CLINICAL TRIALS

GREATER ACHIEVEMENTS, GREATER COMPLEXITY, GREATER COST?

Today, IVF is considered a mainstream medical treatment for fertility, with 500,000 'test tube' babies born every year. But back in 1978, it was a different story. Without privately funded clinical trials, Louise Brown, and over 8 million other children may never have been born at all.

Now, global economic uncertainty is driving up the cost of bringing new treatments to market. In this article, we take a look at the affordability and logistics of trialing complex medicines. And how learnings from the pandemic, including the standardization of mRNA testing, can make delivering more cost-effective trials possible.

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BENEFITS COME AT A COST

Indeed, with ever-more sophisticated medicines becoming viable, clinical trials have never had more potential to make a difference to lives all over the world. But there's a question hovering in the background. Quite simply, with more and more complex treatments to research, how will the increasing cost be met? In this, the first of our new series on hot issues in life science & healthcare, we'll discuss possible answers.

Firstly, it's only correct that, when healthcare professionals talk about their work on clinical trials, good patient outcomes are always their most important concern. Covid-19 has quite rightly been priority #1 but, moving forward, there's no shortage of other conditions people want to cure and plenty of ingenious suggestions for doing it. Medical science doesn't lack confidence. In fact, University College London's Professor Hugh Montgomery suggests the sector is "entering a new world of drug design and of trials".

What might hold back progress however is the plain fact that it all costs money. The average patient probably doesn't grasp the numbers behind the treatments they are receiving. An estimated $196 billion was spent on healthcare research and development, in 2021 alone. Within such sums, the sad truth is that most goes on 'learning curves', not actual treatments on hospital shelves; because clinical trials have an expected success rate of under 10%.

So, the mean '$2.6 billion' which the industry says it costs, to take a new drug from molecule to market, is easy to account for. And would many people bet on that huge price-tag shrinking, as the sector really starts to explore large-molecule treatments like mRNA vaccines or cell therapies?

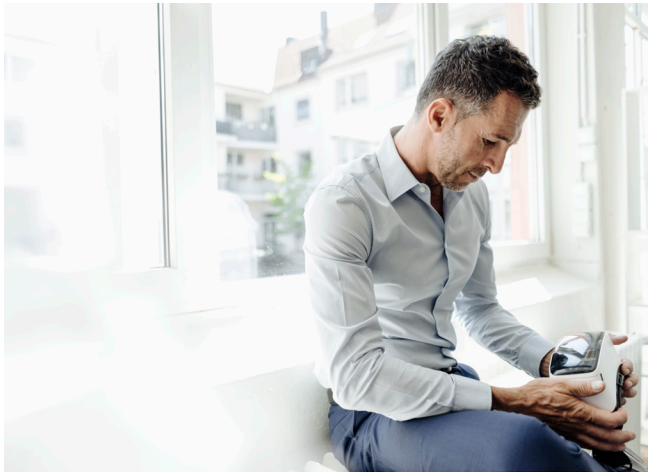
A very 'glass half-empty' prediction can be reasonably made namely, that trials will continue to become more and more involved, and complex, with costs rising accordingly. It's easy to see how a combination of those two things could restrict investment and slow medical advances.

However, we like our 'glass to be half-full'. So, we convened a group of DHL life science and healthcare specialists to brainstorm a few ways sponsors might cover trial costs, in future.

MAKING IT HAPPEN – WHAT ARE THE OPTIONS?

Their first suggestion was probably the easiest to understand, but also to dismiss. Pharmaceutical companies could simply write bigger and bigger checks for R&D, in anticipation of recouping their investment.

Higher investment isn't an entirely unreasonable expectation, from an industry with famously 'deep pockets. However, there are plenty of negative economic indicators on the horizon right now, largely as a result of events in Eastern Europe. So, relying on a so-called 'bull market' to cover the increased clinical trials costs over the next few years may not work out. But here's the good news. There are two ways in which forward progress is being made and savings can result.



Firstly, and simply, we have IT. The exponential development of technology means not just 'clever' but 'fast' too. In just four hours, today's super-computers can learn the game of chess, from scratch, and become able to beat any player on the planet. That same power is finally capable of analyzing all the potential interactions arising within, for example, the millions of proteins present in a human blood sample. The scope of what a trial can achieve is being transformed.

Alongside this, Professor Montgomery says, such trials "will now happen at the speed of light". Intuitively, if trials are faster, they are likely to become more affordable. Affordable trials are more likely to be completed. More completed trials means more new medicines: a virtuous circle.

Of course, the capability of machines to conduct faster trials in future needs to be seen alongside the challenges of reaching and interacting with real human beings, out in the field. And it's here where we see our second reason for optimism.

Based on current and past experience, our firm belief is that standardization of trials practice, particularly where movement of vital samples are concerned, will become possible even in the most challenging areas.

It's already happening. Since early 2021 the world has seen rollout of huge volumes of successfully tested mRNA vaccines, requiring delivery at controlled temperatures down to -70°C and thus highly specialized packaging and monitoring.

Not everyone realizes that not only did most of these billions of approved doses go through carriers such as DHL, but those same globally integrated providers had assisted the original clinical trials in 2020. The new standardized practices created, to enable vaccine development, now have the capability to deliver lower costs into the future.

TRIALS COSTS HAVE ALREADY BEEN TRANSFORMED VIA NEW PRACTICE

Globally DHL 's Medical Express now handles 10,000 clinical trial samples a day. As far as sponsor costs is concerned, the math is surely easy to do.

A decade later and the combination of urgency and breadth needed for the clinical trials programme on mRNA coronavirus treatments soon resulted in a similar step change. In this instance, DHL's solution combined excellent facilities and very strong integration of services. Small batches or individual samples went via Medical Express, bulk deliveries utilised temperature-controlled warehousing and freight forwarding.

Most of the assets required were in place already. DHL had invested in global freezer capacity and partnered with providers of specialist packaging to ensure that the tricky 'last mile' of any delivery remains at the target temperature. Coronavirus tested this capacity. It did not fail.

"We've seen mRNA vaccine clinical trials, in terms of logistics, standardized with sponsors like Pfizer acting as the original driving force," says one DHL customer at a leading CRO. "As with blood samples previously, we expect costs to stay down compared to their old levels".

We are also confident DHL and our sector will continue to innovate cost effectively, in response to the growing requirement for mRNA vaccine trials.

Of course, there's always a new challenge around the corner. In this case, it's called 'cell and gene therapy'. And it's a whole new ball game.

If so, and we're suggesting a historic trend towards standardization of trials, and resulting economies, will it apply here? Let's understand the context, first of all.

"It's a pattern we have seen before. Back in 2009 we responded to demand from CRO's and developed solutions to reduce blood sample carriage cost from $1,000, via specialist couriers, to as little as $200."

Sanjiv Menon
Global and Multi-National Customers
DHL Express

NEW TREATMENTS, NEW TRIAL REQUIREMENTS

Cell & gene therapy, like any new technology, is probably at its most costly right now. And that's certainly expensive – one estimate suggests a $45 billion annual cost, to American health insurers alone, from FDA approved treatments by 2030.

One way to reduce this eventual patient cost and make better outcomes more widely available will be to lower the investment bill for clinical trials, in what is a highly technical area.

However, achieving that will not be a matter of bulk forwarding or anything similar. C&GT samples are completely individual - that's basically the point of the treatment.

Carriage temperatures of -150 C to -196 C are required, implying liquid nitrogen (LN2) packaging as well as peripheral improvements to things like building management standards.

So, we have a growing temperature management challenge for the industry. It's accompanied by a requirement to get treatments, from vein to vein, both at high-speed and with total visibility to the CRO or sponsor.

DHL partner CryoPDP provides ultralow temperature packaging solutions within our current activities in cell & gene. Their analysis of the delicacy of the C&GT task is uncompromising:

> "These products are significantly more fragile and valuable than most small molecule or medicines. Damage to products during shipping is not always evident. Damaged cell and gene products do not change in smell, colour or other physical ways. Slight temperature deviations can render the product ineffective (as can) minor physical damage."

> "In a global environment the specification and diligence in packaging and transportation... vary significantly, resulting in considerable risk and potential loss of irreplaceable therapies".

AN OPTIMISTIC SCENARIO, BUT A LOT OF WORK TO DO

The implication is clear – there is a strong motive to eliminate errors by better practice and standardization would certainly help. If so, however, as we've seen previously, establishing and maintaining high quality standardized logistics will also reduce costs both directly (per sample) and indirectly (through more successful trials).

Sounds great. But what's the scope for actually doing that? We spoke to the Global C&GT transport manager of a leading Biopharma company for their view, the following is what they shared with us:

"We certainly see plenty of room for improvement in cell and gene logistics. Start with the obvious. We need ***transport lead***-times, including customs and HA clearance, between same day and a maximum 48-hours, internationally. ***Monitoring*** is next – chain of custody and identity capabilities need to be supported with scanning technology. And we want 24/7 monitoring and intervention in transit, as standard."

They continued, "We've seen issues in the past with a lack of ***consistent building management standards*** – fixing that is another possible 'win'.

Hospital interaction is another area. How do systems integrate between the cell therapy manufacturer and the supply chain platforms? Is there a good level of ***visibility and management***, on top of the basic courier service execution? Is shipping and receiving, between hospitals and drivers, an intuitive process?"

"Last but not least, who is doing all this? Are we dealing with properly ***trained control tower staff*** and drivers, and are they working on this type of delivery enough to increase familiarity?"

DHL – WORKING HARD TO MAKE IT HAPPEN

Certainly, there is a long 'to do' list there, but providers like DHL are working hard on it and making progress. This is not even an option, by the way – June 2020's ISO 21973 forces trial sponsors to adhere to new standards on cell & gene transportation.

In our experts' view, however, doing the right thing legally is also going to bring down costs in the long-term. After all, as Sanjiv Menon suggests above, 'there is basically a pattern here'. Complication leads to cost, then standardization creates efficiency and lowers cost. We look forward to seeing how quickly we and our sector, can make this a reality.

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