CELL & GENE THERAPY INSIGHTS

SPOTLIGHT

SCALING UP/OUT: COST-EFFECTIVE & ROBUST TRANSITIONIONING THROUGH THE CLINIC TO COMMERCIAL MANUFACTURE

PODCAST INTERVIEW with:

Adrian Lee-Mohan, Senior Vice President, QuickSTAT & Quick Specialized Healthcare, and **David Murphy**, Executive Vice President, Life Science and Cell & Gene Commercialization, Quick Specialized Healthcare Logistics.

Delivering cell and gene therapy: evolving logistics considerations

Cell & Gene Therapy Insights 2020; 6(8), 1215–1224

DOI: 10.18609/cgti.2020.030

Q Adrian, this year you celebrated 30 years with Quick, meaning you have been ever-present during the emergence and development of the advanced therapies industry as we know it today – can you reflect upon that long journey, and share your key concerns as you look at the ATMP field today?

ALM: It has been a long and eventful journey, and I feel like I have had several completely different careers in that time. I wouldn't pretend that it has not been very hard work, but it has always been rewarding and varied. Just when you think you are close to knowing most things, along comes a whole new field of medicine, and the learning process starts over.

With regards to the ATMP field, at Quick we have been at the forefront alongside the customers, and I believe we have effectively learned together. My main concerns would probably relate to the establishment of protocols for commercial distribution by the sponsor based on clinical phase experiences, without the inclusion of the logistics provider.

What we have experienced is that what works on a small scale, clinical phase is not always practical, or possibly even necessary at a much larger commercial phase. Therefore, I think that clinical and commercial need to be aligned from the get-go, and the logistics provider should absolutely be involved at the earliest possible stage.

Q David, you spoke to Cell and Gene Therapy Insights back in the Fall of 2017 about the role of shipping and logistics in the commercialization of cord blood-based therapies – can you share your thoughts on how that particular field and its supply chain has evolved since then, and what issues it still faces on an ongoing basis?

DM: 2017 seems like a decade ago even though it has only been three years, because this industry, including cord blood therapies, has evolved so rapidly. The ongoing development of allogeneic therapies is exciting to observe, but there are important differences between autologous and allogeneic therapies that must be acknowledged and understood.

> "...clinical and commercial need to be aligned from the get-go, and the logistics provider should absolutely be involved at the earliest possible stage."

The technical details associated with autologous therapies are slightly more challenging, whereas allogeneic is more structured and scheduled. You can easily schedule collections at cord blood banks or blood centers throughout the country, or the world for that matter, traditionally sending these collections with high integrity to contract manufacturers throughout the world.

With autologous therapies, it is all based upon scheduling a patient, which can be a challenge. These are often very ill patients so

DOI: 10.18609/cgti.2020.030

there could be delays, or they could be too ill to even go through an apheresis process. To work with this level of potential variability we have worked very hard with the industry for many years. For example, back in 2010 and 2011 when the first cell therapies were approved, we were right there to support the developers and we continue to do so today.

Turning to COVID-19, we have seen interesting events happen in the last four months in terms of challenges. We have had to deal with a shrinking airline industry, a trend that we do not think is over, as we expect that the airlines are going to continue to right-size.

We have made incredible efforts to save the day in many cases for this industry. We have chartered a lot of airplanes and made a lot of long drives. It has really been interesting and through this crisis management, I think it has validated what Adrian and I have put together on a case-by-case basis to clients; it has validated our processes.

You never know what is going to happen next year. We can only continue to work hard with our clients, be creative, and find solutions.

Q Adrian, you are UK-based – what are your expectations currently in terms of the repercussions of BREXIT, and how can or will you prepare for them?

ALM: This has been the biggest question we have faced over the last four years, which has been preoccupying both our minds and the minds of our clients. It has been overshadowed since March, and COVID-19 has taken the number one spot. However, it is still very much an issue, and one that we still don't really know the answer to.

As we all know, until the end of 2020, there will be no change. But that deadline is now fast approaching, and we will not be in a position to accurately assess the potential repercussions until the final trade agreement between the EU and the UK has been established. We don't know how close to the 1st of January 2021 this will emerge.

Personally, I was hoping for considerable alignment in the medical field, and I was cautiously optimistic that any repercussions would be contained. But in recent months we have seen the two sides lay out their frameworks for negotiations, and they do seem to be at loggerheads. Certainly, in the rounds of talks that have been held so far, both parties have sounded fairly intransigent in their negotiation red lines. We will continue to hope for a last-minute agreement, but so far, we do not have any progress.

In the UK, Quick is an official customs broker. We clear all of our own inbound shipments at all of the key airports. We are electronically linked and connected to HM Revenue & Customs, so any import or export customs functions that are needed with effect from January 1st next year should be smooth and rapid.

Additionally, we have been increasing our staffing levels in this key area, so that we are able to respond to the additional pressures and potential changes that are coming.

Q What are the key components that you feel make for a good logistics provider for the advanced therapy sector?

> "The technical details associated with autologous therapies are slightly more challenging, whereas allogeneic is more structured and scheduled."

DM: Without getting overly technical, the reality is that experience matters. Between Adrian and I, we have nearly 63 years with the Quick Group.

We have been working in this area for 35 years, and that makes a big difference – we have acquired a great deal of experience working with organs, tissue, blood, and the pharmaceutical industry. In many ways, the requirements for cell therapies and organ transplant are very similar – the expectations, the chain of identity and custody, and the required temperature integrity are all very similar.

Tenure in our organization is incredible. It is very common to have groups of people in all our centers of excellence and control towers, that have 20 or more years of experience in special logistics throughout the medical community.

When you work so closely with these medical organizations, you must demonstrate honesty and integrity. You must be frank with them, particularly when you are dealing with risk-mitigating situations. The industry in general has changed, in a good way, in that the interaction between vendor and pharmaceutical or biotechnology company is now very open and honest. I am very encouraged about that, because whenever possible we should be on the front line with our clients.

Transportation is critical to the success of these therapies, and at the end of the day, we are all working for the same patients. Every patient deserves our most concentrated effort.

Q How do you evolve as an organization to meet the changing demands of this sector?

DM: One of the most important questions received from us by our clients is around scalability. We are involved and engaged with these organizations from a clinical perspective, and on into a commercial perspective, and it is important for the client to understand our scalable abilities.

On the clinical side, we are dealing with perhaps 15–30 patients as you go through the clinical stages. But of course, the goal is to get to a commercial position. Suddenly you could be talking about tens of thousands of patients, and each patient requires three shipments at a minimum, and potentially up to 10 or 11 shipments. You can understand the concern that clients may have in terms of our ability to scale to those levels.

In 2010, when the first FDA-approved therapy was developed, we had to demonstrate our ability to scale to 90,000 patients per year. It was a daunting task, and this is when employees with 20 years of experience is huge advantage.

We are also seeing changes in the airline structure. Some airlines will likely not be in existence for much longer – or at the very least, they are going to be a skeleton of an air carrier compared to what they were six months ago.

DOI: 10.18609/cgti.2020.030

In these situations, clients deserve options, and those options need to be very in-depth and practical. If you are going to experience potential delays and you want to mitigate risk, you must be able to offer other options that are perhaps very expensive. But it is still an option because we are focused on the patient. If we all continue to focus on the patient, I think it is going to be a very exciting ride.

Q Autologous cell and gene therapies are now a global commercial reality. What would you pick out as your top three key learnings on the logistics side, that may be drawn from the experience of the trailblazers in this area?

DM: As we discussed earlier, for both the autologous and the allogeneic therapies, there are strong similarities to the transplant community, which we have been handling for between 35 and 40 years. We are the pioneers in transporting organs and lifesaving drugs for the industry, and what we have learned over the years is very valuable to the solutions that we provide today.

The other important thing is to engage – engage with your logistics provider both early and often. When you start talking, even before the clinical stage begins, identify where the manufacturing is going to be done, and then look at the logistics. Learn what expectations you should have of your service provider. You might think you have it all spelled out, but when it comes to logistics it is not always that simple, and you may have gaps. If you do this early, you can flush all these issues out, mitigate risk, and come up with creative ideas on how to approach things.

This becomes even more important as these therapies grow globally. We have done an outstanding job between Adrian's team and the center of excellence in the UK, and our team in the US. We have handled some very complicated logistics solutions in Europe and in North America. The next evolution is going to be in Asia, and we are certainly prepared for that.

Lastly, from a biotechnology or pharmaceutical company perspective, logistics partners need to be viewed as a true partner. We act as a partner, we work with our clients as partners, and we must have the same mindset. This is what we are experiencing today in this industry, and it is a breath of fresh air.

Another thing is that we need to be good stewards of these therapies. We need to be able to educate our airline partners, our ground handlers so that they are as aware of the therapies they are handling as we are.

Q How is Quick seeking to develop its solutions further to support autologous therapy chains on a worldwide basis?

ALM: For Quick, this would really focus on what is effectively a reset of the supply chain involved in delivering these therapies, and in meeting the specific demands of each individual client.

> "...engage with your logistics provider both early and often."

We are still in a relatively early phase, particularly for CAR-T. We must fundamentally build an entirely new supply chain model for the cell and gene field and the CAR-T field.

We must take into consideration the scalability, as well as the demand for dedicated one-patient-one-product moves – including all of the chain of custody and chain of identity considerations, non-X-ray implications, redundancy planning, and so on. We have to review every available air and road option, and much more besides.

Faster and more streamlined solutions will probably first and foremost be provided by developing the supply chain, in a three-pronged approach. Firstly, that would be by completely retooling the ground network to withstand the pressures and meet all the logistical criteria. Secondly, it would be by working with the airlines and the ground handlers to educate their resources around these products and working with them to potentially develop new services or solutions. And thirdly, working with international regulatory bodies to explain to them why they should potentially make exceptions to some of the existing legislation for products in this field.

We have successfully done some of these things in several cases. For example, from a regulatory body perspective, we encountered a border control authority issue around export, meaning that potentially lifesaving medicine could not be exported in a timely manner within the product's viable lifecycle. We had to work together with the sponsor, and the authorities, and ourselves, in a collaborative approach, to find and bypass this issue. We did this very successfully, and it was very rewarding for all parties.

We have achieved the same thing from a service perspective. Working with an airline and the relevant ground handlers, we discussed issues in great depth and looked at all options. We managed to produce a bespoke handling service that meant we could minimize some of the risks around the failure of freight to be loaded onto the aircraft, by creating an enhanced ground ramp access solution. Again, it was a collaborative approach among multiple parties, and it made a real difference.

We are proud of doing this, and we are excited to push those boundaries and come up with entirely new solutions just by trying to think slightly differently. Can we approach this from a different angle, where can we get better collaboration from, where can we push the airlines, or push the handlers, to do more? That is exciting for us.

Q There seems to be a strong focus right now within the industry on working more closely and diligently to alleviate the increasing pressure on apheresis centers and clinical point of care that comes from this rapid growth of the cell and gene therapy field. What roles can logistics, tools, and service providers play in this effort?

> "The significance of timely collections and deliveries of the apheresis materials, and the product, is critical."

ALM: This is a rapidly growing market, and we are in the main part relying on hospitals and apheresis centers. These institutions have had to find the capability to slot entirely new

DOI: 10.18609/cgti.2020.030

processes into their already hectic clinical schedules. On top of that, they have had to adapt to additional responsibilities.

They may not necessarily be used to handling things such as non-X-ray, and chain of custody and chain of identity processes. They have needed education and help, and it is our job to ensure that we guide them through those processes and assist with the relevant documentation and training. That is something we can do together with the sponsor, through interaction with the hospitals and the sites.

The significance of timely collections and deliveries of the apheresis materials, and the product, is critical. Not only for the patient's sake, but also for the functionality of the institution itself. They do not have endless flexibility. They have tight timeslots, and they need us to produce and perform to what we have agreed.

My second point would be around transparency throughout the logistics process. This is key for all parties, and can be through the logistics provider's information tools, or through a wider platform that links all the stakeholders. As an example, we are currently working with clients who engage third-party organizations to link the key milestones that we might be reporting on, and the key data. That is between the client systems, our systems, and an overarching information platform. In some cases, this can involve booking system for the hospitals, too.

Lastly, as David mentioned, I cannot stress enough the importance of having experienced, specialized, and dedicated team members within the service provider. This is crucial to the sustained scalability of any project.

Q As we have touched upon already, allogeneic cell therapies are clearly on the rise. Many make light of the supply chain logistic challenges that this therapy faces, compared to for example autologous therapies. Where do you see potential issues arising that this field will need to address as it continues to grow?

ALM: Allogeneic therapies can be manufactured in larger batches, from unrelated donor sources, and as such the supply chain is one way, one-journey led. There is more predictability on the source material than there is with autologous, and there is more consistent availability for collection.

Autologous therapy is slightly different. It is vein-to-vein, and therefore has a supply chain that is circular – it has got multiple legs. It is a single source material, often a lengthy manufacturing process, and there is less consistency, or availability for collection. There are also differences in the temperature: normally a single temperature for allogeneic therapies, but often multiple requirements for autologous.

There are some key differences, but in reality, when it comes down to the critical elements of the supply chain, we don't identify too much of a difference at all. Chain of custody and chain of identity are critical in both. Strict temperature controls and the equipment we must provide, produce, and validate to achieve that – this applies to both. The non-X-ray requirements will most likely apply to both as well.

Most significantly, the delivery is effectively to a patient for surgery. We still have the same logistical challenges that apply in terms of hyper-strict timings, and highly detailed individual site requirements, and so on. To our eyes, there is not a lot of difference between the two.

Q Finally, could you sum up for us your, and Quick's, chief goals and priorities over the coming few years?

DM: In a unique way, COVID-19 has validated the processes that we have worked very hard on, and the procedures and logistics plans. What we have learned is that everyone has a role, and it is important to keep our staff healthy and safe. This has served as a reminder that we should continue to focus and concentrate on that.

Our chief goal from a client perspective is to reinforce the early dialogue with a logistics provider. It is particularly important now, in the days that we are living in.

Our investment strategy continues to be very strong, and we have to bolster our staff in Europe and North America. We must demonstrate to every client that scale is important to us, and we want to make these relationships long-term. These are key objectives for us in 2020, and on into 2021.

We will continue to add value through some of our internal functions, for instance, enhancements of our IT systems. As an example, we have just unveiled a redesigned web portal which is very exciting to us and our clients.

The most important thing going forward is to continually refine our quality management program. This is something that could be a pain point if left unaddressed. You must have a very robust quality program.

We are enhancing our ground support in targeted cities. Many of these therapies are being administered by world-class oncology clinics throughout the country, so many organizations are using the same hospitals, clinics, and apheresis centers. Where we feel that it makes sense, we will put our own assets and resources in those cities to help with the process. This takes some planning and investment, and it is something we are committed to doing.

We also recruit and train on-site assets, meaning that if a client is really interested and has the volumes to substantiate it, we will put people on-site, to help them with some of the logistics issues they may have to navigate on a local basis.

Finally, for nearly 40 years we have been patient-centric, and that will continue. I think that is probably the biggest asset that we have – the singular mindset that everything we do is for the benefit of a patient. We will continue with that mindset.

BIOS

David Murphy

David Murphy is a 30-year veteran of The Quick Group of Companies, holding various leadership roles in Quick's Life Science division. Over the past 8 years, David has served as Executive Vice President of Quick's Life Science Division, and works closely with major healthcare organizations to develop specialized logistics solutions to safely transport human organs, tissue, blood and blood products for transplant or research. He also works with biotech and pharmaceutical companies to plan and implement transportation strategies for personalized medicine; including cell, gene and immunotherapy

DOI: 10.18609/cgti.2020.030

treatments. He develops scalable transportation solutions that preserve the product integrity of these life-saving shipments, and most importantly, the overall safety of patients. He helps to ensure adherence to the strict regulations of the life science industry and the chain of custody at every shipment milestone. David was instrumental in the logistics planning of the first FDA approved cancer vaccine, and subsequent commercialization roll out.

Adrian Lee-Mohan

Adrian Lee-Mohan has been with the Quick Group since 1990, and has held various management roles in operations, finance and sales. He develops strategic relationships with pharmaceutical and biotech companies throughout Europe, in order to provide comprehensive logistics solutions for their global supply chain, ensuring product integrity and patient safety. Adrian has extensive experience in clinical trial logistics, cold chain management and packaging solutions. His focus is on personalized medicine, establishing sound supply chain models for Cell/Gene/CAR-T/Immunotherapy, from all phases of clinical trials through to commercialization.

AUTHORSHIP & CONFLICT OF INTEREST

Contributions: *All named authors take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.*

Acknowledgements: *None.*

Disclosure and potential conflicts of interest: *The authors declare that they have no conflicts of interest.*

Funding declaration: *The authors received no financial support for the research, authorship and/or publication of this article.*

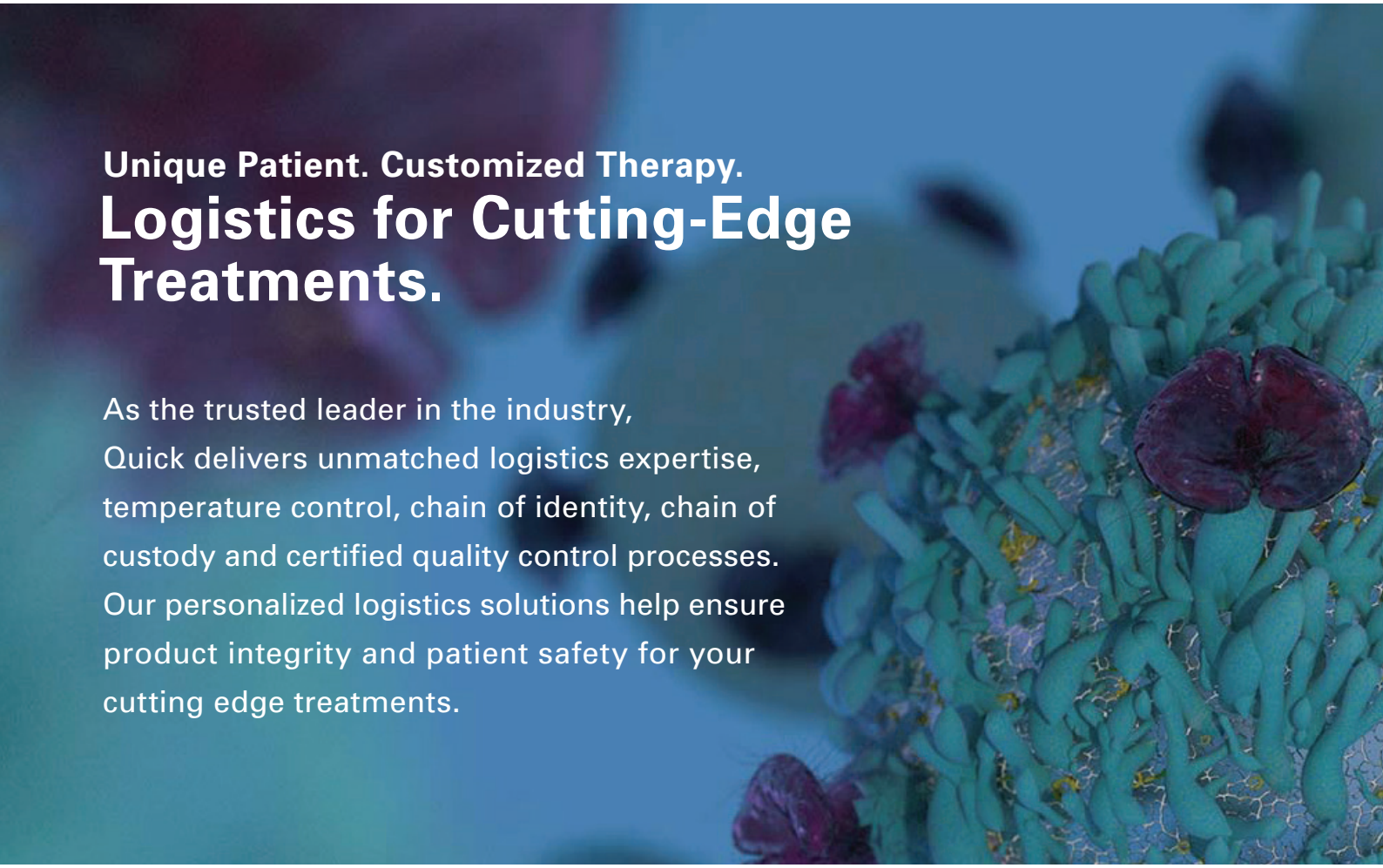
ARTICLE & COPYRIGHT INFORMATION

Article source: *Article written in Partnership with Quick.*

Interview conducted: *Sep 4 2020;* ***Publication date:*** *Oct 1 2020.*

Quick
A Kuehne + Nagel Company

PERSONALIZED LOGISTICS
FOR CELL & GENE THERAPIES



Unique Patient. Customized Therapy.

Logistics for Cutting-Edge Treatments.

As the trusted leader in the industry, Quick delivers unmatched logistics expertise, temperature control, chain of identity, chain of custody and certified quality control processes. Our personalized logistics solutions help ensure product integrity and patient safety for your cutting edge treatments.

- Global leader in personalized medicine transportation
- Preferred partner for the first FDA approved immunotherapy
- APH to infusion, clinical to commercial, scalable solutions and supply chain planning
- Temperature control and procurement of packaging systems for product and patient safety
- Regulatory expertise, quality and GDP protocols, full chain of custody
- Robust IT systems with real-time tracking and temperature monitoring
- Ability to support commercial growth with scalable IT systems and global footprint.

Learn more

or go to: https://quick.aero/ask-the-experts/

Life Science Solutions from the Quick Group

www.quick.aero