Viroclinics-DDL
A Cerba Research Company

Logistics For Cell & Gene Therapy Trials: Specific Needs Demand Special Skills

As of Q2 2022, there were over 2,800 cell and gene therapies (CGTs) in development across a range of therapeutic indications, covering increasingly broad patient populations.

However, there were still only 78 approved therapies at the time.[1] The industry is still learning its way in many respects. That includes clinical trials.

CGTs are focused very much on rare diseases. They have some of the same requirements as any other drug in clinical trials, but they also have their own, very specific needs with regards to logistics, support, and specialties. One very important challenge around the treatment of rare diseases is that it is difficult to generate economies of scale.

Any clinical trial for a rare disease is bound to be widely spread-out, which dictates the need for a specialized, tailor-made, on-demand type of logistical service support network. It is not possible to plan either in large volumes or around a fixed network. In some cases, it is impossible for patient samples to reach the central lab in the timeframe needed, so there must be a touchpoint with another lab within this to ensure quality and stability is sustained for a longer period. All this is particularly true in the later stages of clinical trials, even though the volumes of material required remain small.

"The demand can occur anywhere in the world," says Marc van Pruijssen, General Manager Clinical Trial Services & Logistic Excellence and Global Head of Logistics, Sample Handling & CTOS, which was founded in 2021 as the company's global logistics and clinical trial services operation.

"And typically, it needs to be reacted to very quickly and in a very precise way. A lot of attention is needed on the conditions to ensure the quality and the stability of the products, and then around the treatment so the trial can be captured in a very stable and secure way. It's not mainstream logistics, it's really specialized."

Extraordinary flexibility and agility are therefore needed. This is particularly the case for viral vectors, which are gaining a strong foothold in the CGT field and account for 80-90% of the total, by some estimates. The ability to deal with very fragile live samples, such as allergy samples, is a critical but rare capability among service providers. In addition, the assays used in CGT testing are unique and specialized. They therefore require a global network of specialized locations.

The other major general issue with trials in this relatively new area with few approved therapies, is that they are both customized and complex. Unlike, for example, an antiviral study or a vaccine study, which can usually be replicated with a little scaling up or down, there are no blueprints on how to deal with these types of studies.

Van Pruijssen cites the example of a top ten pharma client that set up a subsidiary in the cell and gene therapy field and did not know how to deal with the logistical side of it because there was hardly any reference framework.

Eventually, this company came to Viroclinics-DDL because it knew what the company could do for virology trials. Viroclinics-DDL therefore started the cold chain from scratch, and continuously developed and changed the requirements of the post-approval study.

Need for Specialized Providers

The need for a bespoke trial set-up for each product means that it is very important to work with a fixed and stable team. The team members need to be trained specifically on the requirements and to be able to put themselves into the shoes of the different stakeholders in the total chain to understand what is required and how items should be picked up and can be moved forward in order to guarantee the right stability, quality, and timeliness.

“It starts with a dedicated team that orchestrates the logistics activities and the supply chain structure to be applied, and then working with specialized partners in that chain, such as courier companies or import and export experts, in order to make sure that processes are executed in a seamless way,” says van Pruijssen. “It’s not a commodity. We’re talking about very precious services and products that need to be treated with special care and quality concerns. You need to have best-in-class, focused service providers to help execute the processes in the supply chain.”

The single biggest challenge Viroclinics-DDL has faced in terms of the cold chain requirements has been bringing products and services into and out of areas where a structured cold-chain set-up is lacking, including war zones. Partnerships and a creative approach to finding them are more vital than ever in this situation. The company’s approach isto look for local partners, and then link them to the global operators and service providers that it works with.

In one example, it had one of its premium couriers bring dry ice, including packaging, to the main airport of that country in the war zone. A local company that it had established contact with picked this all up, went into the warzone area and eventually brought back a sample that was needed for testing back to the airport, where a plane from the premium courier’s network was waiting.

Wide Geographical Spread

Having worked in most of the world's countries, Viroclinics-DDL has full global logistical coverage for its CGT business, including 40 of its own labs. The challenge is not just that the requirements are different from one region to another, but also that the number of cases are not equally spread across regions.

Whilst these expensive treatments and trials are more likely to take place in developed countries, they can also take place in upcoming economies where a major public healthcare effort is taking place. Moreover, it is very difficult to predict or forecast national or regional demand, or to predict the type and number of activities needing to be pursued.

As the drive for more diverse clinical trial partici–pants accelerates, there may well be more trials in previously underrepresented countries. This will add further complexity, because companies conducting trials have less experience in these countries and because of the weaker infrastructure. Nonetheless, van Pruijssen thinks that this challenge can be overcome.

"You can only gain the experience if you are involved in these types of countries, so that will help out with the development and infrastructures there," he says.

"If you are working in logistics, you have to work in scenarios. That also means that, where the infrastructural and service opportunities are limited or less developed, you have to make sure that you find ways to work around that. This is the intellectual and pragmatic challenge that supply chain professionals need to deal with, and typically like to do as well."

Among the most important tools in managing these supply chains are those related to spreading risk. At a generic level, this means having multiple sources available to cover service needs and agreements with multiple vendors in multiple geographical areas across the globe in order to make sure of having multiple entries of raising purchase orders and getting deliveries secured.

More specifically for CGT-related shipments, which typically travel with passenger flights, demand rose just as the number of flights going fell during the COVID-19 pandemic. This underlined the need to work with different courier companies and operators in order to have multiple access points to the available aircraft space needed to ship to specific locations.

Because it is not always possible to get samples to a central lab fast enough, however, it is necessary to build specific in-between steps to process a sample specifically, via a PBMC isolation or with other samples and by other means at another location in the global network. For example, in Viroclinics-DDL' case, specific samples from southern Argentina cannot reach its central lab in Rotterdam within the 48 hours before they expire. To address these issues, it has created a global network of labs that can sustain sample quality and stability for a longer period so that it can be processsed in the company's central lab.

Regulatory Considerations

Not surprisingly, the regulatory considerations around this complex part of the industry are correspon–dingly complex. Beyond the pharma guidance around CGT products, there are also compliance requirements that must be adhered to, including legislation around imports and exports, ADR for road transportation and IATA for air transportation, and clinical trials. Some of these vary considerably from region to region and from country to country.

In this context, it is critical not only for companies engaging in clinical trials but also for their service provider partners to adhere to industry standards. When making partnership decisions, it is key that they operate in a compliant manner to safeguard the progress of the therapy in clinical trials and development. When utilizing the services of multiple partners, for example in global trials where local lab support is required, it is very important to ensure these standards are also reflected in their operations. Accreditations such as ISO 15189 – which Viroclinics-DDL has – illustrate a commitment to high quality standards and adherence to regulatory requirements.

Finally, any reputable service provider will have its own quality management system and will only work with other partners who they are satisfied are fully compliant with all the regulatory requirements. Viroclinics-DDL itself requires proof of this upfront and also carries out periodic audits to double-check if they are still compliant and that their processes and tools and systems are properly equipped to stay that way. "So, it's not just an 'as is' validation, but also an 'it will be' validation," van Pruijssen says.

Data Management

Sound data management is also critical. Viroclinics-DDL seeks to capture the data as soon as possible upon collection of a sample from a patient, because this helps reconcile discrepancies on time and thus address any issues sooner rather than later and avoid too much repetitive and avoidable communication back-and-forth between sites. This also helps the patient, because it means having a stable, high-quality sample that is usable in trials.

As yet, there is very little existing data in the cell and gene therapy market, because it is so new and is still evolving. For sponsors, CDMOs and even the US FDA, continuous dialogue among all the industry players, on logistics as well as regulation, is essential. This is further complicated by the fact that almost all manufacturing and clinical trials are outsourced to a relatively small group of strategic players.

Quality is equally important as agility and flexibility. This obviously means having the right people on board and working with the best partners, but also relates to preparing all stakeholders, internal and external, about the specific needs of a trial. Service providers have to take time to prepare training materials and instruction sessions for any of the stakeholders or partners in the total chain of activities, including local CROs where they are used.

They must also train courier companies for specific trials to ensure that they understand everything necessary to ensure that the entire process will work seamlessly. Because there are so many things that can go wrong or questions that might arise that someone in the chain not fully understand, Viroclinics-DDL has a 24/7 helpdesk available to ensure that anything that comes to mind or is being considered as a potential hiccup, can be addressed as soon as possible.

Prioritizing Quality for Overall Cost Efficiencies

CGTs are very high value products with very specific requirements. Risks include shipment delays, damaged therapies, and expired patient samples. The consequences of these issues can be the halting of a clinical trial, stalling drug development. They can be ruinous for the sponsor. Worse still, they can be damaging, even fatal, to the patient if their samples are not processed in time, or incorrect data is not identified quickly.

CGTs are largely being developed for serious diseases – and they are mostly developed to cure, not just treat, those diseases. Viroclinics-DDL constantly tells its teams that they are not shipping materials, they are bringing a sample from a patient to a laboratory and the testing results are going to help the treatment of the patient.

Because of all this, it is essential that sponsors partner with the companies that have the right logistical expertise. This comes with a high initial cost but mitigates the risk to the product and barriers to progress that would be even more expensive for sponsors. Investing in logistics services upfront is essential to guarantee an efficient sample flow.

"Quality typically means higher cost upfront. But if you organize quality well and make that a primary target for the trial and for the sponsor, it will pay back in the end because the loss of samples and delays in processing and so forth will all have a huge impact on the outcome, or the timeliness of the outcome of the trial," van Pruijssen states.

"That has financial implications, but also potentially patient safety related issues. These are typically not visible upfront, and the cost associated with them is also typically not something that is openly shared upfront or even afterwards, but it is very relevant."

Conclusion

The rapid rise of CGTs is one of the most exciting developments in the whole pharmaceutical industry. They offer real hope of curing many serious, if rare, diseases. At the same time, however, there are many difficult challenges that need to be overcome if CGTs are to fulfil their promise and many of these involve the logistics of clinical trials for them. The consequences of mistakes can be ruinous for sponsors and even fatal for patients.

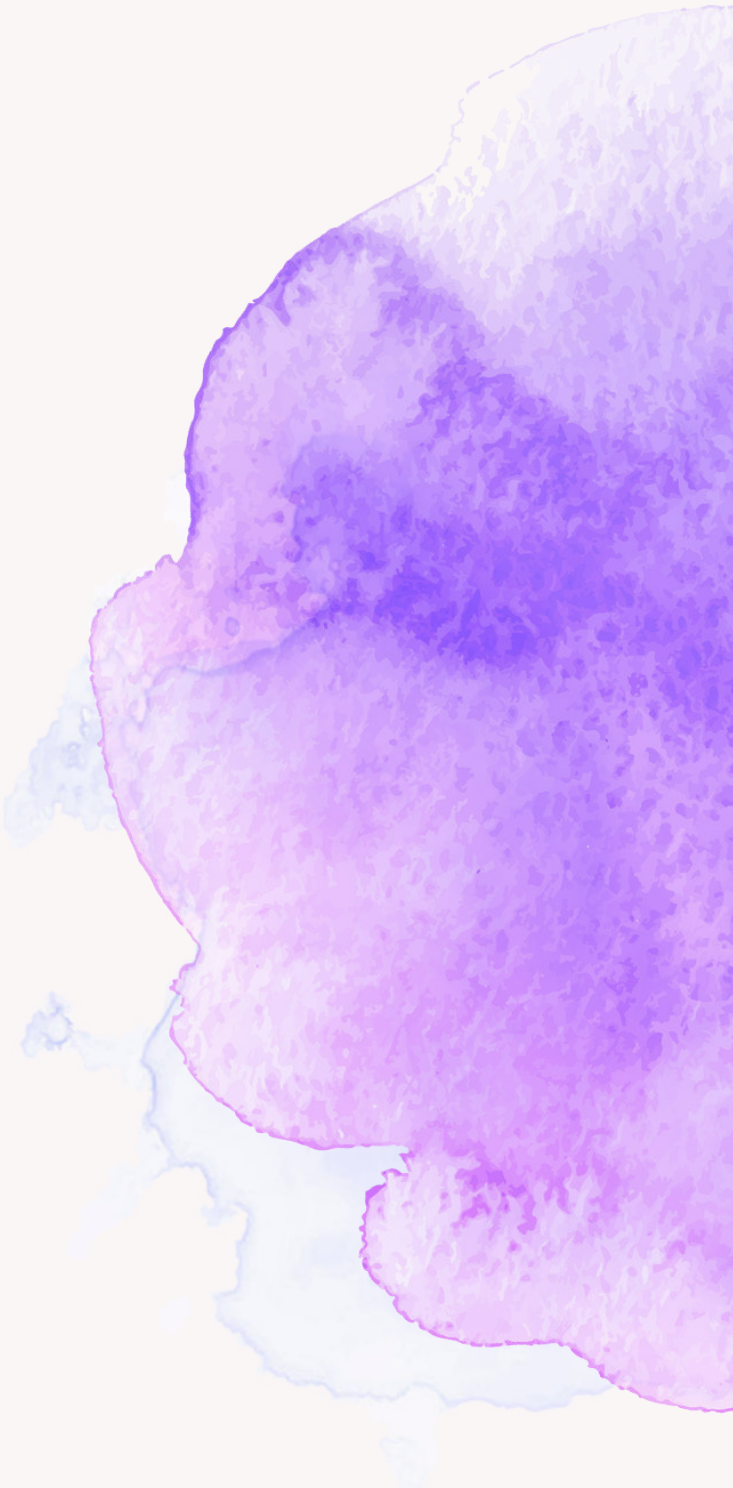
This is not something that all service providers can do. Specialized skills are needed, including the ability to offer a bespoke service for each trial and dedicated cold-chain capabilities. Service providers in this field must have truly global operations because of the global nature of the trials. They must also offer regulatory services in this field where the regulation is still undeveloped and varied, as well as data management services and logistical expertise.

Case Study

Viroclinics-DDLparticipated in the trial for a new viral vector-based therapy for Spinal Muscular Atrophy (SMA). SMA is a rare genetic condition affecting about one in 10,000 children. It is caused by having one missing gene or a deficiency in a functional survival neuron, resulting in rapid and irreversible loss of motor neurons. This then affects main muscle functions like breathing, swallowing, and basic movement. The treatment is administered to children under the age of two via a one-time intravenous infusion over the course of over an hour.

Each patient sample must be pre-screened for antibodies using the assays in the central laboratory. Shipping them from anywhere in the world in a certain amount of time and correctly is even more critical in this indication. The sample potentially represents a baby's life and any delay in transporting a sample may be fatal. Therefore, any logistical challenges must be overcome quickly and smoothly. The company team works seven days a week to bring in the samples, have them tested, then check and report the results immediately.

Because cases of SMA can occur anywhere, there can be severe logistical challenges, from COVID restrictions and closed borders to a lack of local sources of dry ice. Nonetheless, Viroclinics-DDL managed to create supply chains from scratch in some countries. The next steps, as the treatment is being approved in more countries and new markets, will be cooperation with external laboratories. This will allow the company to centralize and simplify sampling and logistical processes for the regions where difficulties were being faced, therefore decreasing transit times for the samples, and ultimately making the treatment available faster.



References

[1]. Pharma Intelligence & ASGCT, Gene, Cell, & RNA Therapy Landscape: Q2 2022 Quarterly Data Report (2022)

Who We Are

About Viroclinics-DDL

Viroclinics-DDL, A Cerba Research Company is the latest addition to the immunology and virology CRO Cerba Research. It supports clients in the pharmaceutical and biotechnology industries with global logistics solutions. The service portfolio is integrated through all phases of the clinical trial process and includes preparation of virology sampling kits, on-site sampling handling instruction, courier transport, sample tracking and tracing, management of sample processing labs, and post-study sample storage. It has an efficient logistical network, all over the globe with 40 operational sites in 26 different countries.

For more information, please see :
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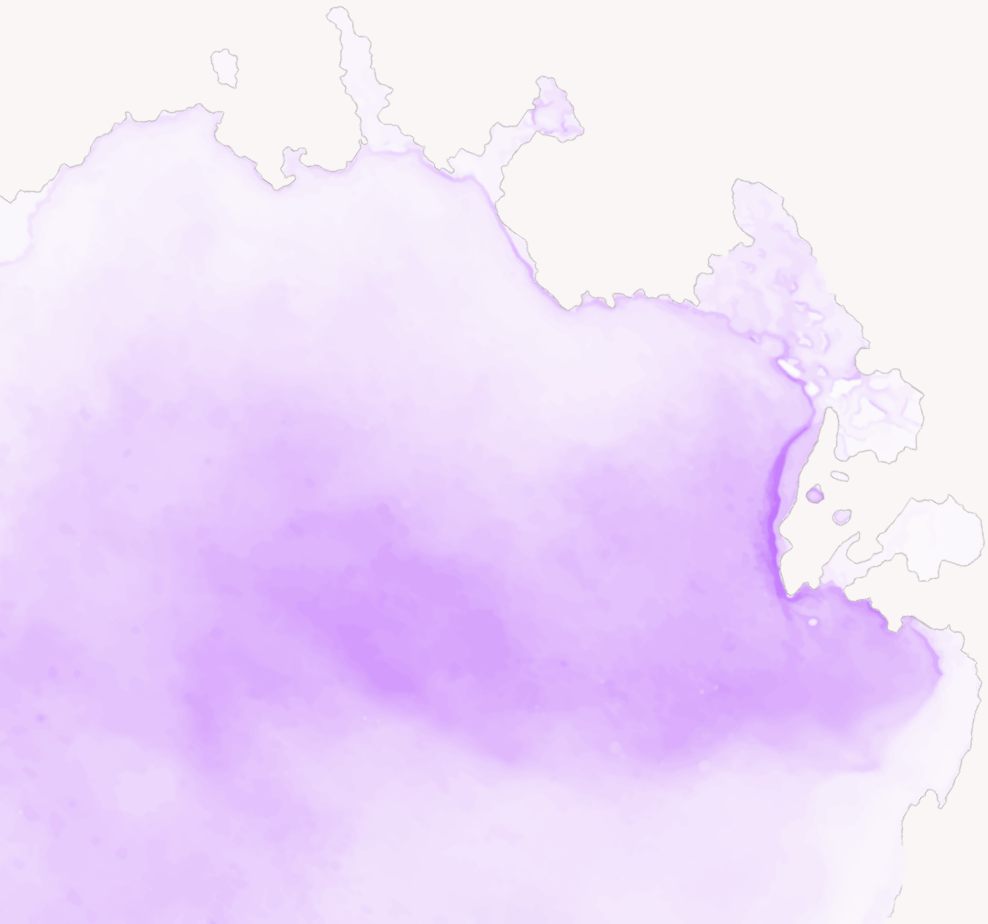

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