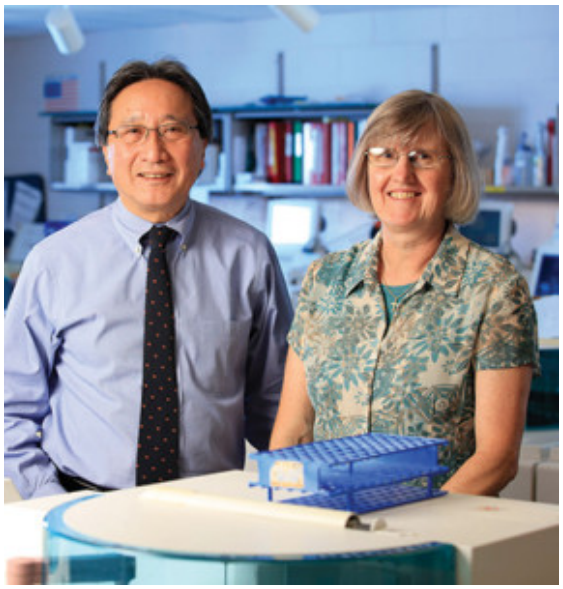
Painstaking process of drug monitoring

Karen Titus

August 2016—As optimists like to point out (in their annoying way), showing up is half the battle. But it's still only half, as other, equally clear-eyed folks might point out.

That leaves plenty to do. And in drug testing for chronic pain management, the work facing laboratories may seem like even more than 50 percent.



For pain management drug testing, the menu will consist of the drugs detected in chronic pain patients on opioid therapy and vary with prevalence and clinic or practice group, says Dr. Tai Kwong, with Barbara Meiklejohn, chief supervisor of the hematology/chemistry laboratory.

While a test can indicate the presence of a drug, "trying to figure out why it's there, or not there, is the complexity we wrestle with," says Tai C. Kwong, PhD, a professor of pathology and laboratory medicine and director of the hematology/chemistry laboratory, University of Rochester (NY) School of Medicine and Dentistry. He's also director of chemistry, UR Medicine. "The fact of the drug being there is not enough."

For laboratories, it's becoming crucial to understand this and other issues related to pain management testing.

Barbarajean Magnani, PhD, MD, professor, chair, and pathologist-in-chief, Tufts Medical Center, Tufts University School of Medicine, Boston, sees a crisis today in managing patients who are taking opioids for chronic, noncancer pain—and the laboratory, she says, has a major role in supporting clinical services.

"Prescriptions of opioids have exploded, leading to misuse, abuse, and adverse health outcomes, including an epidemic of unintentional opioid deaths," says Dr. Magnani, who co-chaired a recent American Association for Clinical Chemistry virtual conference on drug monitoring for pain management. She and others addressed the issues facing laboratories in light of this problem, both at the conference and in speaking with CAP TODAY.

While presenting a typical case and noting the postmortem toxicology report showed, among other substances, the

presence of alprazolam (Xanax), diazepam (Valium), oxycodone (OxyContin), and hydrocodone (Vicodin with acetaminophen), Dr. Magnani notes it's not unusual to see a mixture of medications such as opioids and benzodiazepines in the urine of a deceased patient. "Sedative-hypnotic drugs and opioids together, even at lower concentrations, can provide a lethal cocktail for the unknowing."

"We hear of the increasing numbers of deaths from opioids," she says. "But remember: Every number was a life." The example she gave was from the late actor Heath Ledger.

"If we look at the rate of deaths from drug overdoses between the years 2000 and 2014, it has increased 137 percent," she says (Rudd RA, et al. *MMWR*. 2016;64:1378–1382). The rate of overdose deaths involving opioids has increased 200 percent in that same period, a figure Dr. Magnani calls staggering. "And remember that the data always drags a little bit behind where we are currently, in 2016," she says.

Natural and semisynthetic opioids lead other opioid deaths. In the last few years, however, "We are seeing an unprecedented increase in heroin deaths"—including, she says, in the state where she practices, Massachusetts.

The rate of unintentional drug overdose deaths from 1970 to 2007 has also soared, she says, despite the popular notion that the early 1970s belonged to a so-called drug-culture era. The rate of death at that time was about one in 100,000; by 2007, the rate neared 10 per 100,000. "Prescription drug abuse is the fastest growing drug problem in the United States," she says, and is accompanied by unintentional drug overdose death rates largely driven by an increase in opioid analgesics.

How did we get here? Dr. Magnani notes that pain is considered the fifth vital sign, and patients have the right to appropriate assessment and management of their pain—it's a Joint Commission standard.

Dr. Magnani

Most prescription painkillers are prescribed by primary care and internal medicine doctors and dentists, she says. "I see this in my own practice, where it's mostly the primary care physicians who have difficulty managing patients on chronic opioid therapy and are coming to the laboratory for help in managing those patients."

What do clinicians need from the laboratory? Dr. Magnani points to what are known as aberrant drug behaviors: not using prescribed medications, not using prescribed medications as prescribed, using nonprescribed medications, using illicit drugs, and diverting prescribed medications. "These are the questions that our clinical colleagues ask us when we run a urine drug test and want to know if their patient is compliant.

"There's a good reason to identify these behaviors where possible," she continues. Several studies have looked at urine drug testing and noncompliance. A retrospective study of 470 pain clinic patients, for example, looked at urine drug testing by gas chromatography-mass spectrometry. All results were reviewed and verified against patient charts to check for appropriateness of test results (Michna E, et al. *Clin J Pain.* 2007;23[2]:173–179).

Only 55 percent of the patients were using the appropriate opioid, while 10.2 percent of the patients were missing the prescribed opioid. Moreover, 14.5 percent had an additional nonprescribed opioid, and 20.2 percent were using illicit substances.

Clinical guidelines for opioid therapy call for, among other things, prescription monitoring program reports, which includes urine drug testing. The written contracts/agreements between physicians and patients who are prescribed long-term controlled substances for chronic pain will include notice that patients can be subjected to random drug

testing, says Dr. Magnani. “That’s important, because the presence of unauthorized substances may prompt referral for assessment for either an addictive disorder or may, in fact, even break the contract.”

Another element of clinical guidelines covers monitoring therapy. Physicians need to assess the patient periodically, or with any changing circumstance, she says. Are patients improving? Are they adhering to therapy? Are there adverse events, such as psychological issues or substance abuse? Again, urine drug tests can help with such monitoring. It supplements other tools, such as pill counts, self-reporting, and behavioral monitoring, and can identify problems that might otherwise go undetected. “It really is an objective means to document aberrant drug behavior” as well as a way to check for compliance.

Every guideline recommends urine drug testing, Dr. Magnani says, but the details can be fuzzy. The state of Washington’s guideline, for example, says that urine drug testing is used to “objectively assure compliance,” but provides scant concrete information. What, exactly, does compliance imply? Dr. Magnani asks.

For treating physicians, it meant patients are sticking to the terms of their treatment agreement. Urine drug testing can help with this, but isn’t perfect. It can’t determine if a patient is adhering to exact dosing intervals, for example. “This is a problem for us when we do our consultations,” Dr. Magnani says. “All I can really say is if the drug and its metabolites have shown up in the urine, then it’s most likely they’ve taken that drug prior to the urine collection. I don’t know exactly how much and whether they’re taking it every day. I can’t determine whether they’re taking more or less of that prescribed dose.” As to whether they’re taking a nonprescribed medication, it depends on what the assay targets, though most labs can detect use of illicit drugs.

An equally important issue for urine drug testing is clinicians’ interpretive skills. Dr. Magnani cites a seven-question, multiple-choice survey that assessed the skills of 150 physicians at an opioid education meeting. Among this group, 68 percent used drug testing, and 76 percent prescribed opioids; 19 percent were board-certified in pain management and six percent in addiction medicine or psychiatry. Of those who ordered drug tests, says Dr. Magnani, none answered all seven questions correctly, and only 30 percent scored more than half correctly.

The implications are clear to Dr. Magnani: Clinicians can’t manage their patients’ pain without help from the laboratory.

Dr. Krasowski

Matthew Krasowski, MD, PhD, would second that notion. At the University of Iowa Hospital and Clinics, Iowa City, the laboratory performs basic immunoassay drugs-of-abuse screens in-house; the panel covers amphetamines, benzodiazepines, cocaine metabolites, opiates, oxycodone/oxymorphone, and THC, reports Dr. Krasowski, clinical professor and vice chair of clinical pathology and laboratory services. Confirmatory testing by mass spectrometry is referred to a commercial reference laboratory.

“What I’ve been asked more in the last year or two is to give more education to family medicine, surgery/trauma, and other areas where this is starting to come up,” he says. “Patients may be seen in a pain clinic, but they’re often followed by primary care physicians, who want to understand what testing they need to do to follow these patients.”

There’s data to show that pain isn’t always managed well, Dr. Krasowski continues. At the same time, national data point to opioids being overused, he says, with a dramatic rise in the past decade for overdose deaths attributed to prescription opioids.

The lab helps on two fronts: the analytical service and the consultation service.

The former will be laboratory-specific, based on a lab's resources and the practice area. Test menus and drug lists, as well as appropriate screening/confirmation assay sensitivity and specificity, are, of course, crucial. As for consultation, the lab needs to let clinical colleagues know what it can, and can't, detect. Labs need to review test sensitivity/specificity with clinicians, as well as drug testing limitations. "Most importantly, we want to provide an interpretation of those test results," says Dr. Magnani.

Given that drug testing is critical to monitoring aberrant drug behavior—"Not too many people would volunteer that they were doing drugs," notes the University of Rochester's Dr. Kwong—laboratories need to closely consider the issues involved in such work.

To decide on a test menu, says Dr. Kwong (who focused on urine assays in his talk), "We need to know what drugs are detected in chronic pain patients on opioid therapy." One study showed the drugs detected in close to 11,000 pain clinic urine specimens. As expected, there were high positive rates for opiates (82.4 percent), and lower but still significant positive rates for other medications used for pain control, says Dr. Kwong, namely the barbiturates, 2.8 percent; carisoprodol, 5.6 percent; fentanyl, 4.2 percent; methadone, 11.1 percent; and propoxyphene, 3.5 percent.

For testing in 2016, he notes that propoxyphene has not been available since 2010, and that buprenorphine was not available at the time the paper was published, in 2008. "Finally, with many states passing the use of medical marijuana, we should expect that positive rates for cannabinoids in the future among chronic pain patients may go higher" than the study's 8.9 percent.

For pain management drug testing, the menu should consist of the typical illicit drugs, like the amphetamines, the cannabinoids, and cocaine, as well as opioids and benzodiazepines. In some programs urine alcohol is included.

Commonly prescribed opioids for pain management include the opiates morphine, hydromorphone, codeine, hydrocodone, dihydrocodeine, oxycodone, and oxymorphone. Opioids are agonists for the opioid receptors and include both opiates and non-opiates. "In other words, all opiates are opioids, but not all opioids are opiates," says Dr. Kwong.

Opiates are the naturally occurring alkaloids morphine and codeine, derived from opium poppy, and their aforementioned derivatives. All are structurally related.

The non-opiate opioids, on the other hand, are structurally unrelated to morphine and codeine. For example, methadone, fentanyl, buprenorphine, tramadol, and tapentadol are structurally not related to the opiates. The non-opiate opioids are not detected by the opiates immunoassay and thus require separate assays.

The benzodiazepines are a structurally diverse class of drugs that includes diazepam, oxazepam, and temazepam; the latter two are also metabolites of diazepam, or Valium. "But these days the most prescribed benzodiazepines are clonazepam (Klonopin), alprazolam (Xanax), and lorazepam (Ativan). And they should be included in the test menu," says Dr. Kwong.

For testing by immunoassay, the menu is limited by commercial availability of FDA-cleared kits. "The menu depends on local prevalence, and of course it will vary with clinic or practice group," he says, though it will likely be some combination of the following immunoassay tests: amphetamines, benzodiazepines, buprenorphine, cannabinoids, cocaine, methadone, opiates, oxycodone, and fentanyl.

Providers, including those involved in drug treatment programs, can help. "They're directly dealing with people who they suspect are abusing their prescription or using some other medications, or even illicit drugs," says Dr. Kwong. It can make sense for laboratories to develop several different test menus, each one customized to a particular practice group or treatment program. "The laboratory needs to be flexible."

“The test menu and methodologies must meet the needs of the pain treatment programs,” Dr. Kwong says. What are the drug positivity and negativity rates, and are the results expected or unexpected? Can the laboratory handle the test volume? Does the laboratory have resources and expertise to do confirmation testing?

Dr. Kwong identifies two basic testing strategies: 1) screening by immunoassay, and 2) skipping immunoassay screen and going directly to mass spectrometry.

“Pain management testing is clinical testing. And unlike workplace or forensic testing,” says Dr. Kwong, “confirmation of the initial immunoassay positive result is neither mandatory nor always necessary. Ordering confirmation is at the discretion of the ordering physician,” who may forego it if the positive test result is clinically expected and if there is no suspicion of aberrant drug behaviors. “Needless to say, proper interpretation of an unconfirmed positive result requires a good understanding of the capabilities and limitations of immunoassays.”

Immunoassay screen—and, if positive, reflexed to confirmation by mass spectrometry—is probably the most widely used strategy, says Dr. Kwong. Confirmation may also be ordered when a specimen screens negative for the prescribed drug (an unexpected negative); if a specimen tests positive for a drug that is *not* prescribed (an unexpected positive); if a specimen screens positive for illicit drugs, such as cocaine; or if the provider suspects aberrant drug behavior.

Direct testing by mass spectrometry is an alternative strategy. One advantage of this approach, says Dr. Kwong, is that immunoassays are class assays, whereas mass spec assays are analyte specific. “For example, an immunoassay positive tells you that there are benzodiazepines present, assuming it is a true positive. But the mass spec will tell you which benzodiazepine is present.”

Mass spec assays are also analytically more sensitive and have lower cutoffs. For example the opiate immunoassay cutoff is 300 ng/mL, but LC-MS/MS can easily go down to 50 ng/mL or lower.

Finally, immunoassays are qualitative, while mass spec assays can give quantitative measurements of drug concentrations.

But mass spec assays have the disadvantage of slow throughput, he notes. Most assays require sample preparation and extraction steps, which are labor-intensive and time-consuming. And “if you want to analyze for 10 or more different opiates, you will have to separate these opiates chromatographically,” which makes for a long run time.

Moreover, he says, “If you have one assay for the benzodiazepines, a separate one for the opiates, yet another one for other drugs of abuse, then you’re talking about doing three assays per specimen, if that specimen is positive for benzodiazepines, opiates, and cocaine.”

Finally, “We all know that mass spec instruments are not cheap.” And assay development, validation, instrument operation, and maintenance require highly trained technologists.

Dr. Kwong’s laboratory performs urine drug testing for the common drugs of abuse and some of the commonly prescribed medications for chronic pain patients, doing screening tests by immunoassay and confirmatory testing by LC-tandem mass spectrometry. With a handful of prescription drugs, “We go direct to tandem mass spec,” he says.

Test menu and strategy are based on other parameters in addition to analytical methods. “We have to consult with clinicians and other providers to make sure their clinical needs are met,” says Dr. Kwong. “We can go into the lab result database to review the positivity rate [and] the negativity rate, to see if changes to test strategy can be made.” For example, if the screen positivity rate for “PCP or methaqualone is low in your area, then propose to drop these drugs from the test menu.” On the other hand, if clinicians feel that a positive result has serious consequences for the patient, like dismissal from treatment programs or discontinuation of opioid therapy, then

tests for drugs such as cocaine and amphetamines should be kept on the menu, even if positivity rates are low. “The point is, let the clinicians have their say.”

If a high percentage of patients are on certain drugs, so that immunoassay positive rates are clinically expected to be high, and the positive results reflex to confirmation, “Then one might consider bypassing immunoassay screening and going directly to mass spec confirmation testing,” he says.

And if the false-negative rates are high? This is common for some drugs, especially the opiates and benzodiazepines, Dr. Kwong says. “For example, hydromorphone at 1,000 ng/mL will test negative by the opiates immunoassay used in my laboratory, even though the patient has been compliant with his or her prescription.”

How often do his menus change? It depends, in part, when new drugs become available (or disappear). “There are a few changes that I’ve made over the last several years,” Dr. Kwong says, such as when use of methadone shifted to buprenorphine. And when propoxyphene was taken off the shelf, so was the test for it; likewise, when oxymorphone, a metabolite of oxycodone, appeared as a prescription opiate, “I had to add oxymorphone,” Dr. Kwong says. When clinicians request testing for a drug that’s not on his menus—which happens occasionally—“I’ll send it out.”

Stacy Melanson, MD, PhD, associate director of clinical laboratories and co-director of chemistry at Brigham and Women’s Hospital, Boston, says she and her clinicians re-evaluate the testing menu roughly once a year. “Maybe there are newer drugs they want to add, or they want to take away things that aren’t as clinically useful anymore.”

Thanks to the current opioid crisis, clinicians also ask for help with identifying designer drugs—not that clinical laboratories can keep up with evolving substances. “They don’t have the time or resources to develop all these new designer opiate assays,” Dr. Melanson says.

At Brigham and Women’s, the lab will send samples to a reference laboratory in cases that fit a designer drug profile. “The clinicians will give us the clinical picture and say, ‘We think it’s X drug, or it seems to fit that pattern. Can you help us send it out to see if our clinical suspicion is correct?’” Dr. Melanson says.

Most of her clinical colleagues are pain management experts. About 90 percent of their testing is ordered by the pain management group; the other 10 percent comes from primary care physicians.

Even with that high level of expertise, says Dr. Melanson, the lab is still asked to provide fairly detailed interpretations. “They know the drugs they’re prescribing, but they’re not familiar with what the pattern should look like in the urine,” she says, noting that her lab tests not only for the parent compound but also the metabolites. “And they do not understand what are the appropriate metabolites, and at what concentration or ratio.”

She cites a relatively simple example of a patient who is prescribed morphine. It’s reasonable to see hydromorphone in the sample, she says. “But that concentration should be less than five percent of the total morphine, or it’s suggestive that the patient took hydromorphone on top of taking their morphine.”

Dr. Melanson

For pain management testing, results are automatically confirmed, says Dr. Melanson. But since that requires a longer turnaround time (roughly four or five days), physicians will sometimes call with questions about a screening result, before the confirmation is complete. “They may follow up and say, ‘The patient says they didn’t take

cocaine, yet I see a positive screen.' So we run through the scenarios with them: what drugs may cause a false-positive result, or how the assay works, what the molecules are, what the antibody binds to. We go through the limitations." Clinicians also ask about sample adulteration, she says, in cases where patients might be trying to simulate compliance.

Many of the questions Dr. Krasowski fields have to do with opiates, he says. "The metabolism of opiates is complicated, and every physician in family medicine or emergency medicine can't be expected to know the subtleties of toxicology testing and interpretation." That's why it's appropriate, he says, for pathologists and clinical laboratory scientists to be proactive in educating clinicians in toxicology testing.

Beyond test menus, clinicians have two primary areas of concern, in Dr. Kwong's experience. "They call me for two reasons," he says. One is a lack of understanding of drug metabolism and pathways, while the other involves unrealistic expectations of what an assay result can tell them.

If a clinician calls Dr. Kwong after a patient tests positive for an opiate on an immunoassay test, for example, "That means the physician is facing a decision." Such decisions can range from keeping a closer watch to discontinuing opioid therapy or dismissing a patient from the treatment program.

He also notes that in this arena, "providers" encompass more than clinicians, including drug counselors, who may lack scientific education in drug metabolism and testing technology. "It's important for the laboratory to educate them, particularly on the limitations of drug tests specific to the ones they provide," he says.

The capabilities and limitations of immunoassays are fairly straightforward, Dr. Kwong says.

Obviously, they're qualitative—but that point can be misunderstood by those outside the laboratory. He points to the opiates assay, with a cutoff of 300 ng/mL of morphine: 300 ng/mL is positive, but so is 30,000 ng/mL. Likewise, 299 ng/mL is negative, as is 0 ng/mL. "So a negative does not mean that the specimen is devoid of drug."

A positive result can be a true positive or a false-positive. The amphetamines assay picks up bupropion, for example, and the opiates assay can detect ofloxacin, an antibiotic. Only a confirmation test can tell if the result is a true positive or a false-positive.

Assay immunoreactivity for a drug determines the drug detection limit, Dr. Kwong continues. Class assays have varying reactivities to members of the class—a drug that has lower immunoreactivity will have a higher detection limit.

In his lab, morphine is the calibrator (300 ng/mL) for the opiates assay. Codeine is more reactive and can give a positive result at a lower detection limit of 150 ng/mL. Hydrocodone is less reactive than morphine and has to be present in concentrations greater than 650 ng/mL to trigger a positive result at the 300 ng/mL cutoff. It would take more than 10,000 ng of oxycodone and close to 40,000 (37,000) ng/mL of oxymorphone to give a positive result. "Therefore, the opiates assay in my laboratory cannot be used to monitor patients on oxycodone or oxymorphone." Other FDA-cleared opiates assays, however, have different relative cross-reactivities for the nontarget drugs. Consequently, the same urine can test positive or negative, depending on where the testing is done.

Some immunoassays are cleared by the FDA for two cutoffs, he notes. Choosing the lower cutoff will increase the detection rate. "Another reason for not using the higher cutoff is that. . .you will miss the detection of some drugs because they have lower reactivity." Using the 2,000 ng/mL instead of 300 ng/mL cutoff for the opiates assay, for instance, will miss more hydrocodone and hydromorphone. Similarly, for the cannabinoids, the low cutoff of 20 ng/mL may present a problem, because this is too close to the typical confirmation cutoff of 15 ng/mL of 11-nor-9-carboxy-Δ9-tetrahydro-cannabinol.

Each class assay has its own considerations.

The amphetamines are a specific class of drugs sharing a common phenylethylamine structure. Amphetamine and methamphetamine are the target drugs of the amphetamines assay. “They are very potent central nervous system stimulants,” Dr. Kwong says.

The amphetamines immunoassays target the *d*-methamphetamine and *d*-amphetamine and have varying ability to detect the *l*-isomers. Of greater concern, he says, is that different assays have different abilities to detect MDMA/MDA and the sympathomimetic amines. “Thus, a urine containing MDMA or MDA may test negative depending on which amphetamines assay is used. So you need to check your package insert.

“Many false-positives have been reported for the amphetamines assay,” he continues. “A common one is bupropion, or Wellbutrin, a quite commonly prescribed drug. Of course, a confirmation test will eliminate the false-positive.”

What about patients on methamphetamine- or amphetamine-containing medications? They will test positive by both the screen and the confirmation tests. “And when you take it to confirmation, it will show methamphetamine and/or amphetamine. So they are analytical true positives. But it is a clinical false-positive,” Dr. Kwong cautions, “in the context of suspected illicit amphetamine or methamphetamine drug use.

“So we have to know the medications that contain methamphetamine or amphetamine for proper interpretation,” he continues. Such substances include Adderall and Dexedrine (*d*-amphetamine or *d*, l-amphetamine), Desoxyn (*d*-methamphetamine), and Vicks inhaler (*l*-methamphetamine). Other substances are known to metabolize to methamphetamine (benzphetamine) or to amphetamine (selegiline and clobenzorex).

The various benzodiazepines immunoassays exhibit cross-reactivities for the different drugs as well. The relative cross-reactivity of benzodiazepine varies between and across assay manufacturers. Among five different makers, the cross-reactivity of alprazolam ranges from 67 percent to 308 percent; within the range of one manufacturer, cross-reactivity varied from that aforementioned 308 percent to nine percent (for 7-aminoclonazepam).

Many of the benzodiazepines immunoassays target either oxazepam or nordiazepam. As a result, they may do a poor job of detecting drugs that are not metabolized to either one. Commonly prescribed benzodiazepines, such as alprazolam, clonazepam, and lorazepam, may not be well detected, depending on the assay; newer drugs for insomnia, including Ambien and Lunesta, are not detected by current assays.

All FDA-cleared opiates immunoassays target morphine, with varying reactivities with the semi-synthetic opiates, such as hydromorphone, hydrocodone, dihydrocodeine, oxycodone, and oxymorphone. And, warns Dr. Kwong, false-negatives are possible with these drugs after pain-control doses are administered.

In his own lab, he says, “The opiates assay I use has hydromorphone that has 20 percent the reactivity of morphine, which means 1,500 ng/mL of hydromorphone is equivalent to 300 ng/mL of morphine in terms of reactivity. Thus, a patient on low-dose hydromorphone or hydrocodone—for example, 10 mg/day—may have urine drug concentration that is not high enough to give a positive result.”

Dr. Kwong says laboratories must be careful about interpreting cross-reactivities. He cited, as an example, a buprenorphine immunoassay with a 5 ng/mL cutoff, with a claimed 0.01 percent cross-reactivity with morphine. “In other words, the assay is 99.99 percent specific for buprenorphine when it comes to morphine.

“This looks fantastic,” he says.

As it turns out, however, 0.01 percent relative reactivity for morphine is insufficient, because morphine can reach a very high concentration: 50,000 ng/mL of morphine is not uncommon among patients on moderate doses of morphine, Dr. Kwong says, and 0.01 percent of 50,000 ng/mL is 5 ng/mL, which is the cutoff of the assay. In other words, 50,000 ng/mL of morphine will give a false-positive. And this same scenario isn’t unusual with common concentrations of other substances, such as codeine, dihydrocodeine, and hydrocodone.

As compelling as the technical challenges are, Dr. Melanson cites a particularly low-tech aspect to the lab's role in pain management testing.
"We're clinical consultants," she says. "We need to develop relationships with providers." There's plenty of work to be done on creating best practices for reaching out, she acknowledges. "We have a good relationship with our colleagues, but I think others may be struggling with that."

Education can be particularly tricky—and especially important—when it comes to "providers who think they know everything, but they actually don't," Dr. Melanson adds with a laugh.

Even within the laboratory, says Dr. Krasowski, "there are not many who understand the interpretation in great detail." Thus the importance of building relationships with clinicians to educate them and so they'll know whom to contact when questions come up.

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Next month: mass spectrometry and oral fluid testing

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Dr. Melanson urges her laboratory colleagues to simply start a dialogue. "Let them know that you're there when they have questions. Let them know the tests have limitations, so when they're taking care of the patient, they understand false-positive. If they're withholding a prescription renewal based on a false-positive, and the patient is not being medicated properly, that's not the best patient care."
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