative and compared to the chromatography mass spectrometry so the one that stood out to me as cocaine and this particular immunoassay missed 50% of the cocaine positive and it could have a serious effect on the care of your patient

and also propoxyphene as well and 23% and it did not do so great on the benzo and you can understand, we alluded to that a little bit the opioid opiates and bends and they can be problematic but the bottom line for this experiment was there was a real risk of false-negative with the immunoassay compared to the chromatography mass spectrometry and it was due to the cross-reactivity we talked about for a which can be great for forensics and can be a nightmare for the clinical community and much lower cutoff for the chromatography mass spectrometry because in the clinical setting you are not stuck at the SAMHSA drug testing cutoff they want to go as low as they can go to provide you, the provider a reliable result and it can be different from the immunoassay. So the risk of false-negative as an example on the right and we look at the point-of-care that we argued there is a home in a place in an appropriate use for point-of-care and we're going to compare that to the gold standard the study was done 2011 and it was less specimens of 1000 the patient population again is relevant and the pain patient on the drug they were looking for an illicit drugs, what they did, they compared point-of-care testing in the gold standard to what is actually written in the medical record and in terms of opioid, the a, it did okay, it did good to the LC MS and this is agreement to the medical record and not to the point-of-care and chromatography but to the medical record and 80% agreement between IA medical record 89% and they look for nonprescribed opioids what they found, 40% or 44% false positive by the immunoassay is what is that mean to your patient population if you got this result? Squarely it lands in the unexpected category and you're probably going to in some cases follow up with a $600 chromatography mass spectrometry to clear up confusion in the last thing they looked at was a list of illicit drug false positive initiatives illicit drug false positives by the point-of-care relative to the gold standard and so that actually does not look so bad and so the bottom line is a little over 30% of the specimens that were initially tested by the point-of-care immunoassay required $600 confirmation test but in some cases maybe for the illicit drugs the Tier 1 testing in some cases the point-of-care and immunoassay was sufficient.

Last if you did not get confused enough, you had the qualitative and the quantitative and you have cutoffs and you're ready to go in there are just a few other confounders and I should not have put covered in part two, it may not be accurate but you knowing about them is quite important it particularly if it is your lab downstairs if you're looking at the talks lab and who is running the chromatography mass telemetry and detection units they can affect ABBA test regardless of what bucket they are in and that still applies and certainly knowing the detection limits and the cutoffs Hand in Hand can help you understand what we're talking about here when you expect a positive and then the metabolites, [Indiscernible] is a beautiful example of how you should not see the parent but the metabolite nevertheless the take-home message is know what your assay measures and are you saying the metabolite when you should see it with the parent or what are you measuring and make sure you know your interpretation is correct and the patient is safe.

Specimen integrity, the one caveat to urine is it could be adulterated and it could have a serious effect and definitely affect the result terrestrial non-detected immunoassays can become will we will just say they are denatured and some people can enter their urine so they can get

a no result in the determinant for you will see, it may be if you have reason to believe he took the urine from the patient and it is cold or does not seem warm or something does not seem right and turn them specimen integrity there is a whole slew of tests writer fingertips that you can run on the core lab instrument downstairs to help tell you if it is really urine and we're talking about pH but maybe not temperature but pH and creatinine and specific gravity and all of these things can help you determine in my actually testing urine into my patient give me urine or something else and the recommendation here from the practice guidelines is validity testing should not be routine, it really should be, it is not forensic and in the forensic world it's interesting but for the clinical community it is not routine and less yes for suspicion when you can use validity testing with the other trolls maybe the other trolls can help point you toward validity testing but again the practice guideline said to gather the tools do work well together.

So is it urine or not and we tend to us that in the next thing is that the idea of [Indiscernible] affect how you can measure it so hydrolysis in this really focuses, there was no official recommendation other than to know about these because you cannot [Indiscernible] from your test and being able to detect and measure the metabolite increases accuracy but not required and the burden on your laboratory it is to provide consistent quality UDT especially if hydrolysis is part of the methodology and surf you're getting results that don't make sense and you know your metabolites needs to be hydrolyzed you may want to have a conversation with your lab and they should be able to have the conversation with you and pharmaco genomics, super interesting and this speaks to objective number 10 and the support for routine genetic testing for your pain management folks they did suggest you may want to look and a foreman is gnomic, genomic if they are experiencing adverse drug reactions. You can certainly use and academic medical centers they will differently use the quantitative testing we talked about the gold standard to characterize a known variance for one of their patients. And then there is a slew of enzymes that correlate to rapid metabolizes in slow metabolize ours and you may want to be aware of those. Retract okay so we talked about things that confound your ability to interpret your UDT and what are some evidence based things that help make that easier and first and foremost is the quality lab report and one that does not tell you negative and one that includes cutoff values and one that says this is a screening assay or this is a confirmatory test and so that burden is [Indiscernible - low volume] it is on your clinical laboratory and also UDT results clearly understood, this speaks a lot, actually it speaks directly to the qualitative and quantitative marriage and I will not give you a whole bunch of numbers I will tell you exactly what I looked for and was it present or not detected.

The incompleteness of the testing is clearly communicated and I have never seen this be problematic but it did make the guidelines and this is an reference to the two-step testing and you have to screen and it did not match the clinical picture and it is being sent off for confirmation in your laboratory needs to in the EHR clearly communicate that with you so you know there is no definitive answer yet and you delay whatever medical action and my favorite, report out numerical numbers when necessary. I don't know any numbers that are not numerical

and what that was supposed to say is as a result they report out numerical numbers only when necessary and we'll talk about that on the next slide in the last couple of things are know what you don't know and that is what we try to cover here in sort of know your UDT. If your Quicken point and [Indiscernible] are Genesis, find out about the test you ordered and the burden here is on your laboratory and to answer your questions about that stuff.

Good ideas that can go bad if you don't know your UDT, this is usually medical centers but you need to have an algorithm and I don't know where DTS came from and I'm not traveling but I don't know but this is a UDT algorithm set in stone and your drug testing algorithm needs to reflect her capability and limitation of your patient population and it needs reflect the capability limitations of the UDT itself and particularly when using point-of-care UDT and it can't be since on it needs to move with technology and move with your patient population and remember how we alluded to the second-tier testing and one of the indicators was drug abuse in your geographical region, an algorithm is good because standard is usually good and it costs less than everyone tends to be happier but it cannot be set in stone and the second thing is using the juror, urine drug testing to get the last dose and on the laboratory gives your number the temptation can be to try to correlate the number with the drug concentrate concentration they gave you with the time of the last dose and again the assessment of compliance, just don't do it. You can't make the analogy with therapeutic drug monitoring for urine drug testing unlike with blood UDT is not recommended for trying to approximate the time of the last dose and then lastly and probably one of my favorites the practice of normalization of the UDT to try to construe compliant it has been normalizing and [Indiscernible] microloans and in order to assess the completion of the 24 hour urine collection, these are spot urine and they are not 24 hour urine and so the result to try to normalize your drug concentration to creatinine or specific gravity is not recommended and they are not saying it cannot be done it is just there is no good evidence of it being truly useful yet and so don't go there paragraph mark the end of the presentation I want to say the true measure of the urine drug test is, its ability to improve the outcome of the patient and that should always be the focus and one of the biggest risks is the provider misinterprets the UDT and we want to do everything we can to make sure it does not happen to our providers taking care of our patient's and so that ends my presentation and if you have any questions at all I am more than happy to answer those. And thank you very much for your attention.

I think we have a question in the chat box.

So is that Miss Rubel, I can send those to you, I can send it to you it is a PDF and you’re asking for the UDS practice guidelines and that is not a problem.

Just send me an email and I will shoot those to you. >> Okay, any more questions?

Thank you so much and you have my email, and I am always available for questions and we will take a 15 minute break and she will monitor activity and it will be Lt. Col. Castaneto.

We asked everyone to stay connected to the audio and we will be back here in 15 minutes.

Thank you so much.

The event is on a 15-minute recess. Captioner on standby]

Hello everyone. We will be starting in a few moments okay.

Guide it. Got it. Welcome back to the second part of the workshop today and I will hand this over to Lt. Col. Marisol Castaneto.

Yes, ma'am Burt loud and clear. Direct I apologize I cannot go live with you guys as far as my web cam is concerned but I will go through the slides and it will probably be a rehash and I think it is actually good because I know it was a lot of information and going over some of them we are at least reviewing what we discussed and I can go into detail as far as how you can strategize or you strategy when it comes to urine drug testing or drug testing for pain in your scope within clinical or pain management and I think our job is to make sure you understand the purpose of the urine drug testing when you have it in front of you. A quick background about myself as mentioned earlier I actually I am a toxicologist but I have worked in many areas and we are Biotech's by trade with the United States Army and we have gone through some clinical to research and even forensic drug testing for the Army and we also assist MROs when it comes to performance her duties when we are doing results and these are actually something we constantly have to work with the doctors whoever is the assigned for the unit specifically drug testing. Without further ado quick disclosure I have not nor my spouse or any of my family members have had in the past 12 months expect to have any upcoming mints or any financial relationship or gift in kind with particular industry relevant to the subject matter of my presentation, none of them I don't have any financial ties whatsoever in the disclaimer these are my opinions and we put our heads together to make the presentation as appropriate as possible and easy to follow through as much as we can and if you have questions, feel free to type in the chat box and I can address as I see it or we can actually address it towards the end but bear with us.

For most of my presentation I will actually extract information primarily from the clinical drug testing in primary care and this is actually provided by SAMHSA and it is a little dated, but the concept has not changed, and you may hear some terminology we are still using up to this point there will be new technology and we will provide [Indiscernible] as far as instrumentation is concerned and my focus today is break down the technical aspects of urine drug testing. Again, why do you think it's important or why is it important we have drug testing and primary care and these are the reasons for the most part however you want to carry out whether family practice or some other who belongs to a pain management clinic and they have a predefined or very logistic algorithm to follow it

is important to have tools to provide the best care. The clinical drug testing not only as mentioned initially affect the clinical decision but also about safety and what you don't want is your patient taking other things you have no idea or no knowledge about and you are about to prescribe something that could cause adverse reaction or actions toward the patient so it's important the, at least a urine drug testing before you put them into some type of regimen whether pain management or something where their substance abuse disorder or anything that would require to actually give someone any kind of medication you want to know exactly what the risks. I'm not saying you have to do this for everyone who use in the clinic and again I think it went into detail as far as what needs to be done and what things you should consider and again we advise that you consult with your Nunnally or clinic but also with your clinical director and the standards and expectations because it could be ordering a lot of test for a person for your patient because of safety reasons and if the mechanism is not there you ought to consider what other avenues can you actually approach then it may not be simple as far as putting it in or in the computer and sometimes you actually have to coordinate with the lab to see if you can actually send a sample for testing and as far as identification of illicit drug use it varies from state to state and for example marijuana and for our patient population if there active duty it is pretty straightforward and if there National Guard and reservists they are still considered in uniform and so they still fall under the active duty service members but if you have dependent and they are accessing another doctor also primary care it is important to find out if they are receiving medical marijuana or some states actually now prescribe a [Indiscernible] mushroom and [Indiscernible] is something people actually now get outside primary care and offer to military hospitals and there are some out there but again probably it's important to know the history or the patient history before you actually get involved with pain management or even a urine drug testing per se because you may be surprised when you get the results something shows up and it is good to have the open discussion with your patient before you make any assumptions.

The methods, this is a quick history and overview and drug testing has been around for a long time and it did start ideally with people with problems with addiction back in Vietnam where people were coming back with heroin and opioid addiction and it became law in 1986 and for us we were already during this in the late 70s but it became mandatory for everyone coming in the military to be drug tested and all the federal employees depending on the job they do especially in positions where they have to be tested, they either do it randomly or sometimes fit for duty but for those who are actually working or applying for federal jobs most can remember or for the civilians they are in positions that are required to be tested before you can start your job. And for other industries like the pilots under D.O.T. or Department of Transportation they also have to be tested as well.

Just a quick definition for everybody and again we mentioned window detection this is actually referred to as the time it could be hours or days or weeks or months but basically the time we can detect in a specific matrix whether it is your end, hair, blood or fluid or saliva and nail clippings they are doing that now, you name it, the detection

times, really most of it depends on Nunnally the dose but it depends on the sensitivity of the equipment or the instrument. The administrative cutoff threshold, every instrument has its own limit of detection however in order for us to roll out certain things for example and again this is actually dependent on the method so they can be very sensitive or they could be a [Indiscernible] and while some can only go through a mammogram and what we want, nanogram what we can rule out is the [Indiscernible] versus active administration or someone smoking versus someone ingesting so the window of detection or the administrative cutoff not only works on the sensitivity of the instrument but detection and when people actually have a cutoff for the sake of the work resource testing you're looking at years of research pick for they come up with a number and for the clinical side we typically basted on the method with the vendor saying they are able to or other standards we can go by and we could either adapt SAMHSA or the laboratory can actually establish its own cutoff based on the sensitivity of their method. Cross-reactivity is when one compound actually cross reacts with the antibodies designed to actually look for a specific [Indiscernible] and you'll see most of these happening with immunoassay and for specifically and I will cover this but drugs that caused more cross-reactivity than others do when you look at the results and look at your lab results you have an idea why the result is positive even though the patient says they're not taking any other medications.

The test matrix again is what biological sample you're getting and what are you testing for adult rent is really explanatory and in the department of defense for the most part whenever you do the urine drug testing for the workplace environment specifically for the federal we need to know the validity testing and that is actually to make sure it is from a human person and not adulterated and the [Indiscernible] is considered valid but there are other things considered when it comes to validity testing like gravity in creatinine and whether the urine actually has an oxidant or something which will trigger that.

Test reliability, again this is depending on the method you are using and I will not spend too much time on this but I will give you some time to do examples and we covered in the beginning the assay screening and testing in confirmatory testing and it is really the end of, basically something you want to know your answer now yes or no but also quantity and as mentioned by Colonel Heady we will get, it is pretty difficult and we will get questions for example where this concentration in the report and the first thing that the provider or someone else is receiving, we can actually reduce or at least estimate the dose of the medication or the dose of the drug and if you are telling me I have to do that from a urine standpoint the answer would be no in urine because we are only looking for, it depends on what you're looking for you can be looking for the metabolites or you could be looking for both the parent and the metabolite but in any given time if you actually don't know how often the person is taking that it is hard to determine the concentration that is based on a single time point or a single collection point and we try not to focus too much on the dose but definitely as an example of someone is positive for an amphetamine which we see with Adderall and the cutoff is 100 and the urine drug testing typically most of the immunoassay will start with 500 and then they will have a confirmation

of 100 or maybe [Indiscernible] come if you're patient actually comes back and says the dose is 200,000 nanograms with amphetamine that is the first urine drug test you collected, what is your baseline and you really don't know and if you actually tell your patient to come back two days later and tell you they took Adderall but today you know the dose and it comes back to 1 million then that is something I would look into as far as how often are they taking the Adderall so without having the baseline or a number two a concentration it is hard to tell whether that concentration is high or the concentration is low it's also possible you can get a negative result which means it does not mean there is nothing in there but it means the instrument was not enough to detect the drug or the urine and that is why when you look into the methods you consider the sensitivity of the method pick something you guys may not hear all the time but for us lab folks we like to use the terminology as far as true positive or false positive or true negative or false negative and this will only work if you have more than one method of testing.

A lot of times what it was covered earlier we do screening first and use immunoassay and all of the present and positives go into confirmation and the positive is the confirmation and it is still testing positive basically equal or above the cutoff it is the true positive. If the positive for example it goes to confirmation and confirms negative for what it was to supply the for and let's say the drug classes [Indiscernible] and it is a negative that is what we call a false positive. True negative same thing and a lot of times we don't see the true negative because if the threshold in the beginning was a screen negative we don't go further that is typically what happens for you only say true negative if you say the patient is taking let's say they are taking oxycodone and they screen negative for oxycodone and the provider, if they are allowed they can request to have it confirmed because the person is a high risk and the specimen goes to confirmation and the oxycodone is below the limit of detection are below the cut off and then it is a true negative because now you have the screening negative and you have confirmation negative in the false-negative basically, a lot of times this is when you actually set the cut off to high and we don't really see that either and so again it goes to confirmation to where let's say the same sample it is negative for oxycodone but you have confirmation and there is oxycodone but it is below the cut off of the screening so you can see most of the time when your screening cutoff is much higher than your confirmation cut off. Again you and the see that to the provider asks for that specimen to go to confirmation and a lot of times the algorithm will set to negative in the laboratory is comfortable to say we did our validation and decided the threshold will be set and we know the patient is supposed to be taking a medication and that cut off ideally should be able to catch the majority of people there taking the medication on a known frequency and so yes the cut off of the threshold it actually affects the [Indiscernible] whether the true positive or that negative or false negative and this is just a general idea.

This could vary based on drugs and this is not all and it does not mean they are able to be detected and you can only detect them when a day or two but for the example the restrictions, smoking marijuana, one joint it

may be 60%, versus eating cannabis chocolate that is 15% and they would of detection will be longer for the oral ingestion than the smoking. White that is, one not only the person is able to ingest more and the availability of the drug and it is actually, it stays longer in the system and it can get expensive to digest in your stomach but again if your liver is not able to metabolize all of the drug gets recirculated and it is known to be [Indiscernible] and it stays in your fat cells and the more you actually see the drug or the cannabis, the longer it stays in your system and we have had patients who have actually had [Indiscernible] when I worked at the national [Indiscernible] and they said they were actually of stained or they have not smoked marijuana or even eaten marijuana in the last 30 days we can still actually see the metabolite him in their urine even after they stop using the drug so it depends on the property of the drug and how long it stays. The [Indiscernible] whether it is immediate or long acting they can also stay in the system and the Metabolife specifically some of them can be a week or two weeks. Keep in mind and I know you almost have to review drug pharmacology or pharmacology to understand how they actually affect the window of detection but get that in the back of your mind when you look for or looking at your dose.

This has already been given and this is how we typically do this, and you get a sample, and the sample is subjected to initial testing which is some other point of testing and then it is false positive and goes to confirmation and this is ideally how it should happen but sometimes again if your screen positive you take that and basically stop there but ideally if you want to get confirmation you have to get [Indiscernible].

Lateral flow is different from this one lateral flow is still in antibody but the concept is this book any time you have a drug in the system or anytime you have something that competes with a label drug or typically a label drug, it is concentration dependent and some of them would be inversely proportional to the compensation and it means the higher the concentration of the drug the Lord the signal and while others the most common thing we see is the more drug they have in their urine the more [Indiscernible] it gets and so what we typically do along with the cut off and as I am looking at the one in the gray area, 100 is a normalized value and that is the one abuse in the DOD it could be any number, whatever you think you need to review for your method but in this case a simplified thing if I see a specimen that tested equal or above 100 it is a presumptive positive and anything below 100 is a negative. It is possible urine can still be positive and still have drugs in the urine and still read below 100 and yes it is concentration dependent and sometimes it is also possible where there is nothing in there but something could cross react with the antibody and you can still read above 100 and those are the things that sometimes is not, is not straightforward and you really have to know the limitation of your case and suffer the providers you will not know that you have to call the laboratory or whoever the POC to explain that and in our realm and forensic drug testing specifically the laboratory the witnesses [Indiscernible] they can go ahead and answer questions and so if you have questions later on and even after this webinar if you want to ask about these things we are open and you can email us and we will be happy to actually address those questions.

Again not only the immunoassay with the calibration could be saved for many days we don't have to do it every day but you can have it once every week and that's great and it is cheaper if you produce or you can actually test more for a short amount of time and it's cheaper and again one of the limitations as far as sensitivity is concerned as I mentioned the activity and it is qualitative and it could be quantitative it just depends on how many calibrations you're going to put or that you used to calibrate your instrument and a lot of these immunoassays are the ones that run those they have algorithms that have [Indiscernible] to actually do more than one point or two point calibration and you can do as many as nine however the manufacture are validated so you could do those in the only caveat is whether the manufacturer providing [Indiscernible] or making it in house if you make it in-house then you have to have other requirements to actually use your own calibrator's.

The point-of-care testing and again I don't want to go through too much of this is we cover this quite a bit, here's a question that we always get asked with or on and immunoassay causing a false positive. We have been asked this before or if you are a pharmacist and someone says someone is taking [Indiscernible] or Sudafed and they tested positive for amphetamines do you think that is right or do you think the test is acceptable and if you did not ask them how was the sample tested it may say it is positive and in your mind you can say that could be a problem because it had a cross-reactivity with the [Indiscernible] kit but if I say the urine actually went to confirmation or testing that's the difference in the area and I will cover that while that is because if you are doing screening and this is mostly applicable for confirmatory testing it is possible some of the over counter medications can result in a false presumptive positive and that is not necessarily a conformed or false positive that went to confirmation and it will attribute the immunoassay and then the question is then what and that's the algorithm covered a while ago if you have a patient high risk and positive for XYZ was the next moved to Houston for confirmation, par probably I would like to and we doubt whether the patient is taking cocaine or and phentermine or whatnot.

These are some of the drugs that could cross react if you have an amphetamine case and Adderall if you are not aware it is actually a mixture, three 21 and three part D amphetamine and one part L and so you will not know that but the laboratory during the confirmation needs to be able to separate the trial separation. Another thing is which are not aware Vix inhaler with the L [Indiscernible] and Ed Service Members were they were masking the [Indiscernible] by saying they had a Vix sinus inhaler and fortunately for the drug testing labs where they can separate their able to [Indiscernible] the commanders that the test is actually positive for the methamphetamine and yes we did see [Indiscernible] but we also see D and Nate L did not [Indiscernible] and vice versa so people have done other ways to actually either mask [Indiscernible] so keep in mind these are things that could cross.

This is terminology for the GC or LC MS and pretty self-explanatory, gases gas and liquid is liquid and one thing for sure part of the [Indiscernible] for a very long time and until two decades ago LC MS

and now I think most of the clinical labs are moving forward primarily because the separation in the process you use could be more [Indiscernible] but these are the two typical confirmatory testing you will see and anything that has to do with mass spectrometry has to do with the drug and that is where that's the reason why people actually prefer to have a mass screening rather than immunoassay because it is highly sensitive and better and specifically we also have definitions like LOD or limit of detection and limit of quantitation and most of the time when you see a report they may say LOD. And the forensic world LOD has its own standard and in the clinical LOD may be a signal to ratio for the [Indiscernible] and on the forensic side we make sure we are not only able to meet the three criteria, but the result is repeatable. Again, depending on how the laboratory carries out the test, what it is used for, if you see something a role or result below LOD or the limit of quantitation odds are the person is actually taking the medication is not detected at all, but I would like to point this out even though LC MS is better not only identifying or detecting the drug and also you have a number to go along with that there actually it could very between the test groups or it could be opioid is one group in amphetamines is another group and if you don't have an idea exactly what you want you could be sending a sample for amino acid screening first and then all of a sudden it is screen for something positive and if you do not specify what you need to confirm the laboratory could send samples or confirm five or six type of drugs and it adds up. So again if you're not in the lab, that is something you don't have to be involved in but if you have to be the director and you have to be tasked with putting a program together for clinic this is something you need to be aware of whether you can do it in-house or you want to send it out to Qwest or lab core and the cross benefit of these you will not see the rate of return you may see it for five years later depending on how many examples are testing versus being able to send it out so it depends on your population and the scope and if you're only looking for one class of drug like opioids it will be depending but if you want to look for everything I recommend actually doing in house so you can get, well it can get expensive and hiring people who know how to use the instrument and it is really establishing a very robust quality control and assurance program in the lab itself.

This is a picture of the GC and LC MS if you Google there are lots of pictures as far as they are schematic that this gives an idea of what we have learned when it comes to GCMS.

The advantages, again the bottom line the sensitivity. The limitation, most of the time that only you require a highly technical person to run it and upfront it will cost a lot of money and depending on your method, sometimes some methods can only run maybe six samples per hour it depends on the method. Some samples or some methods can run 10 samples per hour and if you compare that to the immunoassay the analyzer for example that they use the laboratory one module can run about 100 specimens in 15 minutes so there's a difference. So, yes, it depends on how extensive you want your method but they have limitations and not as fast as [Indiscernible] assay in there is another technology that you can do and we call it rapid fire training and it is like an onboard skipping the sample preparation we basically inject the urine and you get a mass

spectrometry screening results and it is not necessarily quantitative but it is only a screening but the capacity technology is much bigger than what you would do if you can go for LC MS screen right off the bat. You will hear a lot of that in the terminology to say I want to have MS based screen capability and again these are the limitations if you want to do that. Most of the time they will come for confirmation.

We already went over this so this is a review of the DOD of what we use.

The challenges, it was mentioned about synthetic urine and it is actually a problem and if your laboratory is not looking for them the patients can actually replace their urine with synthetic urine and if it is not an observed collection it can be easily done. Even if it was observed in the collection we actually did this and we had are we evaluated a class to where if someone wears I don't know if you have heard of a [Indiscernible] but we had a person at least two people where synthetic urine, mill parts, that [Indiscernible] we made sure the urine was warm and when the person actually donated their urine there was no discussion of it being adulterated or substituted and on to hold some or not observing properly and I had a guy actually successfully able to use that to provide synthetic urine and again this is not , it was just an exercise it was not live but an exercise to see if it can be done in our success rate was about 40% and there are people who will see it but I am sure practice over time people can actually [Indiscernible] their urine with synthetic urine and it will pass the test. They're getting better actually and there are kits that will detect synthetic urine but for the most part laboratories may not actually be using the kits. There are some point-of-care testing in the urine cups some of them come in that test for specific gravity or creatinine oxidants and those are also available nowadays in strips and if you are a small clinic and do decide to do point-of-care testing or you have your patient in a cup with a strip those are available also and if you want to do it that way that's one way to know whether your patient is giving you authentic urine or not. Again, like I said if the process or the positive collection is not observed it could be easily done.

Again, the specificity these are some of the drugs again and if the specificity is really bad most likely you could reduce them to the lab for confirmation it come back negative and it will give a lower confirmation.

Novel psychoactive substances or we call NPS and they are synthetics and the drugs in the 60s are no longer the same as yesterday so we have not only synthetic [Indiscernible] [Indiscernible - low volume] we have analogues of LSD and it is not your typical LSD and we also have some analog of cocaine and other stimulants and there are also other serotonin or agents that are actually synthetically made and if you want to know the list of the synthetic names if you go to the website there is a log and you can actually go to the scheduling and there is a whole lot and probably up into the 300 maybe close to 400 synthetics. Why does it matter? It matters a lot. If your patient is not actually getting the release they need they could easily be [Indiscernible] and be getting something from the street because they may be cheap enough but it still gave them relief and unfortunately most of the synthetics do

not cross the immunoassay and summarize for the most part actually the majority of the labs they or their only designed test for a hand full of [Indiscernible] and maybe a handful of synthetic catheter zones and [Indiscernible] the son , something some states are legalizing and some labs may offer that as well and there are lab kits specifically [Indiscernible] hydroxy and you also have LSD and it is making a comeback. If you or your lab whether the core lab or the clinic is getting results from a laboratory that does not include some of these synthetics there are things that you will not know. If you don't test for you don't know. Again, this is where it can get complicated as far as treatment is concerned because of all of the things readily available to the public.

Here are the questions you have been asked before. Can CBD lead to positive THC and this is some of the articles that we found and typically people go to, especially I am in San Antonio and CBD in this state they tell them [Indiscernible] [Indiscernible - low volume] and the problem it depends on how they purify or were they get the CBD from and a lot of times you can actually strike it or we can extract it from the actual leaf or plant material were you extract but the rule of thumb if you are going to have problem or products with CBD you make sure it is below 3% what the 3% what does it mean, is it by the weight or the plant or the constituent compared to the rest of the [Indiscernible] they can identify. A good example if I have a plant down and it is one kilogram and I extract CBD what is the .2% coming from? I mean one kilogram is quite a bit and that is 1000 milligrams. They only need about five milligrams to actually test positive for the cut off or above the cut off in the urine and again we actually tell military members if they are going, CBD is basically off-limits and if they have [Indiscernible] they want to bring home, especially edibles they need to be careful because they will test positive and we just don't know the level in the product and even if you ask for an analysis from the vendor and they go to a local shop, I don't know how many people actually have a certificate of analysis under a CBD product but again, the patient they need to be aware of what they are taking and also need to be aware of what they are taking and when the result comes back positive is good to know what they're actually eating and this is the reason why.

For the DOD as far as the communities and the medical officers, I review results for people who are actually taking [Indiscernible] and I am sure some of you will have patients and that is a synthetic THC and if someone is taking THC and the [Indiscernible] the five or 10 milligrams depending on how many they have to take. Day, so far if I have to look at the concentrations that we see the concentration it is 1000 and sometimes between [Indiscernible] medic [Indiscernible - low volume] the entire bottle, there is literature and if you're interested in the articles let me know and I would be more than happy to emailed the articles but this is something you will see more and more now because states are actually legalizing recreation use of cannabis and of course CBD as well.

For pain management, I think for the most part we need to know: again this is based on the drug, how often do we test and so if I want to know Mr. Smith is taking his OxyContin on a regular basis and not having any problem with it do I test him once a month or do I test him

twice a month or do a test him every time he sees me in the office which is more than once a month, those have to be discussed within your group and we don't have any recommendation as far as that is concerned but definitely understanding the role of pain management and the frequency of how you carry out the tests is important and it leads to the interpretation. And this is a question as far as if it is made from him it is legal and that is correct and that is for [Indiscernible] and the CBD, not all of them are made from hemp even though it is actually the same plant [Indiscernible - low volume] one goes into vision one goes to a tree and the premise is the folks , the farmers who are supposed to be extracting CBD based on the law they are supposed to following what is required and how often are they check? I do not know. Who does a QC, we don't know and one thing for sure the only FDA approved CBD we know is the one that is prescribed to children with the pediatric epilepsy. That is the one that we know and if a Dowlex, other ones that are plant-based that are sold for public consumption without prescription there is no knowing whether they are actually processed from hemp and [Indiscernible - low volume] or something else. Again, the legality is really based on the state and of course the active duty or anyone in uniform, CBD is off-limits and hip is off limits and again for your patience and actually veterans it may not be so in they could probably take as many as they can as long as the state allows them to.

In this particular article is actually a good read and if you need a copy of this or have access to this it's great and if not let us know.

I apologize the resolution on this is blurry, but this gives an example how a clinic carries out pain management program. Basically it is an algorithm and if you are a positive you have different groups and if it is positive for XYZ and if that is a yes it goes to with it is not compliant in you do more stuff and so it's important to actually, I mean ideally every clinic should have something like this where what you should do but I understand it is also not a cookie-cutter scenario because the criteria of what is a high risk versus low risk varies state to state and it could be [Indiscernible] and keep in mind what we provide in the clinical setting we have the tool and there are limitations that we provide people. It may not be what you are looking for and if that is not the case I am sure you can dig that up through your chain or lab director or clinical director and I would point out the limitations you have. If you have more than just you if you have a group that experiences the same thing, I think you would probably get a better or stronger solution when it comes to what makes the pain management and here's a good example in Hawaii, [Indiscernible] they are still following what the CDC would say is first pain management is concerned, however there are other people that completely who would forgo drug testing because they believe they will not give them pain relievers and they will stay away from opioids and they will try and [Indiscernible] and my question to the group at that time in the seminar is that is great if you can actually can venture patient not to take opioids anymore and to wean them off the prescription, however how do you know they are actually not taking your old medication which are not testing them and again I did not get an answer and they basically said we don't know, and exactly you don't know so even if you believe what your patient is telling they no longer take [Indiscernible]. Again, that's

the relationship between you and the patient or the doctor and even if you try alternative needs of treating people for pain or managing their pain keep in mind there are other things available to them and if you're not testing them they may be taking that.

Another is a could also be conducting diversions or be carrying drugs to someone else and making money and that's another way of putting it.

This is an example and I don't know how will you can see it and for this, the data was collected did at the beginning of this year and the scope covers from October 2018 until March 2020 and as you can see for the providers in Hawaii, more than 40% where the populations are actually or 40% of the prescriptions are opioid.

If you look at the breakdown of opioid there's a long list.

If your patient is taking five or even six of these medications and you are going for drug testing, how many of these things will light up? That's a good question. Is your drug screening sensitive to tramadol can it be [Indiscernible] or do you want your [Indiscernible - low volume] and how about melodic cell and some say it's important if it's not available then what.

Here's the benzo and muscle reacts in muscle reacts, relaxant and the medications being prescribed. [Indiscernible - low volume] some of the compounds actually are metabolized and also [Indiscernible - low volume] and the slide is coming up and I will go over those.

Here is a good example. The question is scenario number one patient is taking [Indiscernible] which is coding with Tylenol, codeine with Tylenol and it is tested positive for the opioid and you want confirmation and when you get the confirmation result it tested positive for codeine and morphine and [Indiscernible]. You are thinking wait a second the person was not taking hydromorphone so why am I thinking this? Will there is a minor pathway in the liver where if we take a lot of codeine and you take, you produce a lot of morphine as well there is a chance you can still detect concentration of hydromorphone and sometimes, you'll see codeine for example the morphine could be 15,000 typically much higher than that and your hydromorphone would be in the sub thousand maybe it could be three to 500, very small percentage.

Again, this is just an example and if the person is taking codeine multiple times a day or for a long time, the [Indiscernible] could potentially it is a little higher than what you would expect. If someone is also, there are some people who are fast metabolized others and there are people who are so metabolized others and for someone who is actually, let me look, someone is taking codeine and they are slow metabolizing means they have CYP2 06 is not working as good as normal people, it is possible that not only they may not only get the release they want as morphine was definitely the drug you want to give them, they may be producing more the other metabolites like the Nora codeine or the Nora codeine and Hydra codeine and this is the actual codeine and those are the things between urine so we have to consider hydrolysis

in the lab and you actually have to clean the [Indiscernible] and you can actually detect the morphine and why is that? Because the [Indiscernible] when it comes to the success, they are not stable because my issue is compared to get the free morphine to tell you how much potentially they have Metabolife Weiss. Before anyone who was and [Indiscernible] [Indiscernible - background noise] the chart I'm showing here it would actually change the species of the metabolites you will see and for someone who is actually inhibitor and they are taking codeine for example that pushes the reaction more towards this and someone taking codeine and all of the sudden you don't see codeine you just a lot of morphine and they are probably taking a couple of things and ultra-metabolize her or they are taking something that is [Indiscernible] grapefruit juice is one example and there is a long list of medications that could actually affect the metabolism of opioids so keep that in mind when you have patients on opioid medications and these are some of the [Indiscernible] which are responsible for the metabolism of the drug and can be affected depending on what other medications you have given in the same thing with the hydrocodone and same thing for oxycodone they all work the same.

For the benzo it is actually interesting. This, I just wanted to emphasize that if someone is taking oxycodone most likely they will see oxycodone and if the lab panel or the lab is also testing for the oxycodone that is there to and hydrocodone or hydromorphone for someone taking oxycodone that is not going to be oxycodone and that is on the flowchart or the diagram if you can print this out feel free to do so and if you want to memorize that is great if you know it that's even better. For the benzo here's an example someone is taking Valium and someone taking [Indiscernible] you can actually detect three, a [Indiscernible] and also [Indiscernible - low volume] and keep that in mind pick someone taking the Meza Pam it can also produce temazepam in the group could have [Indiscernible] occurring. So yes, the interpretation can get complicated based on what drugs you're looking at and when you get some of these drugs, they share metabolism with the Metabolife with other drugs as well. So, keep that in mind.

This one I want to have a quick overview and this is actually a unique assayed but form just a biochip array and if you’re familiar great and if not I thought I'd give you an idea and one thing [Indiscernible - echo] [Indiscernible - background noise]

That is okay we are almost there and almost and so hang in there but one thing about this the biochip array technology it is similar to the immunoassay but you only need a sample to be able to test and I think they came out with one [Indiscernible] and the one I evaluate is 20 and it is still more expensive than the amino acid that you run in the core lab however one thing about this is the sensitivity is comparable to [Indiscernible].

I'm not quite sure if you can see that clearly but the red font that represents something equivalent to LC MS and I'm using lab core limit of detection and the one in blue represents the biochip has a lower sensitivity than the lab core which is actually contributory in this column here shows what the DOD workplace drug testing used and what we

are looking for and this column right here tells you what lab core can actually do and at that time when I evaluate [Indiscernible] what it can give you an the highest range it could detect if it is higher than the limits they will give the maximum value so if it's possible for whatever it is you have a choice of working with that number or you want to go for confirmation and one thing that I also identified that was not listed in this slide just like some of the immunoassay, the minor connectivity with other drugs but so far they did well and the amphetamine, they do not overlap and if you have someone testing positive for amphetamine using this chip, I would confirm it. If they are not supposed to be on if amphetamine. Another thing the chip provides is it also has an you can also if you want to look for other drugs like [Indiscernible] or the trip to lean over nortriptyline [Indiscernible - low volume] and I checked that and it did not and it was actually two milligrams is concerned and again if you have this already if you have the ability or capability to run the chip the analyzer itself it is also a Baller, a solid version of this but it only does one sample at a time nothing the, I think I have only one sample and you get the results after 15 minutes I believe in the analyzer you run about 90 samples at a time and get results about an hour and half later. Something you need to consider.

Okay again the summary this is the same workplace with a urine drug testing in the clinical and the MRO function is important and unfortunately for the clinical you are the MRO and you are the doctor and basically the MRO and you get the results and have to [Indiscernible] pricked the MRO get their training for the civilian side I believe, if it is a minimum of three days it could be a week-long but for the Army we have to provide but they have to be appointed and they are supposed to be an MRO training and San Antonio but because of COVID we have to control that but keep in mind there is a lot of things that you have to keep in the back of your mind for interpretation of results because it is not just what they are taking it is understanding the pharmacology of the drug specifically how the body basically metabolizes and that is the most important thing so if you are not aware on the metabolites how they could be made or how it is produced from one drug you could actually be misinterpreting the results. And so if you feel you think you need to consult someone for those results if you're laboratory has a toxicologist, sometimes they do and sometimes they don't I am sure we can ask around who you can talk to and I can't remember if SAMHSA has a clinical cup from ecologist but again for the most part those who have someone to consult with, if not, like I said you can email me or talk to us and actually we can help you out and again we are providing you with service we're not giving you a course of action as to what you have to do we're just giving an idea what it could be and depending on how aggressive or how thorough you want your pain management to be it is really up to the facility whether they are able to [Indiscernible] or send the samples out for additional testing. That is where we are at.

And that is all I have. Any questions?

So, you want to go over the test? Sure.

Can you hear me okay? Loud and clear. Great at this point if there are will go over the test now.

I am going to summarize them right now. For the get to know your question, so, there were two. What was your classification? 5-Star, seven? The majority of the folks responded that seven, that they were other, so they were something other than resident or primary provider or pain management provider. It was equally sick plate between primary care provider and Pay Management at three and three. We had one resident. In terms of the question about formal education on proper interpretation, roughly house said yes, they had had such education and I-9 had said, no, they had never had formal education on interpretation of UDT.

How many UDTs does this provide a population review per month by and a large? Most of you said provided between one and attend or that you review and interpret between one and attend UDTs per month.

In terms of confidence in your ability to accurately interpret a UDT, all over the place pick we had three saying they were not confident at all. Most people, six, said they were somewhat confident. Once had neutral. We had four Rock Stars who we're like, yes, I got this. I am confident. Ideally, I guess you would do a pre- instruction, sort of an opposed instruction survey. Unfortunately, it did not quite work out that way for us. So, we did do the survey to get a feel for our audience, but when I'll be able to see a Delta with you guys, unfortunately. Maybe, if you invite does back next time, we can do that. Let's get to the quiz.

The assessment.

The first question that is interpretive in nature is number 62 falls, taking [Indiscernible] can result in a positive urine drug test for THC? True false.

True or false.

As we alluded to you cannot really answer this question without knowing how it was tested. So, if you screened with an IA or maybe even lateral flow test, chances are, and you're CBD contains more than that .3% you could end up positive by THC. In addition, as Colonel Meadows said, if you've got CBD that exceeds the .3% of THC and if on the confirmation [Indiscernible] you could still be positive depending on the limit of detection and the cut off for the assay. I said, true. Most people actually said true but not everybody. LTC Marisol S. Castaneto, what do you think?

It's a trick question.

It is. It is a trick question. A lot of them end up being a trick question. The current State the way we are at now someone is taking CBD like a dialect's odds are you should not test positive for THC. Again, that's only strictly limited to children with epilepsy, but any CBD that you get from the outside source, not one that you get from your pharmacy prescribed to you.

It's a higher probability because actually take it, in just it. Not something you put on as a body oil, lotion or here or whatever, but if you he did have highest potential to test positive for metabolite THC. It's a lot. We're talking about more than several milligrams. Some of them could have, the [Indiscernible] that I found could be as much as 2000 milligrams of CBD. That's amazing. So, yes. It's interesting when people say, CBD actually helps me make goat to sleep. I'm thinking, Jacob CBD doesn't have that characteristic. Maybe it's something else. There you go. Because it's in there. In reality it would cause confirmed positive. For the immunoassay it's yes or no. It depends on where your cutoff is said. If it's set at lower, lower than 50, yes it would. If you set it about 50 to a hundred it may not. It just depends.

Do you want to take number seven?

We have number seven. Number seven, patient prescribed with Tylenol T3 and may test positive for what analyte in your? What's the answer?

Most got it right. I think two people got it wrong, but I said, D, all of the above.

In most cases we typically see morphine and codeine.

True, true.

Most of the time we see that but there will be a few that will have Hydromorphone. As I commented want to go you'll see how do more phone much, much lower than morphine and codeine. Ideally use encoding and morphine but it is all of the above.

But it's the right one for misinterpretation.

Yes, it is.

Number a true or false, Pseudoephedrine can cause a positive urinalysis for the Amphetamine? This one is tricky. What test is that screening or confirmation test? I said it's true, it's true if you are looking at an IA top immunoassay test or lateral flow test that really certainly isn't specific for the isomers a pseudoephedrine. [Indiscernible] if your test is in fact one of those chromatography Mass spectrometry tests that can distinguish out and DNL Amphetamine.

And a little bit about ephedrine and other things. Something I did not touch on a while ago people taking [Indiscernible].

This comes up and they say taking the supplement, pre- work up supplement and all of a sudden test positive for to 24 or Amphetamine. Supplements you don't know where it came from. Some of them they do have some contamination but for the most part they are sold at GNC we're any reputable place like Vitamin A world or something like that, keep in mind that Amphetamine, [Indiscernible] will be more schedule two drug. [Indiscernible] sell the product they have to have a license to do that.

Good point, excellent point, excellent point.

The next one is right up your alley, Colonel Castaneto. If a person adjusts 100-milligram of THC from a cannabis at the bowl, how many days can the primary metabolite of THC be detected in urine?

-- cannabis and double.

-- cannabis edible.

Drumroll could be longer than four days.

Why?

Primarily because 100-milligram. Two, because THC as I mentioned can be recirculated and could also be sequestered in your fat cells. It does take some time for your liver to clean that out. If you smoke typically [Indiscernible] but for the most part what we have seen people actually ingest THC as edible is three to four days per keep in mind there are edible out there that are [Indiscernible] labeled. It to be over and it can also be under. If you are interested in these articles let me know. I could share those articles with you. It's a good read but somebody adjusted THC, don't trust the label unless they get some kind of certificate of analysis that's what it is. Both of them would probably be more. Now there is some, but most will be less. Typically, it's more than what the label would say. Even if the person only took one time. Not for chronic use but just one time.

Okay. Number 10. True or False. Vix sinus inhaler can lead to a positive D Meth and D Amphetamine?

Elle Amphetamine so answer is false.

Correct.

Benzodiazepine, a rich source of misinterpretation. Which of the following Benzodiazepines listed below form [Indiscernible] also Benzodiazepine is a metabolite?

The answer is, tran 12.

That's true and it's misspelled. That's right, that's right because Librium will metabolize the [Indiscernible], and then [Indiscernible] which metabolizes nor diazepam which leads to [Indiscernible]. That is how, in fact, D, the chlorine dioxide they had to up [Indiscernible].

Go ahead.

Not everybody cup Librium is not very common.

True.

But there are people that still take Librium. Most the time when you see [Indiscernible] they probably are on, somebody gave them diazepam or

value them. Some people probably on diazepam. Librium is not as common as it used to, but you will still see that.

Okay number 12, which of the following drugs will not form or metabolize to morphine? I did to say that D, [Indiscernible] is Hydromorphone but that should be oxymorphone. It should be like a treat for finding the typo. It is in fact oxymorphone. Given that which of these drugs will not metabolize to morphine? It should be, C and D, right?

[Indiscernible - low volume]

I'm thinking of the other one. I'm probably thinking of [Indiscernible].

If the premise normally when somebody takes coding it does the morphine. Somebody takes morphine goes too [Indiscernible] but anytime they take oxycodone or oxymorphone, [Indiscernible] or Hydromorphone it doesn't go back up.

That's exactly right.

Oxymorphone.

True or False, there is no over-the-counter product available in the United States will cause a positive D Amphetamine and D Meth?

As far as I know if it's legal it's true. If it's illegal?

Is active up.

Number 14 is one we get all of the time. Which of the following drugs will cause a positive D Amphetamine only? Sudafed, Pseudoephedrine, Wellbutrin, [Indiscernible], or none of the above?

And the answer is, B, Mydayis a.k.a. Adderall.

To a false, Fentanyl will result to a positive urine test for morphine. We alluded to this why it could be in fact false because in fact Fentanyl is pretty bad in terms of the opiates in [Indiscernible] out there, write, LTC Marisol S. Castaneto?

It is. It's found everywhere. It ubiquitous.

But in terms of Fentanyl able to register on an immunoassay for morphine, not going to happen most likely, right?

Right, it's just the chemical structure. It's totally different so that's a good thing. But just keep in mind for everybody what we see in the DoD workplace drug testing, Fentanyl is basically, me most of the drugs [Indiscernible - low volume].

That would further confound one of our providers.

So 16, which of the following tests can be run on a urine drug screen to detect certain additives and/or dilution attempts? And the answer is?

All of those.

Yes, pretty much all of those.

Yes. Okay.

To a false top sent Methamphetamine is an Amphetamine chemically, if you test for amphetamines, you do not also have to test for Methamphetamine. For example, if you want to test a patient to see if they are taking their methylphenidate, you can test for either methamphetamines or amphetamines, both would show positive. True false?

Let's assume your testing immunoassay, is that a true or a false statement?

You want to test the patient, um in some cases it would be true.

If this was a screen, yes. If it was a screen think I guess, probably [Indiscernible] activity would pick up either math or Amphetamine. But if you had a more definitive test, that likely would not be true. Because that definitive test will pick up, will differentiate Methamphetamine or [Indiscernible].

Again, it's only if you are hoping the laboratory goes all the way.

Right. If you don't confirm for them, you will said damp or AMP positive is what you will see in the report.

Which of the following, number 18? Which of the following compounds could possibly cause a false positive screen result for methamphetamine? Screen to be synonymous with cartridge, IA, flow. LaBella at all, Dexter more fan, NSAID's or opiates?

It is, A. It is in fact, to 14. It is in the hypertensive [Indiscernible].

So that is what is going to trigger that I a screen for methamphetamine, similar structure.

Looking for that, yes.

Of F is a 30-year-old female with a past medical history significant for allergic Rhinitis with cough, ADHD, HTN, and obesity. The only medications listed in her chart include Claritin daily, methylphenidate twice a day, Lisinopril daily. Our routine drug screening, routine drug screening. Assuming that is IA in a clinic comes back positive for amphetamines and for opiates. What information do you want to make sure that you have to ensure you appropriately interpret the positive result?

You put the [Indiscernible] they are?

I didn't because stole this from one of the old surveys from one of the other published surveys.

We are going to assume it was IA. I'm going to submit was IA.

I think this brings up for me what sticks out the most the fact that the person also screens positive. I'm not worried about the Amphetamine, per se, but if the opiate is the one, I am concerned with.

Being go. That is exactly what I said. What I did is I zeroed in on the call, and so, cough over-the-counter, possibly dextromethorphan for coughing pick my answer to this was to ask her about any over-the-counter medications such as dextromethorphan for her cough. And I would ask her about [Indiscernible] to because I would just want to know. You drink any interesting tea lately?

Yes.

I'm not quite sure for our audience that for DoD with our six-month rule for prescription medication. You can have somebody who has [Indiscernible] maybe two, three years ago.

Good point.

They may take it again because it was something they took and had that incident with the really bad cough, so keep that in mind. Start asking people are your patients what they took. It may not be over the counter. It may be an all prescription. Basically, ask them what they took.

Absolutely, absolutely.

The right is a different topic. They can still test positive for cocaine if they said they are doing right because it does contain cocaine. It is enough cocaine that it will test positive. It will screen positive and come positive for metabolite.

Yes.

Okay.

Number 20, tran 11 is 7-year-old female who was initiated on fentanyl patch is for chronic lower back pain about four months ago. Her last visit she states she's been using patches as prescribed their helping to control her pain. Also performed her annual urine drug screening, ding, thing, Dean, I a letter receiving the results she's negative for all controlled substances, including opioids. Which of the following is the best answer to your reaction? I love this one because we kind of hammered on it coincidentally.

Yes.

I did not realize we had a person with a fentanyl patch.

I'm ago it, D. We already talked about, this says it's a screen so we will assume it’s an eye a screen, everybody trying to get to all of the

opioid screens, but it's not going to catch Fentanyl. We just talked about that. Chances are it's not going to catch Fentanyl.

Right.

I think D is the right answer. Get a confirmation test.

Keep in mind to for the audience if your laboratory is not [Indiscernible] for Fentanyl then, yes. If they are asking for the cut off.

Absolutely.

Ask them if they are looking for the actual parent which is Fentanyl, with a looking for the metabolite, nor Fentanyl. Anybody with the patches on have enough nor Fentanyl in the system should be able to screen [Indiscernible]. Possible this person is probably selling her patches.

No, who knows.

Ideally, if you do have [Indiscernible] I said that does test for Fentanyl it should figure it should, right?

It should talk to the gym.

They are getting a microgram dose. It's quite a bit.

Conferment the goal for confirmation.

Our last one top a 63-year-old male with a past medical history significant for hypertension, hyperlipidemia, chronic pain related to complications after a severe MBA which occurred this past June. Medications he is being prescribed you include Lisinopril, atorvastatin, ibuprofen as needed, and oxycodone immediate release as needed for severe pain. At his last visit, he states he's been taking his Oxycodone only as needed and alternate it with ibuprofen, and that his pain seemed adequately controlled. You also had them do is annual urine drug screen, 1011, and just got the results showing is negative for opiate. Which of the following is the best answer for what your reaction should be?

What is it?

Where is it?

B, I always call the lab. All the toxicology lab and verify the opiate level and the interpretation. Opiate cutoff level and interpretation of what they probably mean here is, so, what opiates our they measuring? Opiates is a broad category, it's a family. You, lab, tell me in that family white Oxycodone, what is the cutoff format Oxycodone for your opiate assay? I need to know.

Yes, so most of the essays nowadays are able to separate the oxycodone from the Morphine/coding and even the Hydromorphone. Yes, the better to go to the lab and see how specific their opioid testing.

That's exactly right.

Let me address the six-month rule because I didn't mention it. For the DoD, for us, the scheduled drugs that is basically schedule one through five.

Yes, one through five.

Those scheduled drugs, we call them -- I'm sorry, two through five.

Well, schedule one.

I did not know that, okay.

We still have some. It is still schedule one, but for the most part DA still have it as scheduled drugs. There is a rule that your patients, specific service members get a urine positive that is outside of the six months then if they can actually show you they are taking that medication and [Indiscernible] if expired will authorize it for now. But if they can show that it's legitimate or authorized.

Right, because now the language, this is DoD instructions that just came out that as this language that LTC Marisol S. Castaneto is talking about. Use of prescription, narcotic scheduled through whatever has six months of the last field date now is considered a nonvalid prescription. -- the last day. Filled there for you don't have valid prescription, therefore it well [Indiscernible - low volume].

That is going to be changed. It's good for everybody to know this because we may have patients who get their refills outside of the pharmacy, Tricare, like DoD pharmacy. They might get it from CVS pharmacy or somewhere else that people track copper say. Some tell me they can access CVS to, but if the pharmacy, these guys, if they do not recognize the six-month rule the expiration can be the expiration of the drug. It could be one-year, a year and a half, but other states are very particular about how many opioids there are able to detect. They can control that but, again, just be mindful that if you have an active duty or even a person in uniform. I would not stick to active duty copper say because [Indiscernible] example but active duty you have the six-month rule.

That's right. This population are folks sitting of this presentation now, some of them very will now be or in the MOs future and something they need to be aware of. Too entity got want to mention one thing and sort of new to me, the pharmaceutical impurity that can also confound your drug result. I know that .04% of Morphine is contaminated with codeine, so that can [Indiscernible] really [Indiscernible] coding can confound some of the interpretation there. Do you know of other contaminations, contamination issues? There are some contaminations as we'll like, I believe, I think the codeine depending on the Company, not had a coding got not codeine specifically, the dihydrate codeine, I think that. [Indiscernible] for example could actually be contaminated with codeine, and even Hydromorphone because of the makeup. I have had somebody who was

taking the codeine was positive for Hydromorphone brought up to me. I ended up asking the MRO to see [Indiscernible] example to ask if we could test for the metabolite that they had the codeine. I did not have this in front of me but there are some percentages. Ideally for the assay they have to be less than a certain percentage, 2% I think, something like that. The overall contamination, but those could happen as well, but if there is a contamination just keep in mind it would be very, very small compared to the actual, the medicine is Oxycodone that is much, much higher than potential contamination.

True, and so cutoff becomes very important there because if you are using IA you are never going to cost likely you are never going to -- right, but if you've got a homespun [Indiscernible] lab developed test in your lab, and they've got real good sensitivity you may just see it.

Yes. Another thing I did not cover was the methamphetamine. Someone on Adderall, most of our folks got most of our service members, those that take Adderall there does per day can vary from person to person. Some Kanav Extended release and have 20 milligrams a day. I don't know how they sleep but at all concentration can be really, really high in urine. And then a little small concentration methamphetamine with it. Again, I would caution those interpreting the results. If you see D Amphetamine, I think .5% of D Amphetamine means you can attribute to the impurity for the Adderall or the pill called the medication, so somebody with 50,000 milligrams of D Amphetamine to potentially be methamphetamine for the 100-milligram per cutoff. Just one of those things.

All right. Do we have any questions?

Very quiet.

I believe both LTC Marisol S. Castaneto and I are easily findable on global. I just want to say a huge thank you to LTC Marisol S. Castaneto because she has been PTS off again, on again, Covid in Hawaii to Texas during this whole process and was still able to participate in this presentation. I am personally extremely thankful.

No problem.

Any questions you may have, just reach out to us with any follow-on questions. We are always happy to assist.

We are always here.

Again, if you need those articles let me know. If you have a question or a question that needs to be answered do not want to give it to the group that is fine. We can answer it for you if you want to do that. If you want to give my phone number in the offices (210)295-4732. That is central standard time for you all in Texas. I am in Texas now. I'm not in Hawaiian now. No more Aloha. Happy to help.

Okay, Carla, I think we are done.

Thank you so much LTC Tiffany N. Heady and LTC Marisol S. Castaneto. We appreciate your time in preparing this wonderful presentation. Thank you so much. What's again, everyone got presentation is available for download in the pod slide. You can upload them directly from there. Thank you so much. Thank you, everyone.

[Event Concluded]