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Originally Published IVDT April 2009

IN PERSON: ONLINE EXPANDED VERSION

Nonclinical IVDs: Growing interest in a growing field

Some IVD companies are venturing into the very busy world of agricultural and nonclinical diagnostics.

Interview by Richard Park

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Manufacturers of human IVD technologies have been contributing their skills and knowledge more and more to the nonclinical and agricultural diagnostic markets. Turning their attention to plant and animal testing can result in big rewards for these companies, but making this transition is not without its challenges.

To learn more about why IVD manufacturers are making the switch from human diagnostics and testing to agricultural and other nonclinical diagnostics, *IVD Technology* editor Richard Park spoke with Rocky Ganske, president and CEO of Axela Inc. (Toronto). In this interview, Ganske reflects on what 25 years in clinical diagnostics has taught him and discusses the main differences between his former field and the world of plant and animal diagnostics. He also offers his opinion on why life sciences companies are looking to nonclinical diagnostics and what the future holds for them.

IVD Technology: **How did Axela first get involved in the area of nonclinical diagnostics and in developing technologies for the agricultural testing market?**

Rocky Ganske: Axela sells to the $20-billion life sciences market with its current platform, focusing first on protein-research applications, and enabling and capturing applications for downstream personalized medicine and human diagnostics.

Our technology allows us to work directly in a variety of sample types that are difficult for other technologies to detect pathogens in without some additional sample preparation.

So that led to people who were doing BSE (mad cow)–type testing asking if we could do tests for protein directly in matrices like milk or brain homogenate, and people asking for testing in plant extracts and things like that because other technologies don't have that capacity.

We came to realize that there was a need for this technology, and as much as we saw the need on the human diagnostic side, there was clearly a need outside of that in agricultural testing as well. That led to more experiments and more collaboration to the point that we have now formed a separate division to focus on agricultural applications.

So this transition has been very interesting because Axela, no different than most diagnostic companies, started in the area of human health. But the markets and the demand for tools and technologies for the agricultural space and in the major areas of animal health, plant and agricultural, biotechnology, and food safety have all grown recently. And that's caused us to take a keen interest in the area.

What exactly do you mean by agricultural and agricultural testing? On what specific areas within those broad terms are you specifically working and focusing?

When we break those terms down, we first see a large direct application of the technology in animal health. That includes both animals in the food supply and companion animals. Those diagnostic applications are relatively similar to their human-diagnostic equivalent.

People working in plant agriculture have been involved in genetics much longer than those involved in human genetics.

They are also now focusing much more in the area of protein analysis—in trying to make sure that the protein contents are there in the feed and in milk products, but also in the development of plants that actually have higher levels of protein output.

Specifically in the area of modifications, most of that pertains to modification of plants and seeds to withstand the climate changes that we're seeing and to feed the world's hungry. Those modifications need to be done.

And we see ourselves playing a role in understanding and helping those people doing that development to understand the output of that mutation work as far as the plant's ability to produce more protein is concerned.

As for food safety and the environment, I think the issue in everyone's mind today is the tainted peanut products—but that is no different than previous food safety issues, whether the contamination occurs in supplies or in any of our plants.

So those are the four areas that we see. There is also waste management and screening of the water supply. We need to have in-process mechanisms that allow us to constantly monitor water and ensure the safety of food and food supply products.

Addressing Demand

Who, specifically, has been asking Axela about its technologies and the possibilities of applying them to agricultural testing?

The University of Research at Creighton University (Omaha, NE) was focusing on some work looking at prions associated with brain wasting. And of course they were looking at things similar to BSE.

We were doing some work in whole brain tissue homogenate to try to find those proteins that cause this problem. And so we worked with Creighton in developing an assay that they could use, enabling them to evaluate the samples that they had.

The folks in the sea groups and agricultural groups, I can't disclose those. But they're groups in the top four companies of those areas. In the area of milk, we were actually approached by some companies that are working out of New Zealand. In New Zealand they have to be very careful about screening for antibiotics that make their way into milk products, and our system's ability to actually detect these antibodies in milk directly was of interest to them.

There is some other work we're doing right now with some of the bird-flu pathogens.

And as you get to some of the viral implications, we're actually able to do some of the direct viral detection. We're doing work with Health Canada right now in early detection of these viruses.

Has Axela had any contact or collaborations with any government agencies there in Canada or here in the United States?

We have definitely had conversations with folks involved with USDA, but we don't do any current work with them. There is work in Manitoba, Canada, that we're doing. We have projects under way with several large veterinary research institutes, both academic and government in Canada. In the United States we have ongoing collaborations in biothreat detection programs with existing installations. University of Guelph in Canada has a very large veterinary program, as does the University of Saskatchewan. There's significant activity around crop improvements as well. While our efforts have been limited to date in agriculture, there are significant collaboration opportunities across academia, government, and industry.

Please provide a little perspective on the history of Axela's involvement in the agricultural testing market. It seems the company's activities are not limited to North America but are in fact global in nature.

That's correct. The need has become very clear on a global basis. Over the last three to four years we have had a variety of involvement with different projects and the customers coming back to us saying they have value that they weren't able to get otherwise. Their inquiries are what caused us to make the business decision to focus on agriculture.

So there was enough of a demand and a need to create a new division within Axela. Did this demand also prompt the collaboration with BioMark?

That is correct. BioMark's group is leading some identification of partners for us.

We brought on Butch Mercer from BioMark because of his extensive background in the agricultural space. He has been associated with each of these agricultural segments for more than 25 years and understands the importance of testing and diagnostic technologies like ours for plant, animal, and environmental applications.

Having that domain expertise is important for us to make sure that not only do we provide the right product to our customers, but that we also get the right collaborations with the right people.

One of the key differences is that we had worked with mammalian sales for human work. Plant cells have nuances to them, and the domain expertise initially was not there.

By working directly with Butch and his contacts in the industry, it gives us immediate access to people who have domain expertise in areas that Axela does not. We will build that and build around that, and fill in where needed as the demand for these products grows.

Making the Transition

Are the agricultural testing technologies on which Axela is working adopted from other previously developed in-house technologies? And, if so, how did Axela adopt the technologies to be used for agricultural testing purposes?

For all IVD companies that have made this move into agricultural testing, the primary challenge is in the area of plants.

When you're moving from humans to animals, the cell biology is similar enough that your systems are readily deployable and can be converted without too much change.

But in the area of plants, there are obviously some different chemistries and reagents that need to be developed to handle the proteins in these plants, keep them alive, and be able to do the detection of these in a very sensitive fashion.

We did not have to manipulate or change the core detection technology. We were actually able to leverage the attributes of the systems, to see things in complex media, so a lot of the advantages that we see on the human side translated rather nicely for us into the agricultural testing side.

On the animal side, there are some quite large markets in that space, both in the area of equine and porcine and in the companion animal. Some of those center on different proteins and testing for individuals who are heavily involved in horse racing and breeding programs.

And I believe now that the spending on companion-animal diagnostics as an out-of-pocket expense has superseded the out-of-pocket spending that people in North America provide for their children. So it's a huge out-of-pocket market. It's a cash-pay market. Because it's an attractive market, you see large diagnostic companies like Bayer Animal Health move some of its testing platforms that it would use for diagnostics into animal health testing. These are attractive enough markets that large diagnostic companies are interested.

Additionally, at the same time pharmaceutical companies are generating human vaccines, the vaccine business for companion animals is also very large. Companies that are heavily involved in human vaccines are also involved in animal vaccines.

What is the process involved in developing agricultural diagnostics? Does an IVD company like yours identify specific pathogens and develop completely new technologies for those agents? Or, would it be more inclined to take its existing products and adopt current technologies that are available to detect those specific pathogens for agricultural purposes?

There are three things that you need to achieve in agricultural testing: speed, accuracy, and flexibility. It is very similar to that of a human diagnostics model, where we have certain things we do in central laboratories and clinics and certain things that are done in a doctor's office. And the challenge is making sure that those data are the same. The same issue presents itself in agricultural testing.

When you talk about speed of testing on the agricultural side, you need to get results fast—especially in a case where problems arise. You need to be able to identify them quickly.

So you have situations where you're dealing with large herds or flocks or hectares of ground that have been planted. And you need to ascertain what your issues are on a global scale, but then you also need to be able to provide individual analysis.

For instance, with mad cow disease, you might hear about entire herds being wiped out on purpose to keep the spread of the disease down. So you need to be able to screen a herd quickly. But you also need to be able to screen individual animals so that you do not waste animals unnecessarily.

At the same time, when you're talking about food and plant stock, you're dealing with a mixed batch. You've got samples coming into feed lots and grain elevators from multiple locations, so when you find a contaminant you need a technology that can look at these in bulk, with the accuracy and speed to move a lot of samples through. But then you also need a testing format to take to the animal or to the specific on-site location and get the same repeatable information. So the flexibility of that format and testing is something that becomes very important. It needs to be usable in a high-throughput application as well as in a point-of-use application.

As a matter of fact, I believe that Axela may have the only technology I know of that can operate in this mutisetting environment, and I've been doing human diagnostic and life science for about 25 years. I believe we have the only system that operates on the same format at the point of care as it does in a central lab.

And we can leverage that to be used in this agricultural area.

It seems that in agricultural diagnostics—and nonclinical diagnostics especially—these technologies have to be used in nontraditional locations, such as in a field, or on a farm, or—in the case of biodefense—in an urban environment. With that in mind, would you say ruggedness is another criterion for this type of testing?

Yes. You do have to be able to operate in multiple settings because the best and fastest way to administer these tests is in close proximity to the food supply or animals, because then you're not dealing with the transportation of mixed samples.

And that does mean that whatever the detection technology is, you need to think through the robustness of the detection—especially in systems for which keeping the environmental influence out of the sample is important.

And the products as we've developed them are all in a closed consumable package that allows us to test in nearly all of those situations.

For field-based testing, you have to take a lot into consideration as well. While we haven't developed a handheld application of the technology yet, we've given thought to doing that in the future. You're going to want something that can withstand the dirt of the environment and that provides the ease of use that's required by the individual who would be doing that testing, because you're not talking about clinicians at the control panel. You're talking about the people that are actually working with the food supply or the crops.

How do the characteristics of a successful agricultural diagnostic differ according to the agents it is designed to detect? Can one diagnostic be used to detect multiple agents?

The major pathogens for which you would test are already available in a testing format known as the traditional ELISA. The key here, though, is that one format doesn't give you the speed, accuracy, and flexibility that I mentioned earlier. So you don't have to develop the antibodies or antigens from scratch, nor do you need to define what those antigens are. You simply need to adapt them to a technology and put them into a format that makes them more useful. Our efforts and our success will be measured by the partners that we bring on and, using their domain expertise, how we deliver a product that is best suited for that application. In the case of companion animals, for example, activists are concerned that veterinarians are overvaccinating pets and that the over-vaccination is causing liver damage and other problems. But we have the ability to look at the level of titer from these vaccinations and actually determine whether a dog, for instance, needs a full booster or a partial, or no vaccination at that time.

Please give us a little perspective based on your previous experience in the clinical side of agricultural diagnostics, then becoming more involved in the nonclinical side: What are your overall views and impressions of the nonclinical diagnostics market?

I've been working in the life science diagnostic space now for over 25 years.

My interest first came—as we, the industry, continue to be challenged in human diagnostics—from needing the sensitivity and the accuracy that central lab testing delivers.

The technologies have advanced the ability to provide high sensitivity and high accuracy in a point-of-care setting or near the patient. That gap now has decreased between those technologies.

Now there are more technologies that have the capability of delivering clinical lab results in a point-of-care setting. And Axela clearly has tried to optimize that as much as we can in work that we're doing with our user-configurable multiplex detection platform. This allows users to test for multiple proteins or pathogens in a single test. This also allows for rapid reconfiguration of the tests in the field to combat any rapidly changing requirements.

Sometimes you can only do the testing at the point of care. Work that we're doing at University of Pittsburgh Children's Hospital is a good example of that—where the central lab test is in an ELISA looking at silent brain injury markers, evaluating Shaken Baby syndrome in small children. It's a case in which the central labs have very high accuracy, but you can't get enough blood from a child to be able to render that test useful. But with the Axela technology, we can work with a very small sample at the patient's location, and we get that determination with central-lab quality.

When you take that relationship and you try to think about it relative to what needs to be done on the agricultural side, you have the same thing again: the central-testing model that is used today across most agricultural testing, where samples go to a central testing lab and data come out. It's very symbolic of what we used to see in nearly all human diagnostic activities. Now what you're seeing is this need to bring the testing closer to where it is needed, whether that's in animals or crops or something else. Some of our point-of-care diagnostic technologies translate to agricultural testing, and other technologies just plain don't. There is still a limited amount of technology that can be deployed in a point-of-testing mode in agriculture.

I think we are seeing that the work being done in human diagnostics, animal health and animal diagnostics, food supply, and the environment are becoming very interrelated. The gaps are shrinking.

We're seeing what happens in our food supply show up in human health. We are seeing it in forms of cancers. We're seeing it in a transfer of viruses from animals to humans.

So that gap is definitely getting smaller. And I think that will drive an even more concerted effort between environmental diagnostics and human diagnostics.

When I was at Becton Dickinson we actually took a device that was used for cell counting and measuring blood parameters in humans and licensed that technology to IDEXX, which is one of the largest animal health companies.

IDEXX still sells that product today; even though the licensing occurred some 15 years ago, I think you'll see more of that type of transition.

Meeting Challenges

What are the primary challenges involved in developing agricultural diagnostics—in plant and food testing, specifically—and how are those challenges overcome?

With animals, as with humans, the matrix you're working with is blood, serum, urine, or stool. As soon as you move to cells for plants, you're looking at taking a piece of a leaf and grinding that up, then administering some chemistries to it to release the protein from that leaf.

This is a very good example of why we've reached out to get domain expertise, because my direct experience has all been in human diagnostics, with some veterinary diagnostics. But when it comes to plants, there is other domain expertise we need, and that's why we've looked to people like Butch Mercer.

With the original work that we had done with some clients in plants, it became obvious to us that there were things about the way cells bind to the testing device—and methods for keeping those cells alive and active to get accurate readings—that are different.

You don't see Bayer, for example, that does a good job in animal health, doing as much work in crop sciences because they're two different sets of domain expertise. For us, it's an area where we're looking to build out and gain more domain expertise, or literally license off, or make it available to someone who has that domain expertise.

You mentioned BioMark. What other individuals and organizations has Axela sought out for this experience and expertise?

We have actually reached out to some of the universities. There are very large veterinary health groups and plant agricultural groups here in Canada that we have reached out to. We have had conversations with groups within the government that need to make sure the food supply for our military is clean and free of any viruses or contaminants. Some of those groups we've gotten involved with right away, and others we're actually still in discussions with.

Looking Forward

Which agents are Axela and other IVD companies still working on and developing agricultural diagnostics for, and what is the status of those efforts?

When we talk about animal health, as I said, there's clearly more work being done to better figure out how to more effectively judge the health of our animals and vaccinate them more appropriately.

There is a lot of work going on to find ways to better ensure safety of our water supply—looking for contaminants, biothreat agents, things of this nature. There is some work in applications specifically that Axela hopes to exploit going forward.

We have some technology that we licensed from Kimberly-Clark that may allow us to do a better job of continuously monitoring water supply. It's an area that we're looking to further develop with a partner.

In the areas of food safety, clearly some of the recent activities around viral contamination are areas where everyone's trying to find better ways to detect those viruses in a faster way. There's a concerted effort on the part of Axela to move some of those efforts forward because they have human health implications as well as food safety implications.

There is a lot of government-driven food safety and environmental and waste management testing that's going on to better assure that water supplies are clean, as well as all of our food safety activities in the way of rapid bacterial detection. Axela is doing a fair amount of work on direct bacterial detection with our platform as well. And some of that is proving to have some early success. The more rapidly we can go through bacterial detection without having to wait for cultures to grow, the better.

What future challenges do you foresee in developing agricultural diagnostics?

There is one issue that may never be resolved in a single sample analysis from an individual source. And that has to do with when the sample is part of a larger population. So when we look at herds or flocks, the analysis is only as good as the sample itself. If the sample doesn't harbor what it is we're looking for, it's going to be missed, or the tainted sample could be diluted by multiple samples that are okay. For instance, think about the way milk is collected. If you've got one contaminated can, it can be diluted if you haven't found a way to do sampling and testing closer to the source of the contamination.

If you've got one cow that is infected that ends up into several hundred pounds of hamburger, eventually it will cause a problem if the pathogen begins to grow in that meat.

But at the point in time that you sample it, it's only as good as the sample that you collect. So smaller sample size, reduced cost, and reagent development will continue to be important threads to addressing this agricultural application.
