

Special Report: The Time Has Come for Automation in Bioprocessing

by Cheryl Scott, with Lorna D. McLeod

This interview didn't make it into the printed report because of space constraints, so we're delighted to offer it here on BPI Extra.

CASE IN POINT: A VENDOR GETS TOGETHER WITH USERS AND THE FDA

In November 2009, Caliper Life Sciences, Inc. was invited to present a training session for about 75 reviewers from the FDA. In December, BPI contributing editor Lorna McLeod spoke with Caliper's CEO Kevin Hrusovsky about the new technology.

BPI: How did the FDA training session go?

Hrusovsky: It was standing room only attendance. We described the role that our new LabChip GX product can play in supporting QbD and DoE testing for FDA submissions and for quality control of production in biologicals, antibodies, and vaccines. It was an opportunity to showcase how this technology is enabling what we think the FDA is interested in achieving. They have a pilot program for biological submissions in the future to actually conform to the QbD standards. That requires a lot of testing, and our technology enables high-throughput, cost-efficient testing with very precise answers.

We had three of our top customers present on our behalf. I kicked it off, and then we had a technical orientation from one of our top scientists. Then we had Amgen, Pfizer, and Biogen Idec actually present their case for how effective the GX product is in enabling high-throughput protein characterizations.

BPI: Do any of those companies use this technology for release assays or in-line quality control?

Hrusovsky: Biogen just began to do that, even though to date it's been primarily used upstream. Just like another product line we had about 20 years ago for automated dissolution and tablet uniformity testing with small-molecule drugs, it started out in the formulation laboratories. After about three years of work, the assays found their way into QC labs, and in the end, 90% of our sales

were actually to QC production labs. We think this new technology will go a similar route with biologicals and vaccines.

The view of the FDA reviewers was, "Hey, could this actually end up even further evolving to become an online test, so you could actually be taking samples directly from the reactor and getting immediate feedback to further optimize processes?"

It wasn't something we'd thought about, but we do think we've developed this technology to be what we call "near line." It's a laboratory microfluidic chip that goes into a benchtop instrument, so we think it could be done at-line.

You know, if the FDA really wants quality by design (QbD) control in place for biologicals, then it's natural to expect that the machine and the instrument enabling those submissions would offer assays that actually run in QC labs.

BPI: Are the majority of people using the chip how you anticipated?

Hrusovsky: Yes. Most reports have been with biologicals and proteins, each month we're learning about new ways scientists feel this can play a role. We're getting feedback saying, "Can you add some additional assays?" And we do. We've found several key installations around vaccines. Our technologies are playing a role in debottlenecking vaccine production by getting better control of processes through experimental design.

I was interested to read Glaxo's announcement that several doctors in Canada advised not using a batch of swine flu vaccine. They were saying it increased the rate of anaphylaxis. I'm trying to have my scientists assess whether our technology could have revealed this type of quality control challenge ahead of time. In the past few hours, we're beginning to learn that we may play a role. So it's not just getting

the supply, but it's getting the supply of very pristine, high-quality material.

BPI: So most people are using this on the research side at this point. What are the barriers to its use in the manufacturing arena?

Hrusovsky: As the new platform is implemented, it creates a data swell that ultimately will help everyone see the role it should be playing in QC labs. So it's probably just a matter of people getting more comfortable with the technology.

BPI: Are there legacy issues? Is this something users can plug into an ongoing process, or is there going to be a lot of reconfiguring required?

Hrusovsky: I don't think there's going to be much reconfiguring. The test itself is just taking a sample from a microplate rather than running a capillary electrophoresis gel. The curves are very pristine and reproducible. So it's really become an analytical tool.

BPI: Is it something that can integrate into a system somebody's already using?

Hrusovsky: Yes. It's compliant with both GLPs and GMPs, and we've got very advanced software to enable those linkages.

One thing we're seeing more played out in Europe — but it's definitely becoming something in the United States too — is the elimination of hazardous waste. Today's technologies require ethidium bromide, acrylamide, and so on. So we're reducing what's required for these gels because ours is just — you can barely see it, how much gel we're using. It's a 100-fold reduction in hazardous waste. I think that's going to continue to get more attention. Particularly in high-throughput testing, that waste level would be so prohibitive that you really couldn't do it with older technologies.