



Challenges in an Uneven Environment

Choosing the correct partner companies for a logistics operation involving biological products is always tricky, and a range of questions and requirements must be identified to make the right decision

Federico Lupp at LifeConEx

The biopharmaceutical sector experienced higher growth in the last five to 10 years than any of its senior counterparts in the traditional pharmaceutical sector. In addition to the regulatory challenges, the growth in the biopharmaceutical sector has brought significant challenges to the transportation of these products. Biopharmaceuticals are medical drugs produced using biotechnology and their drugs comprise the fastest growing sector in drug development; indeed, they are expected to account for more than 50 per cent of new product approvals by 2015 and 71 per cent by 2025.

'-196C-20C228CCRT' is not an encrypted code from Dan Brown. It is the common representation of the temperature change seen throughout the developmental stages of a biopharmaceutical product, from the research infancy stage to the global distribution of the finished product. In addition to focusing on good distribution

practices (GDP), all life science companies are increasingly reviewing this in their effort to ensure optimal delivery to the patients. Packaging companies have been investing significant time and resources to develop better and stronger packaging to ensure that biopharmaceutical products hold up to the extreme challenges they face during a 'typical' journey in Tier 1 (primary distribution) or Tier 2 (secondary distribution).

Challenges of Biologics

In our efforts to provide state-of-the-art services, should we reconsider the use of the word 'typical', or should it be erased from the distribution and logistics vocabulary? Can we predict seasonal patterns? In 2010, Europe started with a very cold autumn and experienced massive snowfalls in early December. Were shipping companies prepared for these extreme weather

conditions? Are we assuming too many steps will happen along the complex global cold chain? Can we trust that a temperature data logger will provide all of the answers?

As the majority of biopharmaceutical products have been developed from proteins, particular considerations have to be taken into account. Finished biopharmaceutical products do not tolerate freezing temperatures; when exposed to these temperatures the proteins denaturalise resulting in crystals that destroy their viability and, ultimately, their efficacy. Transporting early stage products is manageable when dry ice is



utilised, as it supports temperature control. This can only be assured, however, with controlled packaging and applied calculations of the rate of dry ice sublimation. There are additional factors which distinguish biopharmaceutical products from traditional pharmaceutical products; such as a very high value per single dose – ranging from double to triple that of traditional pharmaceuticals and beyond – and the fact that several of these products target very small population groups.

A shorter product lifespan presents additional logistical challenges for the biopharmaceutical industry. Considerations include: provision of the safest and most optimal transportation routes; qualification and utilisation of specialised containers; dedicated security features on the ground and in the air; and last but not least, shock sensitivity. A more thorough analysis of shock sensitivity is required in order to evaluate the capacity of passive solutions, as well as a review of active cool container types to address this requirement properly.

Essential Considerations

A review of the different process steps in the elaboration of a biopharmaceutical product indicates the differing temperature demands of these products (see Figure 1). This would not be a challenge in the event that all of the steps were to happen at the same site. The sobering reality presented by global sourcing, manufacturing and supply have brought unique challenges for drug manufacturers, transportation companies

and regulatory agencies. Are we prepared to support the transportation of products which need to be kept either deep frozen (-20°C), at 2°C to 8°C or within controlled room temperature (+15°C to +25°C) ranges? We should also consider whether the management of end-to-end transportation processes prevents loss and minimises risk, if we have a proper primary and contingency plan in place and whether we are working with experts who are familiar with the global infrastructure of the cold chain. A holistic review would be appropriate.

To be able to ascertain the challenges involved, one should run quality risk assessments with service providers and establish level-frequency of performance management, and go deep into the infrastructure of your chosen providers. Perform an audit, plan a visit, go and see if you are getting what was promised at the sales pitch. Run this exercise with the freight forwarder you will be working with, as it is important to identify their capabilities, how well trained their staff are, whether they have written processes such as training logs, and what lies behind their concepts of the 'control tower' and the 'competence centre'. Are these merely fashionable words? Is the promise larger than the reality?

Visit the trucking companies, airlines and ground handling agents. Ask to see where your products will be kept. What processes do these airlines have for temperature-controlled life science products? Find out what contingency plans they have implemented, how they will handle your passive cooling box and where it will be stored. How would they

know when to store it in a specific cold room? Would the indication of a 2°C to 8°C product be enough that freight forwarders highlight this on the master airway bill, their contract with the airlines? Who exactly ensures that this level of communication is really happening? Continue to dig

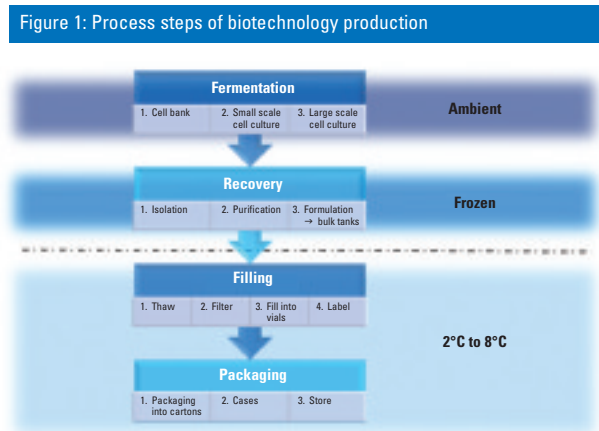
deeper. Is one cold chamber similar to another? Of course not – calibration, size, segregation of products and alarms to trigger when running out of set points all vary. In addition, we should know more than one airport in the chain, as the product that has taken so much time in the research and development phase is finally approaching the market – no failures are allowed.

What about the airlines? The airlines do not use the same type of aircraft. They would have purchased different types of additional equipment, depending on their core business. It is important to know if they are prepared to transport temperature-sensitive products, they have specific processes for transporting your products from their warehouses, to the tarmac and onto the aircraft, and if they truly understand your needs and, most importantly, can they deliver?

We have to be diligent and strive to obtain more and more data, but then what? Some might feel they have purchased the strongest packaging solution available on the market and have given it to the experts. Or perhaps the plan is to rent a cool container from any brand or type, and rely on the technology to manage itself. Are these all self contained? The answer, of course, is that the packaging is only as strong as the process that it follows.

We have identified that clear, standard operating procedures (SOPs) must be designed, implemented and executed. They must encompass all parties along the entire supply chain in order to document the expectations for that very specific biopharmaceutical product profile. The number of suppliers in a global supply chain should be identified – a route between Paris and Jakarta can easily have over 10. All have their own roles in the global transportation process. But how do we ensure that the chosen packaging will navigate flawlessly and maintain the integrity of the products throughout the process?

If the packaging is only as good as the process that it follows, who follows the process and ensures that all steps are followed as planned? Validation times



must be taken into consideration. Does the Jakarta ground handler know when to place the passive cool box/pallet shipper into a specific cold chamber (we assume they know and that they have different chambers with specific set points)? Establish whether the validation of the packaging is still running. Early cold storage would freeze the 2°C to 8°C biopharmaceutical product and ruin its efficacy.

There are similar concerns when ensuring the knowledge of how to handle a cool container is in place, as well as how to check the battery and voltage percentage levels. If the chosen cool container uses dry ice, this method should be available when the product arrives at a less than ideal time, such as a public holiday. Who can we contact? Contingencies need to be put in place.

Of equal importance is the issue of what we do with the 'bad' news. Do we report the problems and wait until the weekend is over? During this time the products might have been stored in incorrect temperature conditions. In the case of finished biopharmaceutical products, the slightest amount of time outside of the product's specific temperature range can affect its efficacy. We need real-time intervention management in order to avoid temperature deviations.

Deviation from the SOP, resulting in temperature excursions, will delay the import and sale of the product. Even a single day of delay in the total transportation can have a major impact on 'non-sales' resulting from failure to sell the product. Do we believe the following expectations are achievable? We need to create macro-SOPs which involve all parties in the entire transportation chain, regardless of the size of their role. All participants can create significant risk for your temperature-sensitive product. We need to ensure that every party is aware of its responsibilities and duties, and they need to make themselves accountable. We need to ensure that all expectations are met as per the agreement. In the event that problems do arise, we need to ensure that appropriate contingency protocols are in place and operating correctly.

Basically, we could say that there is a need for constant quality assurance, in order to achieve process qualification, and that every process must be monitored and measured to ensure that it will ultimately deliver the requested level of quality.

In a 2008 study, participants were asked to discuss the financial costs which arise from non-compliance (temperature excursions in the logistics process) in the global transportation sector (1). Individuals at several mid-sized life science companies estimated that the overall costs amounted to 180 working days per year, with the addition of costly personnel expenses. This is a staggeringly high cost to be paid for non-compliance of transportation industry standards – and this does not include the costs involved in the potential loss of product, loss of sales and the health authority's intervention.

However, after collecting experiences, what shall be done with the information? Do not underestimate the importance of understanding data and seeking a retrospective analysis. Post-shipment evaluations, and even claims, should not be seen as a financial dispute, but rather as a continuous improvement process leading to root cause and corrective actions. This is also why biotechnology and pharmaceutical companies should see freight forwarders, airlines and ground handling agents as an extension of themselves – a true partnership leading to continuous quality improvement.

Transportation companies must understand that a temperature-sensitive supply chain is not just a matter of a nice marketing campaign, but rather of operational excellence. Performance is not going to be demonstrated in meeting rooms. Sooner or later, the temperature monitoring device (or temperature data logger) will reveal the weakest link in the process. There should be no reason to over-sell a

transportation solution. The aim should be to realistically present its strengths and weakness, in order to collaboratively select the most appropriate option.

Last but not least, regulatory control from health authorities is growing and will continue to increase in the future. Pharmaceutical and biotechnology companies will have to continue to prove that their designed shipping processes are able to meet all labelled storage requirements for their products, including during transportation. This can only be achieved by building a good partnership, robust process definition and continuous control of shipments.

Conclusion

Have we been diligent? Have we taken all steps into consideration to eliminate the risk along the temperature-sensitive supply chain for our high value biopharmaceutical product? Collect data, and don't let encrypted codes paralyse you. Bring all experts to the table and share information. Proper collaboration and a well-designed, solid plan will be the key to success.

Reference

1. Cost incurred through insufficient logistic quality by Novumed, www.lifeconex.com/Apps/News3/Uploaded/novumed_press_release.pdf

About the Author



Federico Lupp has been the Head of Sales Europe and Latin America at LifeConEx since September 2007, and was previously a Sales Manager at the company. Before joining LifeConEx, he was a Global Industry Manager for the Americas at Lufthansa Cargo. Prior to his transfer to the US in 2002, he was based in Buenos Aires, Argentina, where he served as a regional Business Development Manager for the pharmaceutical, automotive and telecom industry for Lufthansa Cargo's South American operations. He attended Veterinary Medicine School at the Universidad de Buenos Aires, where he obtained his Master's degree. Email: sales.marketing@lifeconex.com