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Setting up a robust CGT supply chain (Part 1)

Intro:
I'm Chris Riback. This is Logistics Live: Conversations & insights on the global supply chain.

Cell & gene therapies hold incredible potential for improving – if not saving – human lives. These CGTs have been called "living drugs" and can heal diseased organs and – we hope – fight diseases that currently have no cure.

Because of these incredible possibilities, related research and development is growing exponentially around the globe, with increasing numbers of complex clinical trials – complex because they require complicated and precisely timed pickup and delivery of specimens and deliveries. A single hiccup anywhere in terms of pickup, drop-off, temperature, contamination – anything – can cause significant challenges.

So what, exactly, does it take to set up a robust cell & gene therapy supply chain? What should manufacturers, labs, pharmaceutical and biotech companies, and logistics providers consider?

Mike Sweeney can explain. Mike is Global Head of Strategy for CGT and Direct-to-Patient products (CGT and DTP) at QuickSTAT Global Life Science Logistics. He joins me now to discuss why – for CGT supply chains – planning in advance is the best medicine.

Chris Riback:
Mike, hi there. Good to see you again.

Mike Sweeney:
Good to see you as well, Chris.

Chris Riback:
Last time we talked about all things DTP and DFP, direct-to-patient and direct-from-patient. And it wouldn't be a podcast without a new acronym and today's three-letter acronym is CGT, cell and gene therapy, specifically exploring the unique complexities that are part of developing a CGT supply chain and implementing that supply chain, both sides of it. So, let's jump right in.

I read Mike recently that there are more than 1,500 cell and gene therapies registered for clinical trials. I feel like all of these trials represent something that's part of the CGT supply chain because they represent hope and I know we'll get into it, but you almost could add an H to CGT; it's cell and gene therapy and hope. It's hope for the treatment of challenging and incurable diseases – really challenging stuff. I imagine you agree. So, with that in mind, at the highest level, can you walk us through the state of CGT today?

Mike Sweeney:
Sure. It's exciting. It really is. I think there is a great reason to be hopeful, more so than any time I can think of over the past 30 years of being involved in clinical trial logistics. Cell and gene therapy is a science that we've been hearing about for decades. There's been toes dipped in the water for a long time on this front, but now we're really here with therapies getting approved. The FDA is excited about the possibilities of the numbers that we'll see approvals over the next few years; even by the end of this year, we're expecting some more. So I think where cell and gene therapy has really evolved has challenged us certainly within the supply chain, but the science has been truly amazing and I think we will see more great things coming out of this. I do think that we need to be careful about how quickly it's moving and how we're supporting it because it's very complex on the supply chain as well as all of the talent that's required to make the engine move.

Chris Riback:
So let's talk about that supply chain and let's start with, we're talking about living cells, aren't we?

Mike Sweeney:
Absolutely. There are a couple ways in which I think the science is really driving these therapies. One is through one individual's own cells, and then another is from donor cells. We'll talk more about this, but the key is that these are cells that are being manipulated to attack the disease, which is really incredible when we think about that actually being done scientifically and actually helping and potentially curing disease in some cases. Truly amazing stuff.

Chris Riback:
So tell me, what would be some examples? What would be some of the diseases that we are talking about? I'm certain there are a number of them that many of us are just not aware of and then probably others that we hear about quite regularly.

Mike Sweeney:
I think the big one is definitely oncology, so various types of cancer and there's been very interesting results throughout. Whether it's pediatric cancers or multiple myeloma, there's several drugs that have come out that have really shown promise, and I think that it extends into various therapeutic areas. Once the developers – therapy developers – are able to really take a look at what these engineered therapies can do, you can look at cardiovascular, you can look at so many other therapeutic areas, and they are. There's great results that are happening. I think one of the best things I've seen is just in terms of the types. So you have gene therapy, you have cell therapy, you have RNA-based, for example, three different types and all three of those have seen approval over the last year. So I think that's a great really acknowledgement of how robust the science is and the variety of ways in which it's being delivered.

Chris Riback:
Mike, in our last conversation, we touched on how much things had changed post-COVID. Is that the same on cell and gene therapy? Has the rapidity of it picked up since COVID? Because my question ultimately is, what was the process on this pre-COVID, and what has happened now post-COVID? Because I want to understand the supply chain complexities. I'm going to get into these questions with you around materials and worldwide locations. I mean, really, the complexities are really mind-boggling to an outsider. But first, maybe you could take a step back and give me some context. How did this work once upon a time?

Mike Sweeney:
I think the COVID question is a very good one here and it does extend throughout clinical trials. There were a lot of tough decisions that had to be made, can we continue to run this trial throughout this pandemic? And in cell and gene therapy, there were a lot of trials that were kind of getting ready to start that were paused, and that was for a good reason. I think there's a lot of tricky components to the supply chain that we're still seeing the aftermath of from COVID, frankly. So to answer your question, there was big momentum before COVID. It slowed down certainly at that point, and it's picking up steam again, but there has been some economic challenges that have definitely hurt the industry to a degree. A lot of this is still in the investment phase.

It's similar to the kind of the '90s biotech boom where there were scientists in small rented office space who were doing this virtually and getting together and figuring out the scientific part and then pulling in suppliers to help. This isn't entirely different from that in some respects. There's also cell and gene therapy developers that have been acquired by bigger companies, so getting a push that way. But I do think that there is a great outlook now, even though we've hit some bumps in the road. The numbers of the trials you mentioned before, 1,500, it's going up, and it will continue to, but there was a really good trajectory for this prior to COVID. We've definitely had some challenges coming through that and out of that.

Chris Riback:
So as you talk with biopharma companies and you talk to them about – maybe it's establishing a supply chain, maybe it's improving a supply chain, maybe it's around the various logistical challenges. How do you talk to them? What's the high-level strategy? And then, as practically and literally as you can, how do you talk to them about managing two areas of challenges? One, materials. So, as mentioned, we could be talking about living cells. In our last conversation, you talked about temperature. I can only assume that's a key factor again, but also locations. How do you talk to biopharma companies about those aspects? Particularly because they need to make sure that they have a commercialization plan in place.

Mike Sweeney:
Absolutely, and I think the challenge that they have and will continue to have is looking at all of those variables. Where will the cells be manufactured? Where are the patients going to be located? Logistically, is it possible to get to those individuals with their treatments or to get their materials in the case of materials that are drawn directly from those patients? So the key is looking at all aspects of this and it's high risk in some cases. So I think what we need to do is help our customers understand that there are limitations. Particularly right now, the airline industry is fractured. We may not be able to rely on that as much as we were able to 2019 and prior. It's never been perfect. So we've always had to manage things.

So, I think there are two key components. One is location and so point A to point B, what are the timelines for that? And then the temperature, how do we manage the temperature piece? And they vary – precision-based requirements around both temperature and timing. And there's also an additional consideration I would say, around how we're managing pickups and deliveries. So, our drivers going somewhere too early can be problematic in cell and gene therapy. If there are staff that are actually dealing with the patient, whether it's extracting their material, their specimens, or if it's for the treatment that's coming to them, you want to make sure that they're dealing with the patient first. And we're conscientious of that.

So, it is challenging on a lot of levels. It's very unforgiving, and we do have to have contingencies in place because, invariably things go wrong. Flights cancel. There are weather problems. So we always have to look at alternatives, whether it might be a long drive to make something happen over several hours or it could be chartering an aircraft, sending an onboard courier. These are things that we always could do and have in play in our toolkit, but now it's just become, you have to have that plan ready to go.

Chris Riback:
It's so interesting to me as you talk about patient first and something as simple. The precision involved because something as simple as, exactly, the driver arrives 30 minutes, 60 minutes, 90 minutes early, not only obviously is it impossible to pick up material that has not been extracted yet or some such thing, but it could really be disrupting to that patient. And it's interesting to me that you obviously have to have such a focus on patient first, and that's happening at the same time that the cell and gene therapies are patient-centered therapies obviously. So that connects, and then in addition, the supply chain evolution, let's call it, is moving so much closer to the patient. So everything, every component about it, the logistics, the practicality, the precision, the almost, I would call it the social-emotional awareness of not knocking on a person's door 30 minutes early when they might be having a procedure done or having something done. It really is from top to bottom patient first, isn't it?

Mike Sweeney:
Absolutely. And I think the key in this particular area is the people at the treatment centers that are doing unbelievable work under more stress and pressure than ever before. Again, that's an industry that was fractured prior to COVID, but now, when you look at the hospitals, and with cell and gene therapy, it's a very specialty skillset and division of that hospital that will be even potentially involved in managing cell and gene therapy treatments. So I think the key for us is to make sure that we're helping those individuals that are doing more with less and constantly under pressure. We need to be very cautious of that, very mindful of that and cautious of how we approach the pickup and delivery scenarios.

And then the other part of that as well is you could be early but you could be late. There can be problems with a number of things, right? So I think communication and making sure, again, if we know there's a flight cancellation that is going to put us hours out of that expected delivery time, we need to look at other options, and we need to do it immediately. That's part of it where... I mean, it's exciting in a way that we're able to kind of use those muscles and kind of look at the options that we have and we have all of this documented should something go wrong from each location. However, putting it into play to get a chartered aircraft ready to go, we need to put those wheels in motion as quickly as we know there's an issue. And a lot of this is tough communication with customers and with caretakers; that we really need to be as helpful as we can looking at our options.

Chris Riback:
What's the biggest question that clients ask you?

Mike Sweeney:
How can you guarantee that this will go according to plan, and what will you do if we have a problem? And I think really our clients are more educated and again, folks doing a lot of these, individuals doing a lot more with less resource around it. They're challenging us to be a big part of their planning as well. So we're asked all the time to look at 20 different routes and how can we get it there and how fast will it be able to be delivered? You don't always think about when these requests come in is they're making decisions in some cases based on what we tell them as far as the possibility of timelines of where they extend that treatment.

So they have treatment centers, let's say, in 20 different cities around the world or around the U.S., and they have to make the decision of where to extend that treatment based on the manufacturing timeline. They don't want to be in a situation where if you have 48 or 72-hour timeframes for deliveries to occur, if we tell them, "Hey, this looks like it's going to be around 45 hours," that gets to be a discussion where we need to help them make a tough decision or have an alternative plan.

Chris Riback:
So many tough decisions. Can we talk a bit about autologous and allogenic therapies? What they are, the differences between them, and I guess, more critically, how do those differences impact the CGT supply chain?

Mike Sweeney:
Sure. So autologous is what I referred to before. If I'm a patient and I'm ill, I have samples extracted from me, and then that will be manufactured into my therapy. And allogenic or allogeneic, they're donor based materials. So, materials that one donor can contribute to treatments for multiple patients, for instance, and this does require a matching process. So there is quite a bit to that, but obviously it's more scalable when you think about it in terms of longer term. Provided that the science is there, I think that that's a model that will be pushed more and more, but right now, we're seeing far more autologous, and there are really some great success stories.

But if you think about the mechanics of this with a patient that maybe has a tumor extracted or has a bone marrow extraction done, and that's their chance to have their therapy developed based on those materials. So then it needs to be shipped typically in 2 to 8 Celsius or maybe 15 to 25 in some cases. It varies a bit depending on what needs to happen. But then you've got that manufactured product that needs to go back to the patient, and that's typically something that's cryopreserved in a liquid nitrogen dewar.

So, the science of the two is similar. The supply chain changes in that it's not the circular supply chain of that patient's treatment going back to them as it is in autologous. When you look at allogeneic, you'll have either cryo-storage locations or donor locations in which that material would be picked up. They're still the same similar challenges I would say, but just not as high risk with banking on that one patient's materials to make that therapy happen. If you really think about that, and we've been into some tough situations where the time is tight, and the temperatures are challenging, and we do everything we possibly can to make it happen, understanding it's for one patient. But when you think about the number of these that are moving around and the number of times, these patients are getting treated and even just the idea of 1,500 clinical trials and the number of patients in each, it's staggering to think of how well it's actually working overall. But it comes obviously with challenges.

Chris Riback:
It is absolutely staggering. Mike, let's talk about the manufacturer side if we could for a moment. What are some of the key obstacles that stand in the way of getting the life-saving therapies from the manufacturer to the patient?

Mike Sweeney:
So it starts with often cryopreserved material that is going to be shipped out of that manufacturing location. And again, I think in the beginning, the planning phase of the developers trying to figure out where can we manufacture it. They want to have as much control over that process as possible for understandable reasons, but they also want to reach patients that can benefit. So the challenge is if you have a manufacturing site that's centralized, let's say in the U.S., then you need to consider – can I treat patients in Europe? What are my timelines? I think that's one of the key challenges is just looking at what is my strategy going to be? Where do I have manufacturing capabilities, talent, resources to manage, and how far does that help me extend the reach to patients that are in need? So it starts from there, but then, of course, the logistics of making that happen, once they get the therapy, well, the materials they then need to develop the therapy and ship back. That requires the liquid nitrogen shippers which need to be charged and ready to go.

Again, it's a precision situation where folks like QuickSTAT are going and dropping off these dewars for pickups and they've been charged with liquid nitrogen and have... There are a fairly decent lifespan on those, but still, you don't want to have those not moving after they're charged if you can help it. You certainly want to maximize the lifespan of that dewar and liquid nitrogen. So, from that point forward, it's just then shipping out to the patient location. So, really, the hospitals and treatment centers where that procedure will happen with that treatment for the patient that needs to be treated.

Outro:
That was the first part of my conversation with Mike Sweeney on how to set up a robust CGT supply chain. In Part 2, Mike offers specific system design ideas and tactics for any industry player to establish processes and overcome inevitable roadblocks.
For more information on supply chain logistics, go to QuickSTAT.com.