Ep. 4: Onshoring Drug Manufacturing and TRIPS Waiver Part II

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Matt Hittle: Hi, and welcome to the fourth episode of Akin Gump's *OnAir: Health Care* podcast. My name is Matt Hittle, a senior policy advisor here at Akin Gump.

Dr. Mario Ramirez: And I'm Dr. Mario Ramirez, a consultant here with the firm.

Matt Hittle: Mario, this is unprecedented. We are together for the first time ever. I know we're only four episodes in here, but this is really, really neat, actually being across from you on the microphone as opposed to on WebEx.

Dr. Mario Ramirez: This is great, we're doing it live!

Matt Hittle: We're doing it live. Well, we appreciate all the support we've gotten for this podcast. We have a fantastic one for you today. We're talking about intellectual property, we're talking about the medical supply chain, all interrelated issues. To kick us off today, we've got Clete Willems, who is a partner at Akin Gump. Clete, welcome back.

Clete Willems: Thanks. It's good to be here, and I just want to state for the record I'm also in the same room as you. It's a great feeling.

Dr. Mario Ramirez: And we're joined by Sean Feely.

Matt Hittle: Sean is the “guy behind the guy” making it all function, so thanks for being here, Sean.

Sean Feely: Absolutely.

Matt Hittle: Well, Clete, when you were here on the podcast last, we were talking about the TRIPS waiver, which is the waiver of certain intellectual property related to COVID-19 vaccines. For those who need some review, that's the Trade-Related Aspects of Intellectual Property Rights—or TRIPS—waiver. So I think it's fair to characterize your position then that the TRIPS waiver at best is symbolic; it's a gesture meant to engender goodwill. But at worst, it's a precedent for weakening intellectual property protections abroad and providing competitors like China

access to our trade secrets. Now, since we spoke, the administration has indicated support for the waiver. What did the Biden administration do and why?

Clete Willems: Well, that's exactly right. They came out a couple weeks ago and said that they were going to support negotiations at the WTO on a potential TRIPS waiver for vaccines. This was a huge development, and I don't want to understate the fact that they literally reversed 25 years of precedent where the United States had taken the position of the WTO that innovation was not a barrier to the distribution of all kinds of different products, including medicines and vaccines. They reversed that position, and the reason they gave for that was that they thought that this was an extraordinary circumstance that required extraordinary measures and they wanted to do absolutely everything they could to try to get more vaccines to more people around the world. I will say that is a laudable goal. Of course, that's exactly what we do want to do.

But they've actually taken some criticism on both sides, and if I could start with those who have been opposed to the waiver, the position they've taken has essentially been that this won't actually help achieve that goal and that there are other problems in the supply chain. And really, it is the lack of distribution channels and trade barriers and things like that that have been an impediment to getting more vaccines around the world. Those people have argued what you need to do is you need to fund the export of this stuff from the United States and from other countries. You need to stop putting export controls in place, and you need to put money behind it, and that's really going to help solve the problem. So they've taken criticism, as you articulated, and what is the symbolism that it shows? Not that we're serious about COVID, but that we aren't serious about protecting intellectual property rights anymore.

I can tell you as someone who was firsthand involved with fighting a trade war with China over protection of intellectual property, including in some of these areas, it is a major reversal from where the United States has previously been. Now, they've taken some heat on the other side, and on the other side, basically, the proponents of this—India, South Africa, and others—have said, "Great, you've said you're now going to engage in text-based negotiations, but you actually haven't put any U.S. proposal forward, and you haven't given us direction on your concerns about our proposal." So, again, they're being criticized for just being symbolic and not actually moving those negotiations forward. It's a little bit of a situation where the U.S. has made a major move—it has catalyzed things in Geneva, and there's a lot more talk about what to do—but the negotiations themselves haven't moved all that much since we last talked.

Dr. Mario Ramirez: Yeah, Clete, that's a great point, and this has come up in a couple of different conversations I've had about how symbolic the move was as opposed to something that was actually going to really increase supply around the world. But you've made the good point that the move was made with the intention of trying to improve global supply. Isn't there a role for U.S. leadership in that position? Isn't it our job to signal to the rest of the world that in times of global emergency, that the U.S. can lead in that space?

Clete Willems: I think there absolutely is a role for the United States in that respect, and I do credit the administration for some of the other things that they're doing. They had worked early on with the Quad countries to try to distribute vaccines around the world, and then there was an agreement at the G7 that they would try to get a

billion doses around the world as well. Now we can talk about whether that's enough, and there has been some criticism of the number, but the principle is correct, which is that the United States and the other advanced economies who have the production capacity should produce this and to the extent that others are in need, they can make sure that it is readily exported to those markets. I think that's what a lot of the opponents of the waiver have felt is the better approach, because transferring the IP to these other countries doesn't mean that, magically, manufacturing facilities are going to pop up, that they're going to have the ability to invest in those sorts of manufacturing facilities.

So again, the idea is that U.S. industry has done a great thing by producing this vaccine in short order. Much of the population here is vaccinated; there's a reason we're all in the same room together. Now that we have excess supply, let's send that around the world. If we have to subsidize it with government dollars, let's do that, and that's really the position that the opponents have taken. It's that there's a better way to do this, and even if you get an agreement at the WTO on waiving intellectual property rights, we're looking at—best case scenario—production using that intellectual property a year from now. Hopefully, by then, we are at a different place in this pandemic and it isn't the same global problem that it is today.

Matt Hittle: We all hope that. But Mario, as you've talked about in some of our other conversations off the podcast, with the Delta variant, it's worrying, and we're potentially seeing an uptick in the fall. We don't quite know yet. But all that aside, it sounds like the WTO procedure is a bureaucratic barrier to getting the vaccine into arms in underdeveloped countries. Talk about the procedure at WTO. How bureaucratic is it? Is there a streamlined process they can use? What does the landscape look like there?

Clete Willems: So I would say, in many respects, I think the WTO situation is more along the lines of a distraction rather than a barrier, because I think the point I would make is that the WTO already has procedures in place that would allow for the transfer of this intellectual property if that was indeed the impediment to more vaccines. That's actually the exact point that the European Union is making. So to get to the process now, what has happened is since the United States said that it was open to text-based negotiations—and that wording's very important, they didn't say, "We support the Indian proposal," they said, "We support text-based negotiations"—since they've said that, the Indians and South Africans have revised their proposal and the Europeans have also come forward with a competing proposal. I'll walk through those two pretty quickly.

On the Indian and South African front, what they did is that they claimed to narrow the proposal. The original proposal had no time restrictions on it, it applied to a whole range of medical products, and it also applied to a whole range of provisions in the WTO that go well beyond patents. They said all of this stuff needs to be waived completely. Now, they revised it, and I think a lot of us look at the revision and say, "Well, what really changed?" They made a big point of time-limiting this to three years, but what the provision actually says is that in three years, the WTO can review it, and if by consensus they decide that it's no longer necessary, then they can get rid of this waiver. What that means in practice is that for the rest of history, India can block the removal of this and intellectual property rights will always be waived for a whole range of medical products, not just vaccines, under the TRIPS agreement.

So I look at this as a situation where I think if India and South Africa played this the right way and weren't afraid to take yes for an answer and came back and said, "You know what, we're just going to waive vaccines for a year," or something like that, they might have a chance at getting it done. But they haven't done that. What has happened now is that it's opened the door for others like Europe to come in and to provide a proposal that's along the lines of what I've been talking about already. What they would do is: (1) they would say that countries around the world need to address problems in the supply chain, and they need to get rid of export restraints on these things; (2) they need to look at the existing flexibilities in the TRIPS agreement, and there's a provision in the TRIPS agreement on compulsory licensing that already lets you to turn over intellectual property in emergency circumstances. The European Union is saying that we should use this existing flexibility, and that's part of their proposal. Then they're saying let's put money behind this, and let's really make sure that this works.

I think that, from where I sit, is a productive proposal that actually could help solve some of these problems. But the proponents of the original waiver are opposed to it, and so there's a lot of back and forth. What the WTO is doing is basically telling the members, "We're going to meet every week until we can try to get a solution." They have a General Council meeting, which is the highest body at the WTO, that's going to be meeting this summer in July to take stock, and then the goal is really to try to wrap this up by November when they have the ministerial meeting. But, again, let me just take one step back and say, best case scenario, there would be an agreement end of November, early December. I would hope by that time that the United States and others can do the right thing and do everything they can to help export more excess vaccines around the world that makes this totally unnecessary. And that goes back to your original point, Matt, of why people think this is just symbolic and why it really isn't going to make a huge difference.

Dr. Mario Ramirez: But let me interject there for a second, Clete. I mean, isn't there value in, I won't call it an exercise because I acknowledge that you're right, that this may be largely symbolic. But isn't there value in trying to determine what this road looks like for the next outbreak or the next national emergency that requires international cooperation? Isn't there value in something like that?

Clete Willems: I do think that there's value in the conversation, and if you look at the European proposal, actually, I think that's the way to go because what the Europeans are saying is let's not get rid of the WTO agreements in times of crisis. What they're saying is let's make sure that the provisions that are already embedded in those agreements on compulsory licensing actually work. I do think that that is a useful conversation. I don't want to get too philosophical on you all, but if you think about the trading system more generally and you think about the rules on international trade, they're supposed to work in all circumstances. They're not supposed to just work in the best of times. They're supposed to work in the worst of times. If you go down the path of India and South Africa and you say, "We're just going to get rid of the WTO rules during a pandemic," that doesn't make any sense. That's the law of the jungle.

What we want to see is an agreement with rules that work, and that's what compulsory licensing was intended to do. It's part of the WTO agreements, and I

think that's what should be explored. Now, the counterargument to that is that those provisions do actually require some sort of remuneration for the patent-holder—the person who holds the IP. And my point would be if that's an impediment and the United States wants to make a difference, subsidize that, and that is a way that you can make sure that you uphold the principle that intellectual property is important, it's not a barrier to innovation, and you can do your part in making sure that more vaccines get to more people, which is ultimately what we all want.

Matt Hittle: Well, the TRIPS waiver, Clete, isn't the only hot topic in the pharmaceutical world right now. The White House just last week released a 250-page report detailing the findings of its 100-day supply chain review. This report, among other things, called for federal investment into bringing supply chains back to the U.S., but given that these are spread across various continents and countries, luring these companies back or for the first time into the United States will require, it appears, significant investment in new manufacturing, development of a new workforce, etc. Do you think Congress has the stomach for these kinds of investments at this point?

Clete Willems: It's hard to say, and I want to take a step back and just talk about the supply chain report more generally. I think supply chains for a whole range of products, not just pharmaceuticals but pharmaceuticals and medical supplies, have really been a hot topic in Washington the last year, year and a half. This conversation was already starting before COVID and particularly in relation to what's going on between the U.S. and China, but it really accelerated under COVID. I think it's good that the administration is leading this review, where they're doing a very thorough process consulting with industry to try to figure out the best solutions. So kudos to them on that.

I think, though, that when people saw the report, it was a little underwhelming in the sense that there were a lot of ideas in there that had already been discussed in Washington and high-level principles but, really, that they wanted to consult more before they came with specifics. So this is really just a work in progress. I do want to say some of the highlights that you mentioned are more funding for production, and there are things in there talking about building redundancy in supply chains, which I think is something that would be helpful. But it's short on some of the details, including on how we would work with allies to make sure we have secure and trusted supply chains. So it really is going to come down to does the Biden administration further elaborate these goals and then do they work with Congress?

And to your question, does Congress have the stomach, it's hard to say, and it probably depends on which member of Congress you're talking to. This administration has proposed a lot of funding for a lot of different things, and I do think that at some point you are going to see certain members start to rebel against that and say we need to prioritize. You already saw this happening a little bit with the consideration of the legislation on China, where some of the Republicans who are as hawkish as they come on China and who have been calling for the U.S. to do what's necessary to beat China, including by greater investments in the domestic industry, had said enough is enough, and we really need to be looking at ways to encourage our private sector to innovate more than just having the government come in.

The last point I'll make here is, again, I do credit the administration for what they're trying to do here. I think they're trying to do the right thing. But if I would add two other areas I think they really need to explore a little bit more, they would be: (1) beyond looking at what government subsidies and funding you could provide to encourage production in the United States, I would also look at the tax and regulatory environment in the United States and see whether that's conducive to building more plants here. And then (2) I do think that we really do need a more robust trade agreement strategy and looking at whether we can use free trade agreements and other economic arrangements with our key allies to build a health supply chain and look at things like lowering barriers, prohibiting export restraints, coming up with a common set of standards. I think that is going to be very important in thinking about how we can move forward.

Matt Hittle: That's very interesting, Clete, and I will say for the listeners who heard a weird noise halfway through your answer, one of the perils of recording live together: the dog shook, right in the middle of a question. So let's talk a little bit more about the Endless Frontier Act or, as we now know it to be called, the United States Innovation and Competition Act, just passed the Senate. Does this have legs in the House? Do we expect it to become law, and if so, will it have a real effect on our competitiveness internationally?

Clete Willems: So I do think that this does have some legs because a lot of what is in the Senate bill are the kinds of issues that the administration is talking about. In particular, the Biden administration put in its budget that it wanted to provide $50 billion to deal with semiconductor supply chain issues and, in particular, trying to build more foundries in the United States. The administration included in its budget that it wanted to have a supply chain and resiliency office at the Department of Commerce. Those are both in there. There's a lot of other administration priorities that are included, and so I do think that the Democratic House and the Speaker will ultimately want to take them up on that.

I would also say, from the Republican perspective, this was a bill that ultimately ended up being bipartisan. I think the Senate majority leader did a very good job of including Republicans in the development of this package. Sen. Young from Indiana was a key author of a lot of what was included in the Endless Frontier portion of this, that looked at really enhancing U.S. investments in critical technologies in some of the areas I mentioned, but also other really important areas like artificial intelligence, quantum computing, synthetic biology. So I do think there is bipartisan support for a lot of this, there's administration support for this, and so I do think it's going to get traction in the House.

Now, that said, I do think that there are elements of this that the Speaker and certain House Democrats may feel goes a little bit too far. There isn't really much more popular than trying to make the U.S. more competitive with China or trying to beat China in critical technologies. There isn't anything much more popular than that in Washington, but there are at least some progressives who think that it's gone a little bit far and do want to look at this from a different angle, and don't want to include some of the elements of this package that are more strategic and relate to military cooperation, and also don't want to make it all about China. So what you hear from the House is that they're going to take more of a streamlined approach, try to put a package together of some of the non-controversial elements, pass those in the next couple weeks, maybe before the August recess, and then try to conference the Senate after that.

So, again, I think there's enough there, enough goodies, that there is going to be support for this, but we still have an unpredictable legislative process where bipartisanship has been in relative short supply. Now, I'm finally going to get to your question. Will this make a difference? I believe that it will, and I really do think that the U.S. is at a moment, whether the rationale for it is the competition with China or whether the rationale for it is just we want to as a society prioritize economic growth and investing in emerging and critical technologies. I do think that this, a lot of the provisions in there, some of which I mentioned, will take us down that path in the United States and will set us up for future growth.

But I will add, as I alluded to in the other answer that I gave, it's not just about what the government can give to these companies, Matt, but it's also a question of creating a business climate in the United States that is conducive on the tax and regulatory front and entering into the trade agreements. Finally, I do think we want to see some standard-setting, which is going to be really important to keep the United States in the lead. Some of that stuff isn't fully spelled out on the bill, but hopefully we can start moving in that direction as well.

Dr. Mario Ramirez: So you bring up an interesting point there, Clete. I think the Senate bill was very open about the competition aspect of this with China. The House in their separate standalone bills, is aware or cognizant of some of the xenophobia that goes into the kind of anti-China aspects of this. I think if there's a place where this gets caught up, it's around that issue of the anti-China focus or the xenophobia aspect. Talk a little more about that. I know you mentioned that that's probably the place where Washington agrees, but can we dive into that a little more?

Clete Willems: No, for sure. I do think, again, that there is almost no issue that is animated by partisan cooperation more than China in the last few years. It's sort of the dirty little secret that the way to get things done is to say, "Oh, this is going to help us vis-a-vis China," or, "This is going to push back on China." So I think that is important, and I think, in many respects, it's legitimate. I do think that most policymakers do believe that China poses a serious threat to our economic leadership and national security interests, and they should be doing something about that and they should be looking at it closely. But I do think that there is a risk of going too far, and the view on the left in the House, as you alluded to, Mario, is that some of this either overstates the threat coming from China, at best, or, at worst, has led to some of the anti-Asian violence in the United States. Certainly, those are legitimate concerns as well.

So I do think, at the end of the day, there's a balance. We have to recognize China for what it is, for the threat that it poses, and we do need to counter that. But I also think we don't want to overstate it and we also need to be cognizant that if we paint an entire country and group of people as an adversary, that can have consequences with our relationship with that country but also consequences for the way that we treat our people here. So I think that it's a balance, but at the end of the day, if I take a step back and look at this from a 30,000-foot level, I think everyone agrees they want to make the US more competitive in the world. Maybe they have different reasons for why, and I do think that this is something that still is more likely than not to get done.

Matt Hittle: Well, it sounds like the dog is making another appearance here. I think that means it's time to wrap, but Clete, thank you so much for joining us again and giving us such an informative view into the TRIPS waiver and into the various onshoring issues and the China legislation. We appreciate it, and we will bring you back on as those issues percolate through Washington. We are now going to go catch some dinner, but you listeners are going to listen to our next segment, which is with Jim DeYonker, who is the chief legal officer for Centrient Pharmaceuticals, talking about onshoring.

Well, we're joined now by Jim DeYonker, who is the chief legal and compliance officer and head of intellectual property at Centrient Pharmaceuticals. Jim has a JD from Rutgers University School of Law and a bachelor of science in molecular biology from Emory, and he is a patent attorney, but we won't hold that against him. Jim, thank you very much for joining us today. Why don't you go ahead and tell our listeners about yourself and a little bit more about Centrient?

Jim DeYonker: Thanks for having me, it's a pleasure to speak with you guys. So my practice is largely generic pharma over the last 20 years, primarily in the API and a little bit of final dosage form work, but spread out over the U.S., Europe, India, China, CIS, Russia, so I have a pretty good spread. I think that segues nicely into Centrient. Centrient is probably one of the most important pharmaceutical companies you've never heard of, and by that I mean if you look at what we make, our major molecules, namely semi-synthetic penicillins and semi-synthetic cephalosporins, we're far and away the largest producer in the world. Within the U.S., we supply anywhere from 60% to 75% of U.S. amoxicillin needs, and amoxicillin is the largest antibiotic by volume by far. So Centrient is one of those interesting companies that makes really absolutely critical medicines that you will never see a name brand on a package because we don't sell directly to the consumer.

But what also makes Centrient unique that's important to highlight is we do it all in a really sustainable manner. Our production processes are, I would say, more akin to biomanufacturing than they are to chemical production. All of our products are made via enzymatic synthesis and fermentation, and these are far and away the greenest way of doing this type of production, not just for the antibiotic resistance angle but also for general sustainability and the ability to make drugs that not only cure patients but also don't harm the environment in the process. So I'm very happy to be here to talk a little bit about our experiences, but I think it's an exciting time for Centrient to be looking into onshoring and all the infrastructure-related projects that you see in the U.S. these days.

Dr. Mario Ramirez: So, Jim, you brought up an interesting word there, the "onshoring" word, which has been much in the press lately and certainly in the minds of many of our listeners and is a hotly debated issue up on Capitol Hill. You brought up a lot of antibiotics that I certainly use frequently in my clinical practice and I think a lot of folks are familiar with. How many or what percentage of the antibiotics that Centrient produces are manufactured here in the United States, and where all does Centrient do its manufacturing on the global scale?

Jim DeYonker: Centrient has a unique footprint because the drugs that it manufactures are made at the metric ton scale. These are huge production facilities, way bigger than a traditional standard generic drug API being manufactured. So the scale of these facilities is really multiple times bigger than a traditional facility. Because of

that, we have quite decentralized locations on purpose so that we could spread that risk around. So our main production areas at the moment are the Netherlands, Spain, India, China, and Mexico. Now, to your first part of that question, which was what percentage of Centrient drugs are currently made in the U.S., well, that's pretty easy: none, zero.

So Centrient's drugs would represent about 30% of the total antibiotic market by volume and none of them are made in the U.S. In fact, we're one of the few that even make them in Europe. These are primarily driven out of China nowadays, not even India. It's really been pushed offshore so far. And that fits the Chinese playbook quite a bit because they can put lots of people and get benefits of economies of scale in their low-cost environment. So, largely, most of these drugs, outside of ourselves, have largely been dominated by the Chinese. But onshoring-wise, it comes at a perfect time because, simply, none of these antibiotics are made in the U.S., either in API form or in final dosage form.

Matt Hittle: So let's dig in. I know we're going to talk about what Centrient has been doing in terms of considering onshoring, but I want to get into the current state of play a little bit. With your disparate footprint overseas, I understand you have experiences with intellectual property theft and various concerns with IP. Could you go into what has Centrient's experience and your experience been with respect to the respect for intellectual property overseas, kind of what could be driving you to bring manufacturing to the U.S.?

Jim DeYonker: Speaking for myself, I would say that, as an IP attorney, if I could ever have my large manufacturing facility in the U.S., that's about as good as it gets, because the enforceability of IP laws in the U.S. is good, I would say, second to none. It does get expensive, but outside of the cost—and we don't need to tell lawyers about that—in terms of enforceability, it's really the best. The challenge that we have is ultimately that these plants need to be in different locations to serve their market. So, in doing so, we're forced to have this IP in jurisdictions where it's not very easy to enforce or the timelines are unduly long.

For example, in India, they have very good patent attorneys and patent courts. The problem is it's just an administrative nightmare to get to a hearing. You could go three or four or five years before you even get through the first instance, and that's partly because of the civil procedure practice that's there, which is essentially set a court date, cancel it, then wait two months, set another one, cancel it, and you ultimately never get anything set. The other challenge we have as a company is that a lot of our technology is based on trade secrets, and the reason for that is ultimately that the minute we were to publish something in a patent, it's unenforceable in China, especially when half the companies that we would be competing against are state-owned entities, so you can forget that ever being a fair trial. So one of the challenges we've had is, because of the fact that we keep many of the more business-critical intellectual property items as trade secrets, is simply because we don't have the ability to enforce.

And that becomes cumbersome, right? It's difficult to maintain access control. It's difficult to limit who can go in and out of your facilities, especially when there's quite a bit of turnover on such a giant site. So intellectual property is a nonstop battle against the ability to protect via patent filings or adequate in-house procedures and then, ultimately, the ability to enforce. I would argue that enforcing a patent in China and India, although technically possible, is

pragmatically virtually impossible. And, again, primarily in China, as most of the patents that would be relevant in China would be process manufacturing patents, civil procedure rules there and the evidence rules make it impossible to get infringing evidence against a local manufacturer.

Even if you know for sure that they've ripped off your product, if you don't get a sample, you simply just cannot file anything in court. So there's no burden-shifting like there would be in other places on process patents in particular. India's quite good in that, meaning the bar's lower to bring the case, but then you run into the bureaucracy, which unfortunately, I think, for India, is disappointing for the industry that's there, I'd say, because they have really good pharmaceutical companies but the ability to enforce is still so slow that you have to work that into your timelines.

Dr. Mario Ramirez: It's interesting, Jim, because you also highlighted another issue briefly, which was cost. Clearly, it sounds like, from an intellectual property perspective, it would be advantageous to bring things back to the U.S. But as the White House is undergoing this 100-day review in how they want to try to reposition the U.S. supply chain as a result, what do you think regulators and other government officials need to hear from companies like Centrient or other pharmaceutical manufacturers [about what] would keep you from bringing these plants back to the U.S. market?

Jim DeYonker: I think the thing that policymakers need to understand is that, unlike other industries, tax breaks are not a benefit for us. So one of the first things when people do onshoring is to roll out tax incentives. That's not the reason we're not here. So that helps nobody, and that will never bring back the generic industry. I'll be rather blunt on that because I still see quite a bit of policymakers thinking tax is the issue, and it's not. The challenge is the infrastructure costs that go with these plants, a fermentation unit being $500-700 million to make one or two drugs. That's quite difficult for a company to justify moving to the U.S. solely for the benefit of IP, let's say.

Now, of course, there might be other reasons you'd do that, rationalizing site or looking for technology expansion. But the U.S. government needs to look at this as a public-private partnership because what the government will get is 100% security of supply and what the company will get is the kickstart on the infrastructure to do that. In that case, you don't even need the Defense Production Act because if something goes wrong, you'll have these companies ready to produce 100% of the U.S. needs of these drugs onshore. So it's all infrastructure, CapEx, and that makes all the difference. Because anyone who looks to build, get approved, and qualify and launch and commercialize a product in the U.S., that's going to be every bit of four to five years. So that means you have to spend $700 million upfront in the first two years, and you won't collect that back for a decade, maybe probably even more.

So the business cases for generic drugs, given the so-low margins and so-high infrastructure costs, the only way to onshore is to have these public-private partnerships with the government to support that infrastructure upfront. These businesses will be self-sustainable going forward, especially if they utilize advanced technologies in their manufacturing and not just run-of-the-mill chemical synthesis, which you can throw bodies at in China and India and have a much lower cost of goods. But, ultimately, for us to succeed, the hurdle is always

the same for us. It's the upfront infrastructure CapEx. So I think politicians and policymakers need to look at this as partnerships and collaborations and not handouts and gifts because this is a plant that, once you invest in it as the U.S. government, will be 30-40 years on your soil making these products.

I recently spoke with some of our in-house team, and one of the questions is, "Well, why would the government invest $500 million? That doesn't seem like a really good return on investment." I said, "The key here is the government's not an investor." You cannot look at the government as looking for IRRs or different return levels. Think of the government's investment the same way it invests in the military weapons, the same way it invests in nuclear weapons. You'll hope you never need it, but if it's there, you have it. You're buying peace of mind and security. That's what that investment is for. It's not necessarily a return.

Dr. Mario Ramirez: In addition to that, Jim, certainly here in the United States we have a very robust academic base, but one of the things that I've heard particularly around biomanufacturing is that we have a shortage of either trained personnel who are ready to come in and do some of this work or around things like fermenters, for instance. How much of it is a people shortfall that we have, and how do we address that piece of it, and how much of it is a hardware issue or an infrastructure piece?

Jim DeYonker: Well, you make a good point. This is technically more difficult manufacturing on a unit basis than, say, traditional chemical synthesis. So more things can go wrong, and, again, it's a living organism, so it doesn't always work as perfectly as you would want. I would say that the issue in the U.S. is there simply are no real fermenters of size there anymore. The antibiotics were some of the first to leave because they're the lowest margin drugs. So those are the ones that searched for the offshoring benefits 30 years ago, and there's really very few, if any, at the size of semi-synthetic penicillin needs. I don't want to be definitive because I can't say that there's none out there that I'm aware of, but I'm not aware of any of size that, for instance, Centrient could acquire and brownfield, essentially. We look at the U.S. as somewhere where, at least for the fermenters, you're going to have to greenfield that. It's been too long. You have lots of great beer fermenters but, unfortunately, they lack the GMP [*good manufacturing practices*] and the downstream processing.

But to the second point, to the talent point, I think talent is an addressable issue. Between groundbreaking and early operational runs on that facility, you'll have two full years. So as long as you're in a good university town or a high-tech hub, you can train these people, and I would expect that this is where the state governments probably would get involved and support a collaboration like Centrient and the federal government, that the state government would jump in and say, "Let's do some job training here and make sure you have workforce readiness in place for two years in advance." So I don't worry about the people. Now, that might take a little time, depending on where you locate the facility. But, ultimately, I think that's an addressable problem.

The lack of scale GMP fermenters is a much more serious issue in terms of the speed to onshoring and the cost. I mean, the cost of the fermentation unit is really, really overbearing for companies that, again, are not selling drugs that have 1000% profit margins on them. There's not a lot of room there. So it doesn't mean they can't be successful, but they have extremely long payback period

time. But I do think, realistically, wherever we would look should we greenfield in the U.S., one of the top three considerations after sugar and electricity would be people. So you would look to some of the more well-connected biotech pharma clusters. But also, and this might sound silly, I wouldn't hesitate to look at other industry like bio-ethanol and beer brewing because, in the end, it's the same process. Obviously, we're going to do it at a higher quality standard, but that can be trained. So these operators, I think you could build that workforce, and these will be very good jobs. These are not minimum wage jobs. These are college graduates, biochemists, etc., so these are good, sustainable jobs.

Matt Hittle: Well, Jim, it's clear that the administration is going to have its work cut out for it as it implements the recommendations from the 100-day supply chain review and report. What you've told us today, I think, establishes a decent framework for generic antibiotics onshoring, which I think many believe—and it was referenced in the report—is critical. We know you've got a hard stop, so we'll let you go about your day. Jim DeYonker, the chief legal and compliance officer and head of intellectual property at Centrient Pharmaceuticals. Thank you so much for joining us today.

Jim DeYonker: Thanks again. I appreciate you having me.

Dr. Mario Ramirez: Great to speak with you, Jim.

Matt Hittle: Well, that'll do it for us today. Thanks again to Jim DeYonker of Centrient Pharmaceuticals and Clete Willems of Akin Gump for joining us today and sharing their insights. As always, please like and subscribe if you liked the podcast, and please send us a line if you have any ideas for future episodes. This has been Dr. Mario Ramirez and Matthew Hittle of Akin Gump for this week's edition of *OnAir: Health Care*.