Turning questions to answers in drug testing

Karen Titus

July 2023—As she surveys the opioid epidemic in North America, Christine Snozek, PhD, D(ABCC), could be tempted to think that a ripped-from-the-headlines reality has landed in clinical laboratories as well as on TV crime dramas. With the number of opioid-related deaths increasing in recent years, particularly since the start of the pandemic, drug testing demands have increased for labs as well, says Dr. Snozek, codirector of clinical chemistry and support services and director of point of care and central processing at Mayo Clinic in Arizona.

If only she could turn to the entertainment industry for a technology-based solution. "I wish we had *CSI* lab capabilities," she says, referring to the long-running police procedural. "You could run a sample and find all the drugs known to man on one test. If they could go ahead and release that technology, that would be wonderful," jokes Dr. Snozek, a member of the CAP Toxicology Committee.

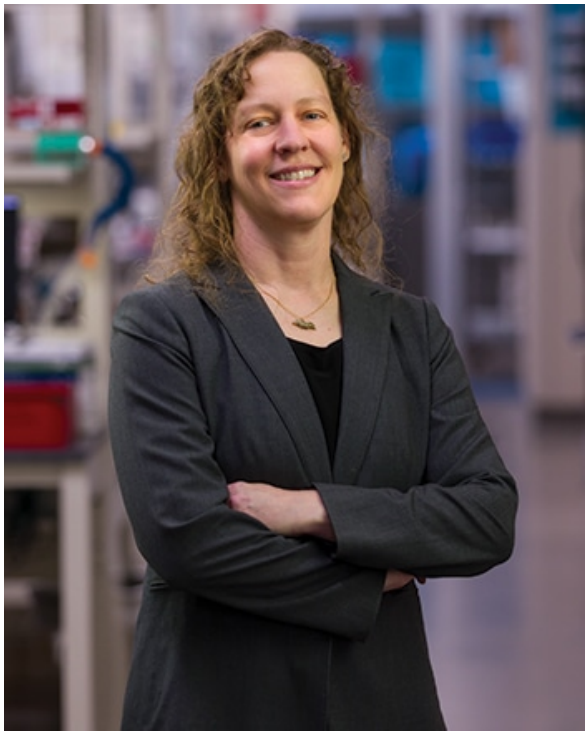
Given that laboratories are unlikely to take a meeting with network executives, Dr. Snozek and others in the field will have to look elsewhere. Fortunately, some nonfictional solutions exist.

Dr. Snozek and two coauthors—Danyel Tacker, PhD, D(ABCC), and Sarah Delaney, PhD, D(ABCC)—explored the laboratory's role in drug testing in a review published recently in *Critical Reviews in Clinical Laboratory Sciences* (Delaney SR, et al. *Crit Rev Clin Lab Sci.* 2022;59[5]:309–331). While keeping up with changing-at-warp-speed testing needs might seem insurmountable to any but the largest reference laboratories, Drs. Snozek, Tacker, and Delaney suggest that any—make that every—lab can be a useful resource for clinical colleagues and patients, not only to help stem the opioid crisis but to manage other drug testing as well.

Dr. Snozek draws on her background at two Mayo Clinic sites when she assesses how labs can help. At her former location in Minnesota, the lab had access to the bonanza of resources that fill any large reference laboratory. At her current position in Phoenix, "I wouldn't call us a small or resource-constrained operation," she says, "but obviously it's very different from Rochester's capabilities."

For labs that don't have access to mass analytic methods, such as liquid chromatography with tandem mass spectrometry and high-resolution MS, or dedicated staff to develop and run drug testing assays, there's still plenty they can do, says Dr. Snozek. Her current Mayo site, for example, is essentially a tertiary center in the Phoenix area. She doesn't offer mass spectrometry for drug testing, nor does she need to for her patient population. But she can and does offer other drug testing options.

And that's the point. "This is my soapbox: Labs can be doing more and should be doing more," Dr. Snozek says.



Dr. Christine Snozek at Mayo Clinic in Arizona. For labs that don't have access to mass analytic methods or staff dedicated to developing and running drug testing assays, there's still plenty they can do, she says, amid the decades-long opioid epidemic. [Photo by Pete Pallagi, Mayo Clinic]

That runs counter to what many might see as a reasonable response to the relentless opioid crisis that's lasted longer than the 16-year *CSI* run: deciding that it's impossible to keep up. Dr. Snozek says she's seen such responses, particularly among laboratory staff who lack specific clinical chemistry or toxicology training. "It's just so overwhelming, they're not sure they can do anything about it."

Dr. Snozek offers a brisk tour of basic steps laboratories can take.

Any laboratory, for starters, can look at its test menu and see if it lines up with, as she puts it, "what's going on in the world." Start by talking to emergency department colleagues. If the lab doesn't offer a screen for fentanyl, for example, would their ED colleagues find it useful?

In some cases, it may be reasonable to subtract rather than add. Any lab can ask its local practice if something is no longer useful. Case in point: propoxyphene, which is usually offered in a kit format, such as a point-of-care cup. "Propoxyphene is pretty useless," Dr. Snozek says, adding that the test wasn't widely used when it was first made available and is even less so now. "It's almost unheard-of to see someone with a propoxyphene positivity. There's no point in testing for it."

She returns often to this common refrain of *any* laboratory—as in any laboratory can take such a step, even those that lack staff with extensive toxicology training. "It just involves looking at your lab information system, seeing who's ordering drug tests, then contacting them" to ask if they'd like to see something different, Dr. Snozek says.

Such steps, though useful, hardly close the case. Dr. Snozek is quick to acknowledge that drug testing can feel overwhelming because it is, in many ways, overwhelming. Keeping up with current trends can feel like trying to outswim a rip tide.

“If you’re talking about novel drugs that come and go, it is difficult to get that information in anything even remotely resembling real time,” Dr. Snozek says. A truly new drug that hasn’t been well characterized may appear as a pocket of overdoses that show up in a metro area and then peter out. The drug will remain unrecognized for weeks or months until someone has the ability to analyze it and confirm it.

Dr. Snozek commiserates with labs that might feel steamrolled by such scenarios. At that point, she says, “It probably is appropriate for most labs to throw up their hands and say, ‘I don’t have the resources to keep up.’ And honestly, if we can’t test for it, we aren’t the best resource,” she says. “As far as bringing up a test for these novel agents that come and go quickly, it’s not feasible for most laboratories to do.”

Coauthor Dr. Tacker also laments the speed with which changes occur in the field. Simply put, “We can’t be as nimble as the changes occurring at the street level in drug use,” she says. “We often find things incidentally and in tragic conditions and circumstances. It’s usually something terrible that clues us in that we need to change something in the lab,” says Dr. Tacker, clinical professor of pathology, medical director of clinical chemistry and mass spectrometry laboratories, and CLIA medical director of blood gas laboratories, J.W. Ruby Memorial Hospital, West Virginia University Health System, Morgantown.

Nevertheless, other clues might appear earlier. Regional trends relate to which drugs are prominent in local circulation, she says; likewise, the CDC’s *Morbidity and Mortality Weekly Report* can indicate outbreaks or clusters of toxicities, offering useful information about symptoms and which agents are responsible. These reports “can help labs triangulate how their services may align, or may even expose gaps in their services and prompt them to try to fill them,” says Dr. Tacker, who is also CLIA medical director at Fairmont (WVa.)Medical Center.

Dr. Tacker has done this herself, noting how xylazine has made its way into street blends of opioids and other drugs. “It’s incredibly toxic, and there’s no standard laboratory screening reagent for it. There aren’t any point-of-care tests that are going to test this for us.” Basically, she says, providers are figuring out the drug based on its presentation in the clinic, then calling the lab to ask for confirmation.

She first heard about xylazine when she spoke with coauthor Dr. Delaney, clinical biochemist at Unity Health Toronto, as they were working on the review article and discussing what examples they’d use. Dr. Delaney mentioned the drug’s impact in the Toronto area. Says Dr. Tacker: “I hadn’t even heard of it yet, but now it’s made its way to West Virginia.” Observing the movement of these drugs is interesting, “but also frightening,” she says. “How do we serve clinicians in a way that’s productive? How do we answer questions for them?”

Longer trends have been easier to track, from heroin to semisynthetic and fully synthetic opioids. But within those decades-long climatic shifts, the specifics are chaotic—one year’s drought is next year’s deluge.

West Virginia has long been an epicenter of the opioid crisis, Dr. Tacker notes, spurring harm reduction efforts. “The most common questions we get on a day-to-day basis are, ‘Is this person using? And what can we do to help with harm reduction?’” she says.

The story of her lab’s response makes a compelling tale of its own.

The lab placed point-of-care drug cups in behavioral medicine clinics, which allows providers a first pass at screening and enables them to have an immediate talk with the patient if something has changed.

Dr. Tacker

But first the lab had to convince a key player: itself. “We originally pushed back against point-of-care–based drug testing,” Dr. Tacker concedes. The lab had doubts about the technology and feared its use would lead to more problems. She was happy to be proved wrong. “It’s been a boon for the clinic—a huge benefit.” Having the results immediately redirects conversations with patients quickly, who tend to respond well, she says. “Usually the patient will come clean because they know this is their chance to get help. It turns things around for them.”

Based on her experience, Dr. Tacker says she encourages labs to collaborate with behavioral medicine specialists in the clinic setting. “We’ve built a strong relationship with them just on creating the point-of-care program.”

Beyond that, the central lab has expanded its urine drug panels, which are offered hospitalwide and in clinics. It’s an 11-component drug panel—covering fentanyl, methadone, buprenorphine, oxycodone, and opiates—with creatinine as a check for integrity. They’ve also created the ability to automatically reflex positive results in the panel to confirmatory testing, primarily on liquid chromatography–mass spectrometry. That’s critical, Dr. Tacker says. “They may be taking an over-the-counter medication that is similar enough to cause a false-positive.”

Or, if a person has an unexpected negative result, Dr. Tacker continues, that could spur conversations about noncompliance. “So the laboratory service has integrated itself without even trying into these care scenarios,” she says. “We’re just trying to support decision-making for our clinicians. There’s so many of them in so many different practices.”

How did Dr. Tacker and her colleagues develop their panel? “I wish I could say it was a deliberate effort, done in a year,” Dr. Tacker says. Instead, it evolved over time, mostly as clinicians asked about testing for new substances. When she joined WVU at the end of 2010, she recalls, colleagues were asking about tests for so-called bath salts, which are synthetic cathinones. “I had to look up ‘bath salts.’ I thought they were literally talking about what you’d get at Bed, Bath & Beyond,” she recalls with a laugh. “I had no idea.”

The lab was also asked about testing for methadone, which eventually made its way onto the menu.

But the drug cups were the catalyst, she reiterates. “Behavioral medicine approached us and said, ‘Look, we have to have something else.’” That launched serious discussions about POC testing. “It caused me to start taking a hard look at what was in the cups, so we could choose the right one. And that cross-informed me [about] what we should be doing with our panels in the main lab.” If a test was important to behavioral medicine specialists, she realized, it would also be important to obstetricians, family medicine physicians, and others who might be looking to ensure compliance for, say, barbiturate prescriptions. By about 2014, the elements started to coalesce, and the lab selected a POC cup with cutoffs that were compatible with the central lab.

Several years later, an upgrade in the lab enabled it to perform mass spectrometry toxicology testing, and Dr. Tacker began to research an opioid panel. The goal was to address the so-called heavy hitters, she says, with an emphasis on high sensitivity.

Cue mea culpa No. 2.

The lab met its goal, Dr. Tacker says, launching a super-sensitive panel. It was so sensitive, in fact, that colleagues from behavioral medicine began calling to let the lab know the panel was detecting morphine in patients who’d undergone minor surgeries a week earlier—i.e. clearly not drug use candidates.

These days, Dr. Tacker makes a point of doing a careful annual review of the panel. She pulls every report submitted in the previous year for every orderable configuration of the confirmatory testing. “I look at the cutoff, how many results came in near the cutoff, whether they were clinically relevant, where they came from—was it an inpatient, was it the addiction clinic setting?” In short: How did the test results affect care and decision-making?

She then shares her summaries with behavioral medicine. “We think we’ve settled on a good set of cutoffs,” thanks to these discussions, she says. “We’ve started to inform our process based on what’s going on in the clinics.” For example, the lab now offers tramadol confirmatories for patients receiving pain control for neuropathies and other conditions. And it’s no longer flagging patients who’ve undergone minor surgeries.

How difficult is it to capture this information? “I’m an Excel spreadsheet girl,” Dr. Tacker answers, adding, “I don’t have any major training in data analytics.” Her approach is simple: “I go into Epic, I run a bench report for the orderable tests that we have built, and it extracts a report for me that I pull into Excel. And then I start counting.” She uses a few simple equations to ask how many results were below cutoff, at or around cutoff, and high above cutoff. It does take time, she acknowledges. In her case, it requires about six weeks, “putting in an hour here, an hour there.”

The close relationship she’s forged with clinical colleagues has paid off in another way, she says. When the lab wanted to bring in-house many of the confirmatory tests it was sending out, it had neither the staff nor the equipment to meet the high demand. When they approached administration for funding, behavioral medicine joined the lab in making the case.

“It helps to have these partnerships,” Dr. Tacker says. “Then it’s not just you asking for cash to build a program.”

Her clinical colleagues have learned to listen to the lab. At one point Dr. Tacker decided it would be useful to add tramadol screening.

“We sold three in the first year,” she says. “We thought, *Maybe they just don’t know we offer this test.* So we reminded them.” Still no buyers. Lo and behold, providers knew the lab also offered a definitive test by mass spec; in fact, the lab had recommended this test to its colleagues in compliance situations, to avoid the double charge. “Well, they followed that instruction to the T. So we turned off the screening test.”

As Dr. Tacker’s tales tell, creating more responsive drug testing requires time and a few misses as well as hits. It’s doable, especially for those who persevere. Her fear—one her coauthors on the *Critical Reviews* publication share—is that too few labs are wading in.

Their article drew information, in part, from CAP Surveys data. As Dr. Snozek notes, in late 2021/early 2022, roughly only 50 percent of laboratories that were signed up for the opiate screen also had a specific result for oxycodone, and only about an eighth had a specific result for fentanyl.

This doesn’t necessarily mean labs aren’t running tests for these drugs, she notes; they might be using a different proficiency testing platform for them. Nonetheless, she adds that the majority of laboratories that participate in a broad Survey of this type tend to be those that don’t typically have multiple, dedicated mass spectrometry-type platforms for this testing. “So it seemed likely to be a good snapshot of routine, regular labs.”

Thus the low numbers are cause for concern, given that use of oxycodone and fentanyl is no longer a new phenomenon. “It’s one thing to say routine labs don’t have the bandwidth to update test menus in response to novel psychoactive agents,” says Dr. Snozek. “But when fentanyl has been the main killer for eight-plus years, that’s a significant lag that’s clinically relevant.”

Speaking from her own experience, Dr. Delaney, who is also an assistant professor, Department of Laboratory Medicine and Pathobiology, University of Toronto, offers insight into possible reasons for the slow uptake. There are, she notes, only so many kits and tests available, and many are third-party reagents. Her lab is currently transitioning to the latest model of its analyzers. “But we use a third-party reagent, and there are no parameters that have been worked up for this brand-new instrument, so we’re scrambling.”

Vendors will also have to find the right incentives (the most obvious being money) to develop tests, but vendors, like labs, can also be hamstrung by shifting trends. Dr. Delaney reports Toronto has seen a tremendous, sustained rise in fluorofentanyls this spring. “It came out of nowhere,” she says. But that doesn’t mean it will continue, or that it will make sense for manufacturers to develop a test. On the other hand, the longstanding presence of fentanyl should induce test development for this substance. “There’s a real demand to make that available on confirmatory or mass-spectrometry–based testing, which might be a little easier to optimize and develop.”

The rapid fluctuations in the unregulated drug supply put another burden on laboratories: They have to work even harder than usual to justify the need for new tests, Dr. Delaney says. “You have to build a case for putting the time

and energy and money into building a new method for xylazine, for instance. And even if something's in the drug supply, you have to weigh the pros and cons of implementing testing."

It's a conversation she has regularly with clinical colleagues. "Sometimes clinicians will say, 'We need this,' but not understand just how dynamic the drug supply is." The only way to possibly keep up, she says, is to have strong relationships with the providers who use the urine drug screen and to meet with them often. "It's a challenging dance."

Dr. Delaney and colleagues have looked at trending positivity rates for various substances over several years, hoping to use the data to decide what to remove from the test menu. It sounds like a good idea, but in practice it may not provide clear-cut answers. Depending on the substance, "you could say, 'We haven't seen it in six months—we're going to remove it from our method.' But then it will come up and have sustained presentation for another six months." It's nearly impossible to predict whether a drug will return, Dr. Delaney says.

With no bright and shiny *CSI* technology forthcoming, laboratories will need to figure out for themselves how to update their test menus for each methodology.

Dr. Snozek notes that currently there are approved immunoassays for fentanyl, tramadol, hydrocodone, and oxycodone. These tend to be more readily available on automated platforms, as opposed to point-of-care screening cups. Labs that have historically relied on POC cups may want to reconsider whether that remains the best solution. And even if it is, newer cup options now offer a better mix of tests.

Given the increase labs are seeing in drug testing, it may well be time to consider moving from a POC cup to automated immunoassays. "They tend to be more customizable," Dr. Snozek says. "You can validate the ones that are appropriate for your practice," and not be locked into what a POC manufacturer offers.

Mass spectrometry tests are almost exclusively laboratory-developed, Dr. Snozek says, adding that more labs are finding this technology within reach. She and others are evaluating Surveys data to understand trends in that area as well. Moreover, the *Critical Reviews* publication highlights the challenges of using various mass spec assays. As the authors note, even with the more readily available platforms, such as standard triple quads, there remains a lack of standardization in terms of what cutoffs to use, whether to report results qualitatively or quantitatively, and what drugs and metabolites to include.

For that guidance to appear, it will require "someone to grab the opportunity by the horns and get it moving," Dr. Snozek says. She points to how matters have unfolded in an adjacent setting: testing for drug-facilitated sexual assault. The Scientific Working Group for Forensic Toxicology, or SWGTOX, though a more forensically focused group, recognized the need for standardization for drug-facilitated sexual assault testing. "They put that guidance out there with the scientific backing behind it to say that evidence suggests this is what you need to do."

It's not a stretch to think of the current testing scene as the Wild West, says Dr. Delaney, in part because there's so little guidance for clinicians.

In her own three-hospital network, recently formed, the clinical practices at the two key hospitals are vastly different, reflecting in part the variations in patient populations. "It's tricky to meet everyone's needs."

She's tried to address this by providing interpretive guidance, including on the lab test catalog website. This involves, among other things, keeping up to date with the cutoff concentrations for the immunoassays, explaining cross-reactivities, and indicating what's included in confirmatory and broad-spectrum testing. The lab also makes it easy for providers to know whom to contact for help with interpreting urine drug screen results.

These efforts have helped somewhat, Dr. Delaney says. "It is so hard. The physician needs are different, and it's hard to understand which guidelines they follow," she says, given that each specialty—ED, mental health services, addiction medicine, pain management—is likely using different guidance. "There are many guidelines out there. None of them agree with each other."

Drug testing requires another essential but often overlooked element: trust. Patients need to trust their physicians to manage test results, which means overcoming the stigmas that cling to drug use.

Fortunately, that metamorphosis is underway, says Dr. Delaney, who notes that changing guidelines from the CDC and American Society of Addiction Medicine and in a couple of Canadian guidance documents are influencing how urine drug testing is performed. “We’re shifting to a less punitive way, to a more patient-centered approach.”

In Toronto, Dr. Delaney has been immersed in harm reduction as one of the leads for the city’s Drug Checking Services.

The premise of this approach is fairly straightforward: People who use drugs go to a safe consumption site to submit a sample of the drug they used or intend to use; the sample is analyzed at her lab, which then returns results to the user along with harm reduction information.

It’s not unusual for someone to submit what they think is fentanyl, while the analysis indicates the presence of other drugs, such as xylazine. Not only is that important from a health and user perspective—“It can have significant unexpected effects on the person if they’re used to using fentanyl, and now they’re using a whole bunch of other sedatives in the mix,” says Dr. Delaney—it also provides useful insights to labs. It’s a fairly novel and underappreciated approach, she suggests, one she’ll be discussing in a talk at this month’s AACC meeting.

Dr. Delaney explains: One of the limits of urine drug testing is that most methods are either targeted (usually mass-spec confirmatory tests) or class-based (immunoassays). But because so many drugs are circulating in and out of the drug supply, unknown to the medical community, “How are we supposed to know what to test for?” she asks. The drug checking essentially works as an invaluable surveillance tool for monitoring trends in the unregulated drug supply. If a pattern of seeing xylazine mixed with fentanyl has persisted for several months—to give an example—“We might want to think about adding it to our confirmatory method.”

With more germane information, clinical treatment improves. If a patient wants to start opioid agonist therapy, for example, having an up-to-date urine drug testing menu or capabilities will allow physicians to manage the patient’s situation more thoroughly—considering the need to manage benzodiazepine withdrawal, for example, if they’ve been taking it unknowingly.

Knowledge is perhaps the best path through a forest where fully grown trees seem to spring up overnight.

“Education is so important to this,” Dr. Tacker says. “So many providers are swimming in heavy schedules, and they get just a few minutes to talk to patients. The last thing they also need to do is double major in toxicology.”

Much of the burden is falling on primary care physicians, Dr. Snozek agrees, noting that this is a group that almost never gets direct education on opioid treatments, or on buprenorphine therapy, which is now being funneled into primary care as well.

Those with less experience may be trying to incorporate drug testing because of guidelines, Dr. Snozek says. “But they haven’t been given a toolbox for how to best do it. They don’t get that information alongside the guidelines saying, *Thou shalt.* Should it be on all our patients? Maybe. Should it be on select patients? Maybe. It depends on the practice.”

Some studies indicate physicians may not have a clear understanding about how to interpret drug tests. Never simple to begin with, it’s only become more complicated in recent years, says Dr. Snozek. And with the growing use of mass spec, which entails a host of new metabolites, physicians are understandably confused.

Dr. Snozek would like to see organizations such as the CAP step in with additional help, given the lack of training in medical school and residency. Pathologists can directly target educational gaps by making sure their own laboratory staff are trained. There is, she says, room for improvement. “I’ve had the experience where bench staff don’t necessarily have training in interpreting drug tests, either.” For those who lack such knowledge, she says it should be easier to turn to the CAP and other professional organizations for help. Bench techs either need to

improve their understanding of drug testing issues, or recognize their own lack of understanding, she says. In the latter case, “It’s not part of your day-to-day job—no big deal. But make sure you have an escalating path to somebody who is trained in it, who can help [answer] those questions.”

Dr. Delaney likewise has found it useful to educate clinical colleagues about the limitations of urine drug testing, both on immunoassays and mass-spectrometry–based or confirmatory testing.

Immunoassays are limited to a select number of drug classes, she notes. The opioid drug class can identify a number of opiates with varying cross-reactivities; the same holds true for the benzodiazepine screen. What’s important to understand is that some of these class-based methods can’t identify drugs like xylazine or emerging novel psychoactive substances. With most institutions using immunoassay-based testing at least as a screen, it’s likely many drugs will be missed.

Moreover, fentanyl requires its own specific immunoassay. “A lot of providers still don’t know that,” Dr. Delaney says, which explains why they’ll order an opiate screen and assume a negative result means the patient is not using fentanyl. This happens even among her ED colleagues, she says.

That lack of understanding remains surprising to Dr. Delaney. Even in more specialized areas, such as addiction medicine, there remain generous opportunities to help clinicians interpret test results. And overall, she’s found, physician confidence in interpreting urine drug screen results “is very low,” despite the resources she and others in the lab have provided. In a survey she did at her own institution, Dr. Delaney asked her clinical colleagues whom they’d turn to for drug testing guidance. Only a small percentage said they’d contact laboratory personnel. “A lot of them said they’d just talk to their colleagues, peer-to-peer”—another surprising (and doubtless unsettling) response.

Dr. Delaney

Nor are mass spectrometry/confirmatory tests beyond reproach, which means providers have to be educated about those limitations as well, Dr. Delaney continues. Most of them are targeted. If a physician orders a confirmatory opioid test but is also looking to investigate potential fentanyl exposure, it needs to be part of the test menu—a point not always appreciated. “You can only look for what you tell it to look for.”

Dr. Tacker had her own surprises involving confirmatory testing and so-called simulated compliance. (This is when a person diverts a drug they’re supposed to be taking, for any number of reasons. “It happens,” says Dr. Tacker. “There’s no judgment there.”)

The laboratory addressed that by adding simulated compliance comments to results for a handful of drugs, including oxycodone and methadone. Mass spectrometry can detect that pattern, since it looks not only for the original compound but also for the metabolite—evidence that a drug such as buprenorphine has been converted to norbuprenorphine, for example. If a result shows exceedingly high quantities of the former, but less than one percent of the latter, the lab flags it as abnormal and adds “potential simulated compliance” to the results.

When the lab first encountered it, “It shook us up,” she says. “The tech would be sitting there wondering, *Why do I have no metabolite? Is there something wrong with my method?”*

This gave the lab another opening to educate its clinical colleagues, says Dr. Tacker. If providers receive only the numbers, they might not think about simulated compliance. “But if we can detect, they can have a different conversation with the patient.”

Like any good conversation, those around drug testing rely on careful listening, says Dr. Tacker, who notes that the needs of every department vary. The emergency department does not routinely do confirmatory testing; it would only slow them down, she says. Instead, if a patient has been admitted and has a positive result from the ED, the lab provides confirmatory toxicology testing for those services, if needed.

The WVU system is also rolling out pediatric toxicology services at its children's hospital, which opened last October. It's a field that places far different demands on the laboratory. In addition, psychiatric medicine is enmeshed with multiple departments, and the lab is adjusting to guidelines for drug testing in obstetrics, palliative care, and oncology. In some cases there are hybrid groups—behavioral medicine specialists who work with oncologists in palliative care clinics to manage pain control.

"Every hospital situation might be a little different," Dr. Tacker says. But every conversation can start with the same questions: What do you need? What can the lab do? What can we do together?

If it's not clear by now, Dr. Tacker is a big believer in talking to clinical colleagues. Perhaps the most common question she gets has to do with false-positives: Is the patient really taking the drug in question, or is there something else going on (like the aforementioned prior surgery)? The stakes are high, particularly as it gets to the heart of patient-physician trust.

Occasionally she'll field questions about why a patient who's taking Ritalin has a negative amphetamine screen. She pauses, then explains: That drug is not an amphetamine.

Another example involves fentanyl screening, a test the lab added a few years ago. It had the lowest cutoff of any drug in the urine panel: 1 ng/mL. (By comparison, THC is 50 ng/mL; buprenorphine, 5 ng/mL; cocaine, 150 ng/mL; and MDMA, around 500 ng/mL.) With that wide scope of cutoffs, there could be cross-reactions with fentanyl that might result in a false-positive.

"We saw a rash of positives in the ED," Dr. Tacker recalls. The clinicians doubted the results and wondered if the test was too sensitive, given that patients who had supposedly taken the drug entered the ED walking and talking.

Dr. Tacker went back to her trusty reports, looking at the raw data for positive fentanyl results.

Her explanation: "We get *a* number, but it's not actually *the* number." She noticed that the positive results that led to the ED's questions were extremely close to the cutoff—1 ng/mL, 1.1 ng/mL. "Low, low positives." she says. "And I reliably found antihistamines in the patient's chart when they presented in the emergency department." Spotting the cross-reaction cleared up the mystery.

She also encountered a disconcerting number of positives for fentanyl in OB patients being treated for hypertension with labetalol, which also cross-reacts with the fentanyl screen. The question from clinicians was swift and direct: *What is going on?* It turns out the beta blocker was going on.

These experiences led the lab to add a comment to its results, noting the labetalol or antihistamines may trigger low-level false-positives and suggesting confirmation if clinically indicated.

"We can do certain things with outreach," Dr. Tacker concludes. "For us, that's been lots and lots of conversations about cutoffs and cross-reactivity."

Some patients may take lower-than-prescribed doses of a drug, for any number of reasons. For example, they might think a medication that has a low dose to begin with can be taken as needed, rather than prescribed. They may think they're being compliant—*I'm taking this when I need it*—but they take so little of it, so infrequently, it won't show up in sufficient volume to trigger a positive screen or positive confirmation.

That means more conversations with providers about the nuances of cutoffs, Dr. Tacker says, and how patients might be unintentionally diverting. "Lots and lots of questions about that."

Dr. Tacker remains upbeat as she surveys the staggering challenges. "If people see the potential to partner up with

clinicians and to turn this into a positive thing, then it gives me hope for our profession."

She had her own learning curve. "The first thing I learned was you have to set aside your biases. And you have to learn from providers that the stigma doesn't help. If you see this as an illness that is treatable, then people can benefit from intervention." Just like any illness, she adds, "they don't want this one. You learn so much more when you push your bias aside and listen to providers and their stories and help with the casework," Dr. Tacker says.

She continues: "That's a big part of this—just removing the stigma. We don't damn people who have heart disease quite as much as the person who has a substance use disorder. We don't go after people who have gout—we don't call them bad people because they like chicken and beef and wine."

Setting aside stigmas should be simple for labs, she says, if they ask questions of themselves as well as their clinical colleagues. "What is the data in front of me? What can I contribute to this team's knowledge? And how can I help them through their clinic day?"

Karen Titus is CAP TODAY *contributing editor and co-managing editor.*