DIY or Survey? Identifying interfering substances

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October 2017—The interfering substance: Whether it's in-laws on your doorstep or lipemia in your specimen, it has to be addressed. Ask Michelle K. Zimmerman, MD.

These days, Dr. Zimmerman uses the CAP Interfering Substance Survey to detect the presence of hemolysis, lipemia, and icterus in clinical chemistry samples at Indiana University School of Medicine, where she is an assistant professor of pathology and laboratory medicine. But before her laboratory started using the Survey, how did it handle those interferences?

"I think we pretended they weren't there," she quips, then adds: "The machine still gave us hemolysis, icterus, and lipemia numbers, and we still appended comments about them [to laboratory reports]. But now we have better proof."

Dr. Zimmerman's laboratory is one of many subscribers to the CAP Survey, which helps determine the susceptibility of individual analytical methods to the commonly encountered interferents hemolysis, lipemia, and icterus. The Survey, which has been around for several years, now features improved precision for lipemia. That's just one benefit.

"I run into situations where phlebotomy keeps trying to draw a patient who's a difficult stick, or for some other reason we can't get a sample that has no hemolysis in it," says Lauren Pearson, DO, MPH, a resident in pathology and laboratory medicine at the University of Vermont Medical Center and vice chair of the CAP Instrumentation Committee. "In that type of situation, it may still be important for the clinical team to have the potassium level, for example. So it's nice to be able to counsel them: 'Here's how much we think the result is affected by the hemolysis.'"

Of course, laboratories can examine the susceptibility of their tests to interferents by also using patient samples known to have high concentrations of, say, bilirubin or hemoglobin and to run a paired difference study with those samples.

"We're giving labs information that would be more labor intensive to obtain on their own," she says. "For example, if a lab designs its own experiment to examine interferences, it has to replicate testing on spiked samples to get information about its assay precision. In addition, the lab would have to perform its own statistical analysis to get an idea of the magnitude of the effects of the particular interfering substance on the patient test results." In the evaluation package for subscribers, the laboratory is provided with a mathematical equation and a graphical representation of exactly how much that interfering substance affected the accuracy of the result.

For 2018, the Survey price is $562 for 23 analytes. "It may be cheaper to spike an appropriate matrix with a patient sample that's known to have a high level of interferent," Dr. Pearson says. "But because you're just taking samples you already have, there are two issues. No. 1, you don't know if there could be more than one interferent in that sample. No. 2, if you choose to do your own in-house experiment, you've got to have a tech who's going to design the experiment, who's going to do the manual work to set up samples and then run the test, and then on the other end, do the analysis. Tech time is really expensive."

Dr. Pearson

With the Survey, she continues, “the samples show up at the lab and it is less labor intensive to prepare and run them. And then there isn’t a lot of technical expertise needed to interpret the results because you get a nicely generated report with both tables and graphs explaining what your results are. So it’s a convenience thing, but also, if you calculate what you would have to pay a tech to do that, the expense of subscribing to the Survey is not as great as some labs perceive.”

Then, too, the Survey can help laboratories satisfy CAP Laboratory Accreditation Program requirements COM.40450 and COM.40500, which state, respectively: “For modified FDA-cleared/approved tests or laboratory-developed tests (LDTs), the results of each validation study include a sufficient number of samples to establish the test’s analytical specificity” and “The laboratory understands the analytical interferences for each test, and has an appropriate plan of action when they are present.”

The Survey differs in some ways from a standard proficiency test Survey, which entails three mailings a year. “This is a service-based product,” explains CAP senior biostatistician Rhona Souers. “So at the beginning of the year, if a customer orders the product, they receive the kit and they can submit it at any time.” For example, laboratories undergoing instrumentation changes can submit their results after the new instrumentation is implemented, and laboratories that need to run an interference study for internal testing can submit their results toward the end of the year.

Once the CAP receives the results, they are typically processed within two weeks. “If a laboratory has additional material left over, if there are some results we need to reprocess, we would generate a revision for a specific analyte,” Souers says. Peer group summary statistics are provided periodically so a laboratory can compare its results to those of other laboratories using the same instruments. “Let’s say you’re detecting bilirubin interference at 20 mg/dL, but you see that 80 percent of your peer group isn’t detecting any interference. That would be useful information you may want to investigate,” Souers says.

Souers

Dr. Zimmerman, a member of the CAP Instrumentation Committee, says the Survey overall does “a pretty good job,” though the higher values of lipemia hadn’t been assessed as well as she would have liked.

In the past, the Survey did yield some imprecise evaluations for lipemia for certain assays, Dr. Pearson says, but that is no longer an issue. “It hasn’t been a perfect lipemia product, but the manufacturers we work with have been helping us to resolve these things as they come up. And the CAP staff is constantly looking at the data coming back from these Surveys to make sure we’re really proactive in identifying some of these issues, instead of reactive.”

In Dr. Zimmerman’s laboratory, the Survey is used not only in its intended manner but also off-label, she says. “It’s kind of crude, but you can use the vials and spike them with the analyte of interest and use that too.” She and colleagues used it to help them develop their vitamin D test.

“I hadn’t even thought about using the Survey for that purpose,” Dr. Pearson says, “but it makes sense, because with our Survey material, we reliably know what the concentration of the interferent is in a particular vial, which could enhance the quality of any type of validation study.”

The Survey's creators and users would like to change a few things about the Survey, mostly pertaining to its scope. "One of its shortcomings is that it's really only for the chemistries," Dr. Zimmerman points out. "There's one immunoassay that's included, but other immunoassays are not included, and drugs are not included. I guess we could just spike various drugs into the vials we get already, but then we don't get the graphs and all that."

Dr. Pearson agrees that laboratories would find it valuable if the Survey were able to identify additional substances. "If we were able to manufacture a product that would let laboratories test for a less prevalent interferent, that would be of huge value," she says. "We do have ideas for how we can extend this particular Survey to other areas within the lab, such as coagulation. We're learning that the methodology for many of the automated coagulation tests is susceptible to some of these common interferents, such as hemoglobin. So we would like to eventually be able to widen the net."
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