Deceptively Simple: Can Urine Samples from CLIA-Waived Urine Drug Screen Devices Be Reused for Confirmatory Testing?

Article:
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J Appl Lab Med 2023; 8(2): 341-6. https://doi.org/10.1093/jalm/jfac094

Guest: Dr. Raj Pandya is a Medical Director of Clinical Chemistry and Toxicology at the University of Utah Hospital Laboratory, and an Assistant Professor of Pathology at the University of Utah Health.

Randye Kaye: Hello and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

Urine drug testing is commonly performed across many clinical settings and is widely recommended for adherence monitoring of patients taking controlled substances. While many clinical laboratories offer urine drug screening and/or confirmatory methods, there are several CLIA-waived point-of-care devices that are often attractive to clinics because they provide immediate results. However, these waived methods provide only presumptive screening results, and urine samples may need to be reflexed to the laboratory for confirmation testing by another method such as LC-MS-MS.

This workflow may raise concerns about the appropriateness of the original screening sample, typically collected directly into the device cup itself for confirmatory testing. The March 2023 issue of *JALM* features a focused report that investigates the question, "Can urine samples from CLIA-waived urine drug screen devices be reused for confirmatory testing?" Today, we're joined by the article's first author, Dr. Raj Pandya.

Dr. Pandya is the Medical Director of Clinical Chemistry and Toxicology at the University of Utah Hospital Laboratory and an Assistant Professor of Pathology at the University of Utah Health. He is an ABCC board-certified clinical chemist with interest in toxicology, interference in lab assays, and renal function testing. Dr. Pandya, welcome. To start us off, can you tell us a little bit about the usefulness of CLIA-waived urine drug screen cups?

Raj Pandya: Sure, but first of all, thank you. Thank you for inviting me and as far as the CLIA-waived urine drug screen cups are concerned, these devices have three main advantages over laboratory-based assays. So, the first one is their simplicity. These devices can have as many as 15 assays built into a single cup, but because they are so simple to use, even non-

laboratory trained individuals such as medical assistants, or even receptionists can administer the test. And secondly from a regulatory standpoint, these devices are CLIA-waived and of low complexity, which means that little medical director oversight is required when compared to moderate- or high-complexity assays wherein you need to monitor QC, enrolled in proficiency testing programs, as well as fulfill inspection requirements. And the last advantage that these CLIA-waived devices have is that they are fast, right? And you get the results within five minutes or so. Therefore, these devices are ideal for the point-of-care applications.

Randye Kaye: Wonderful. So, how do these devices work?

Raj Pandya: So, these devices work somewhat similar to how home pregnancy kits work and the technology that's used is called comparative immunochromatography. So, there are several nitrocellulose test strips built into the cup and each strip is testing for a certain drug class. For example, opioids, stimulants, marijuana, et cetera. And approximately in the middle of each test strip, a specific drug compound is impregnated by chemical conjugation. And at the bottom of each test strip, there are antibodies against this class of compounds.

So, when the test strip is hydrated by urine, antibodies migrate upwards through capillary action and bind the drug conjugates, which gives rise to a red line. Now, this presence of red line indicates a negative result. However, when a cross-reacting compound is present in the patient urine, the antibodies at the bottom already get saturated first with the drug compounds present in patient's urine. And as a result, they can no longer bind the impregnated drug conjugates in the middle of the strip. So, no red line develops when a sample is positive. The *absence* of a line indicates a positive result.

Randye Kaye: Thank you. So, what motivated you to undertake this study? Can you explain what types of experiments you performed?

Raj Pandya: Sure. So, oftentimes, NexScreen test results are sent for confirmatory testing by highly sensitive technologies such as LC or GCMS.

There is a practice at our institution, and we wanted to investigate if drug compounds that are part of the NexScreen assay system, the drug conjugates that I talked about in the previous question, if they could leach into the urine and cause false positives.

Also, if compounds that are present in patient urine could absorb to nitrocellulose membranes or to the plastic cup, it may give rise to false negatives. So, we wanted to

investigate if false positives or false negatives are possible if urine from NexScreen cups is reused for confirmatory testing.

So, we performed two sets of experiments. The first set, we took a previously tested pool of urine, which was tested to make sure that it was negative for all drug compounds, and we incubated it in several NexScreen devices for one hour, and then send it off for confirmatory testing to see if drug leaching is a concern. And for the second set of experiments, we spiked 14 different drug compounds into this negative urine pool at known concentrations and incubated this urine in several NexScreen devices for one hour again to test for adsorption. And again, we sent up these samples for quantitative LC or GCMS assays. So, that was the study design.

Randye Kaye: And what were your key findings?

Raj Pandya: Yeah. So, first of all, none of the negative urine samples that were incubated in NexScreen cups became positive upon LC-MS-MS testing. So, what that tells us is that drug leaching isn't really a concern. And for the second set of experiment, most of the spike analytes, remember, we spiked 14 different compounds. They all pretty much recovered well, about 95%, in confirmatory assays. And only a couple of analytes such as buprenorphine and 11-nor-9-carboxy-THC which is used to look for marijuana use, showed minor adsorption, but that adsorption was really minimal and almost negligible.

So, in essence, false positives or false negatives in confirmatory testing is not really a concern when urine is reused from the NexScreen device is what we found.

Randye Kaye: Very interesting. So finally, is there a message? What message would you have for those who are using and interpreting results from these types of tests?

Raj Pandya: Yeah. For sure. Since these devices have relatively lower specificity and sensitivity, you know, when you compare them to something like LC MS-MS assays, I would say that it is important to keep in mind that positive results coming out of such devices should be regarded as presumptive positive and should be confirmed by lab-based assays. At the same time, negative results with high degree of clinical suspicion should also be tested by more sensitive assays such as lab-based immunoassays or mass spectrometry-based assays. And also, if you have in your lab a workflow wherein you use, or I should say, reuse the urine from such CLIA-waived devices and then send it off for confirmatory test, it is a good idea to perform a validation study such as what we presented in this manuscript.

Randye Kaye: All right. Thank you so much for joining us today, Dr. Pandya.

Raj Pandya: Thank you very much.

Randye Kaye: That was Dr. Raj Pandya from the University of Utah describing the *JALM* article "Deceptively Simple: Can Urine Samples from CLIA-Waived Urine Drug Screen Devices Be Reused for Confirmatory Testing?" Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.