**Paul (Host):**

Hello and welcome to the Rapid Microbiology Podcast. And I'm your host Paul Carton. Today's topic is on the development and manufacturing of lateral flow tests that are currently in widespread use around the world to rapidly detect SARS-coV-2 in workplaces, airports, schools, and at home.

Joining me today is Andre Alfaro, who is director of assay development at nanoComposix, a company that provides medical device manufacturers the knowhow and materials to get their lateral flow test to market. Hi, Andre, and thank you for coming on today to share your rapid test expertise.

**Andre:**

It's great to be here, Paul.

**Host:**

Can you tell me, Andre, what services do nanoComposix offer companies looking to develop a lateral flow test?

**Andre:**

Yeah, that's a great question. So really how we like to position ourselves is full service and full spectrum. This goes from early concept design, marker discovery, rapid prototyping, all the way to high-throughput automated manufacturing. We actually function as both a CRO and a CMO. And this is not something you have to jump in at the start of any particular phase. Lots of companies come in at different points.

Some people already have a target biomarker and some early prototyping on ELISA and want to transition that to something more commercially viable like lateral flow, or they have a lateral flow test that they've had some issues with, maybe it's sensitivity or kinetics, and we come in and help overcome those obstacles.

At the end of it, some companies are finished all that. They've done the hard part, the heavy lifting. They've finished development, they've frozen their design, and they're looking for a CMO to manufacture their test at scale, at a reasonable cost. This is where we come in with automation. And we can manufacture up to 25 million tests. So, we can help you pretty much across the board, I like to think.

**Host:**

You're offering some turnkey solutions, and some modular offerings as well. Have you actually had anyone have a test on the market or develop a test that wasn't sensitive and then say, "We need improvement on this." Is that something you've done before?

**Andre:**

Absolutely. And this is for tests that are on the market and we're helping with gen two, that's something we definitely do. There's always a competitive space, whether you're on the agriculture side, the infectious disease side, the vet space, and across the board. There's always going to be a need to be more accurate, more sensitive and that's what we can help with.

And you hit it right on the head, there, there is turnkey solutions to some things. To expedite development, we leverage our experience to develop platforms that suit most people's needs. And then we tailor and customize those processes and tests to suit the specific requirements of individual tests.

We're scientists at our core, so we like novel solutions. We like creating something new, creating new IP for our customers and building something to overcome different obstacles. Whether you want a fast turnkey solution or you want something new, novel, and custom, we can do both.

**Host:**

It is becoming a competitive market so customers are going to seek out those experts who are on cutting edge of development, really.

**Andre:**

Absolutely. I mean, you almost have to have that edge. And if you could have something, some component, and maybe that's our novel gold nano shells that we produce in house, to give you that extra sensitivity. That's really what sets us apart.

**Host:**

In terms of SARS-coV-2, and there's so many tests coming on the market, what can you offer companies wishing to develop their own lateral flow test for SARS-coV-2 in particular?

**Andre:**

Yeah. I mean, that's a great question and really relevant to the world today. There are a lot of antigen tests out there, but there's not a lot of good antigen tests out there. What we bring to the table is experience developing new generation COVID antigen tests that are faster, more sensitive, more accurate. We've done this through, I'm losing count of how many FDA submissions I've done now. We're about up to six, I believe, with three approved tests that we've helped develop using our custom nano materials.

**Host:**

Very good.

**Andre:**

And that's what we do. We bring experience, we're bringing competitive advantage in terms of integrated solutions to not only the manufacturing development, but also the nano material to really provide customers far and away a better test than what was out there before.

**Host:**

Most of the attention is for antigen tests, but there is an awful lot of antibody tests out in the market. Do you have many customers coming, looking for antibody test development?

**Andre:**

Absolutely. This is one that hits close to home. I can go on a long diatribe on this one. I love these tests. We actually developed one of the most sensitive serological tests for neutralizing antibody out there, that we can use as a platform for other people interested. I've done this for other countries like Brazil and India.

The US is tough, the FDA doesn't know what to do with an antibody test just yet. That information, all viable to me, I want to know what my antibody titers are.

I just got my booster the other week, I loved seeing my immune response change. I could see it in five minutes, in my house. It was great. I mean, I have a newborn and I shouldn't admit it but we were curious of seeing if those antibodies were transferring via breast milk to the baby, Hey, I have a test to do that. I think it has a ton of value. Internationally, outside the US, there are methods to get that to market. I think it's a test that people want. For regulatory purposes, it's really hard to do that in the US though.

**Host:**

But they really haven't hit the market like antigen test. But I think it they just haven't been marketed properly. Or I think a lot of people believe that the results you get from that aren't that accurate, considering there's different antibody tests for vaccine effectiveness, and there's also different tests for post-infection.

**Andre:**

Right. And they do two different things. And then that this is why, coming from the science side, I love having this conversation. Because there's a rationale how you design these tests to make a conclusion on it. There's a difference between the Johnson & Johnson vaccine versus something like the Moderna or Pfizer vaccine, right? These RNA vaccines are specific to creating an antibody that blocks a specific protein. And that's what induces neutralization and when you break the virus's ability to infect cells.

Our test tests just for that antibody specific to that protein, that RBD protein that blocks the virus coming in. Or you can have just a generic antibody test, like Johnson & Johnson. So you'll see on our test, it can even tell you what vaccine you've had, based on the results of the test.

**Host:**

There is some other contract manufacturers like yourself providing a similar service. Why would medical device companies come to you to develop and get your knowhow, and choose you over other similar services on the market?

**Andre:**

Yeah. I'd like to think it's my charming personality.

**Host:**

No doubt.

**Andre:**

But no, really it's the science and the capabilities. This is why I'm at this company. It's a lot of fun to work at a company that gives me all the solution and tools, and our customers those solution and tools. So not only, like I said, not only can we develop an assay and we have a team that does that all day, every day, and that's my development teams. But not only can we do that, and not only have we done that for a very long time, but we also have the manufacturing component. So I'm not transferring it to a CMO, I'm transferring it to the other building, 30 feet from me, who does automated manufacturing at scale.

So those handoffs are all built-in, those integrations that are all built-in to make this quicker and faster. And because we have that integration into manufacturing, unlike a lot of other CROs, our business model is predicated on moving customers through development quickly and into manufacturing. That's where we want to go. So I'm not here to elongate or go slow during

development. I'm here to turn as many knobs as I can, as quick as I can, but within our ISO1345 quality system, to move you into the manufacturing.

We leverage our experience. We leverage our capabilities. We leverage the fact that we also manufacture all the nanomaterials and antibodies here. I shouldn't say antibodies here, that's our sister company, Bethel, who it is great to have, I should say, a antibody or custom antibody development and recombinant antibody developer on our team, which is awesome. We have these integrations to get you from A to Z quicker than anyone else.

**Host:**

You mentioned gold particles earlier on, this is an important component of a lateral flow test. Just tell me how important gold particles are, the ones you have for medical devices?

**Andre:**

That's a great segue. My background was in biochemistry, not in organic chemistry like these guys in the other room. But our company, nanoComposix, it really has three pillars. The CRO services, CMO services, and the products side. The products side have been making nanomaterial now for 20 years. These guys are really good at what they do and the innovation and the novel particles that come out of that side is fascinating to me.

Talking about what sets that apart, we have the ability to customize nanoparticles sizes, surfaces, geometries, to meet customer needs, and create new and interesting particles for people.

Now, because of that, we've organically created really sensitive and different nanoparticles for lateral flow. We have the traditional 40 nanometer gold colloids, we have the traditional 80 nanometer gold colloids. But what we have and other people don't have is gold nano shells, which are just phenomenal for lateral flow. These things are designed specifically for lateral flow because of their optical properties.

What we did, and people know there's, there's an advantage to having larger particles, visually you can see larger things better, right?

**Host:**

Makes sense.

**Andre:**

They absorb more light. But the problem is with flow and kinetics with something that big, it's like rolling a Boulder down that strip. Once the gold colloids get too big, it just doesn't function very well. Now what we did was, and it sounds so simple but it was very complicated, what we did was we knew we wanted to reduce the density of those particles and have them flow a little better, but keep that size. So, what we did was we took a silica core, and then shelled that with gold. Because the optical properties, it doesn't mean the whole sphere has to be solid gold colloid, but the shelling will give it that optical properties. These gold nano shells have the benefits of large gold, but the flow characteristics of small, and they work great.

**Host:**

They're just lighter, making them easier to flow and big enough for readers to pick them up?

**Andre:**

Right. I mean, this is why you get this very definitive kind of... I think my color blindness comes out sometimes, I think they look black, but I've been told they're blue green. So that tells you how old I am. It's a very unique, we'll call it green, gray, green, as I'm supposed to. But it is black.

**Host:**

I am color blind also, I understand where you're coming from

**Andre:**

It looks great on the white nitrocellulose. I mean, you really see these, they really stand out. This is why we use COVID as an example of this, we've done a lot of side-by-side testing for whether it was BD or Abbott or any of these companies with OTC tests. We side-by-side the tests we develop with our customer with our nano shells against these, and it's not even close. There's definitely an advantage across the board for whether it's infectious disease in COVID or something else. If you want visual colorimetric detection, you should talk to us and we can help you.

**Host:**

Quality standards for lateral flow tests, especially for COVID, the bar has been raised several times by medical product agencies and health product agencies. Can you help medical device manufacturers achieve the specificity, sensitivity, and limit of detection that is now required for approval in Europe, UK? I'm not sure about the US if they've changed much, but...

**Andre:**

No, the bar is still pretty high here in the US too. The answer is, absolutely. I mean, like I said, we've done this about six times now, going through regulatory bodies, whether that was Health Canada, the FDA, whether it was in Australia or Europe, Brazil, we know what is required and we know how to design these products to get you through that efficiently and quickly.

That's where we help. We don't put our services in a box, like, "Oh, we just develop the strip." No, we will help you ride those EU waves, we'll help you and hold your hand through those conversations. I don't think a week goes by where I don't have some conversation with the FDA reviewer or a regulatory body. I mean, this is my job. I help my customers. This company helps our customers and so we do this.

One of the reasons why we do this so effectively is the quality at which we design and develop products and manufacture products. I don't need to develop it to manufacture it well. And we have a very high standard with our ISO1345 certified quality management system. We just finished an audit. Our yearly audit was two weeks ago, it went great. This is both for development and manufacturing of medical devices. We have the quality and the experience to help.

**Host:**

Now the term, I'm sure you'll agree, lateral flow or rapid tests has been dragged through the mud in the last 18 months since the start of the pandemic. This was due to unsatisfactory diagnostic accuracy. Can you tell me, in your opinion, what was the main reasons these kits performed so badly in real world settings?

**Andre:**

That's been a hot topic for a while. From someone who's very close to all of it, who knows all these companies and the people who develop these tests and all the recalls that I'm seeing, it is not unexpected. Let me start with that, but there's a reason why it's not unexpected. Really the first company, the companies that are getting recalled, these issues that we've seen with these tests and the efficacy on the sensitivity and specificity that we talked about, is because the first tests that got out there were using two things.

They were using sub-par material because there wasn't a lot of antibodies and good affinity reagents that were developed early on. The first gen products were just not very good. They did the job initially. But really, once we started learning how to validate what we had to look for, you quickly

saw the problems with it. This was the root of the problem. The FDA and these regulatory bodies are finally learning how to accurately or how to truly review and approve tests.

Initially, all they needed to do was get something out there because it provided a benefit to the people to have something. We needed something early on, that something wasn't particularly great and we learned that later. But now, the standards have changed. Now, you have to be great. Not only do you have to be great, but you actually have to be able to, and this is something I get from the FDA a lot, it has to provide a substantial benefit in terms of manufacturing scale. They don't want a test that you can only manufacture 1000 of, they want a test that you can manufacture a million of.

And not only that, it used to be 80% sensitivity and specificity. Now it goes through redundant independent validations, those numbers have to be above 90%, or they just put it in a pile with all the other ones. There's a substantial difference now on how the reviews are getting done. But early on, there was no standards. Now there is.

**Host:**

I think also part of the problem was that I think some of the pilot projects where they tested how good these lateral flow tests were, those pilot projects weren't managed properly. Where they were testing someone once and expecting negative results and then that was it. That was how the project was done. And I think now, everyone's starting to realize that if you use a lateral flow test on someone every two days, that's just almost as accurate as your PCR test.

**Andre:**

Right.

**Host:**

And I think that's why they got a bad rap, I think

**Andre:**

Absolutely. The design of the studies was very poor. Mainly because they didn't know how to design them. Now there's very strict rules for OTC and POC clinicals. I mean, we've done it enough times now that I can probably regurgitate all the requirements here, but I will save you and the audience that pleasure.

**Host:**

I'm sure you're available to email and phone, if anyone wants to hear you.

**Andre:**

Of course. I think all my information's on the website for nanoComposix. But I mean, I love talking about this stuff. I have a passion for assay development and what we do. It's a lot of fun to bring people's ideas and products to market.

And I've been doing this now for 17 years. And I'm pretty darn good at it.

**Host:**

Very good. So, in the early days of the pandemic, test kit manufacturers couldn't fulfill orders. And so there was orders sitting on desktops and they just weren't being completed. And this was due to shortages in supplies, materials and reagents that are used in SARS-coV-2 tests. Can you tell me what are nanoComposix manufacturing capabilities and how robust is your supply chain if a similar strain on the supply chain happens again?

**Andre:**

Yeah, that is of particular importance when, as I mentioned before, scale of manufacturing is a requirement for COVID, maybe not so much for other tests. But for COVID, it definitely is when you talk to these regulatory bodies. You don't have manufacturing without supply chain control. Early on, you alluded to the issues that they saw with manufacturing and getting raw materials. That was just a byproduct of the systems that were in place at the time.

There was this crazy influx of material needs and simple things, paper, swabs, tubes. Now these companies had the capacity to manufacture, and now they're actually doing it at scale and meeting the needs. Earlier on though, none of the systems for any of these companies were designed for that kind of production. Thus, you had that big lead times. Nowadays, it's not nearly as grievous as it was back then. It's not I get everything I want in a week, but you plan ahead.

I mean, this is where our material management and manufacturing team really comes to help with that. We set up these supply agreements for our customer. We develop manufacturing plans to account for these lead times, to ensure that we have everything we need ready for our customers. So that's where it's at now is, with proper planning we have the capacity to do all the manufacturing at scale. Like I said, up to 25 million here at nanoComposix, we can do that. We do that with organization, management, and really proper planning.

**Host:**

Is it 25 million per year, I assume?

**Andre:**

Per month.

**Host:**

Per month, per month. Just to be clear on that. Okay.

**Andre:**

Automation a wonderful thing, my friend.

**Host:**

Now viruses mutate by their very nature. The latest Omicron variant, which is spreading already in our communities, and medical device companies need to ensure their kits are variant-proof. Is this part of your development program?

**Andre:**

Absolutely. Our job is to keep up with all of that, the second we find out about a new variant or a new cross-reactive species or interferon that the FDAs requiring for testing, we're on top of it. We do this all the time. We have a BSL-2 onsite to work with infectious diseases. We don't grow them so we don't have a BSL-3, but we can test them in our BSL-2.

What we did is create partnerships with companies that do grow and culture the virus. And then we work with them to secure these new strains immediately. They inactivate them and send it to us. So we can do our TCID50 measurements and LoD measurements with the new virus. We have that system built-in and ready to go.

**Host:**

Saliva based tests for SARS-coV-2 in high demand because they can be self-administered, and they're in high demand because of their non-invasive and user-friendly design. Do you have any experience in developing a saliva-based test?

**Andre:**

Absolutely. Now you're talking to of one of our sweet spots. Being a nanoparticle manufacturer and having novel nano-shells and having the most sensitive colorimetric particles, it was a natural transition into being a big player in the saliva diagnostic space. Because if you're doing saliva and you're choosing a very non-invasive matrix, it's usually because you want it to be simple and at home test. If you're going to do that, you want to avoid costly things like readers. Thus, you're going to move away from fluorescence and into colorimetric readouts.

We've done on quite a few saliva-based tests over the years. This is not that we just developed a strip and not that we just work on normalizing the matrix, which as anyone working with saliva knows is not the easiest thing to do in the world, both with viscosity and pH and all those fun constituents in there that make it a difficult matrix. We help with all that strip design, but we also help with the engineering of that cassette. We help with the selection of whether it's swabs or tubes or these consumable portions. We'll help build that system with you, with the strip and, and provide that experience to do it.

I mean, honestly, the writing's on the wall in terms of empowering people to do surveillance, monitoring, tracking of their health independently. I mean, the insurance companies see the benefit of empowering people to do testing, preventative medicine as they call it. Being able to take tests home, as in OTC, is going to really help people and keep people healthy. Saliva would be a great way to do it. We don't want people having to take blood draws at home if we can avoid it. This is nanoComposix's stance, we want to help you get your test, saliva test, to market in that space.

**Host:**

Sure. And even the lower nasopharyngeal swabs aren't too bad to use.

**Andre:**

The lower ones, yeah. You don't want those brain ticklers.

**Host:**

No, for sure. Now the rapid lateral flow tests have been on the market, as you said before, for in many industries, agricultural, veterinarian and stuff like that. But in the medical device field, for HIV, there's a lateral flow tests on the market that can detect HIV antibodies in 60 seconds. Can this be achieved with SARS-coV-2 antigen tests? And if so, why isn't it being done already?

**Andre:**

The interesting way to put it in a good example, and I mean it really is something like HIV, we've been developing rapid diagnostics for 40 years. And we've had the time to really develop novel solutions to that very question you brought up, "How can I get a high-sensitivity, very rapid test?" It took time to get there. It took time to develop those affinity reagents and that platform to do it.

We've really only been working on COVID now for almost two years. In time, I think it's going to go there. It will almost assuredly have to go there. We want to help customers get there. Those are the interesting projects, if we have those custom affinity reagents, and I love working with antibody companies that are developing these and helping them get a platform out there. I think it will happen. It hasn't happened yet and the reason why is just time, time to develop that material and time to develop that platform. But it will happen. I think that's going to be a very commercially viable test when it's ready.

**Host:**

Okay. Can you give our listeners some peace of mind who may want to get in touch with you to develop a lateral flow test, by telling us what ISO standards your manufacturing site and products are certified to?

**Andre:**

Yeah, of course. It's one thing to develop an assay, it's one thing to develop an assay correctly, as in with all the right design controls to ensure that the safety and reproducibility of the test is there. That's why nanoComposix is proud to be an ISO13485 certified company for both manufacturing and development and medical devices. It provides us the guidelines of developing assays to make them truly what we're claiming they are. So, rest assured that we do things not only fast, but we do it right.

**Host:**

Great. And do you have any final words of wisdom for any company looking to get their tests to market?

**Andre:**

Oh man, how much time do I have? There's definitely a lot of advice.

**Host:**

Okay. Any brief words of wisdom?

**Andre:**

I would say it's never as straightforward as you may think at the start. And what you need to do is talk to the experts in the different spaces, and really understand that landscape first. And create a good plan. The success of a product is, I wouldn't say 100% dependent on it, but there's a correlation between success and proper planning. And that's where we help. And I can definitely, nanoComposix and myself can help with that planning.

And once you have a good plan, once you have that strategy and not just, "Hey, I want this assay to detect this marker at this sensitivity." Go beyond that and think about things from the finish line back to the start of the race. And that's really where I come in. I have an excellent development team who thinks about the micro and making that assay meet the specifications it needs. My job is to think about the macro and why are those specifications what they are? What, what is the intended use population? How does test fare against its competitors? What do we need to do to get there? And I developed the plan from from the finish line backwards. And I have best scientists and chemists in the world working it on from the other end and looking at the micro.

**Host:**

Great.

**Andre:**

So that would be my advice.

**Host:**

Thank you very much, Andre, for coming on today. You're obviously-

**Andre:**

Oh, of course, this is a pleasure.

**Host:**

You're obviously the go-to guy for lateral flow tests. So don't expect much sleep for a while, as I imagine you're going to be quite busy, if not already.

**Andre:**

Sleep is just a dream these days, Paul. I have a three-month-old, so it is all just... I forgot what sleep was, is. Can't even say it straight, that's how tired I am.

**Host:** these lateral flow assays are an important weapon in our arsenal against COVID-19 and are now part of our daily lives and might be for some time to come. And thank you to listener for making the time.