State of the Industry Report

Pharmaceutical Supply Chain Challenges
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Executive Summary</td>
</tr>
<tr>
<td>4</td>
<td>Introduction</td>
</tr>
<tr>
<td>6</td>
<td>Respondent Demographics</td>
</tr>
<tr>
<td>10</td>
<td>Logistics Challenges: Overview</td>
</tr>
<tr>
<td>13</td>
<td>Logistics Challenges by Area</td>
</tr>
<tr>
<td>14</td>
<td>Cell and Gene Therapy</td>
</tr>
<tr>
<td>16</td>
<td>Clinical Trial Logistics</td>
</tr>
<tr>
<td>18</td>
<td>Commercialization</td>
</tr>
<tr>
<td>20</td>
<td>Direct-to-Patient Trials</td>
</tr>
<tr>
<td>22</td>
<td>Market Access</td>
</tr>
<tr>
<td>24</td>
<td>Orphan and Rare Disease Drugs</td>
</tr>
<tr>
<td>26</td>
<td>Pharmaceutical Storage</td>
</tr>
<tr>
<td>28</td>
<td>Conclusions</td>
</tr>
<tr>
<td>29</td>
<td>Content Library</td>
</tr>
</tbody>
</table>
The pharmaceutical supply chain is rapidly evolving with innovation driving new trends such as Advanced Therapeutic Medicinal Product (ATMP) and Direct-to-Patient distribution, together with the rise of specialty drugs. These new approaches and treatments are considered value-add services to patients, however they also bring new challenges to both clinical and commercial supply chains.

To get a better understanding of these challenges, World Courier produced a survey of 481 pharmaceutical professionals to learn more about their daily logistics challenges. The survey targeted primarily decision makers such as managers, directors and senior executives, which equated to 65% of respondents within the Nordics, Central and Eastern Europe.

Results from the survey showed a strong consensus among professionals in regards to the challenges faced. Regardless of country, therapeutic area, company size or type, 60% of respondents agreed that temperature control and packaging is the biggest challenge they are facing. Import-export documentation (39%) and risk management (37%) were rated the next major pain points among professionals.

Respondents also recognized knowledge gaps as a key logistics challenge; 20% see knowledge gaps in clinical trials, 18% in Direct-to-Patient services and 16% in cell and gene therapy. The former comes as no surprise as the complexity of clinical trials within the highly-regulated pharmaceutical industry is constantly increasing; whereas the latter two are growing trends of the pharmaceutical industry.
About the Survey

This research was conducted to analyze current challenges within the pharmaceutical supply chain. To accomplish this objective, a specific geographic location—representative of language, culture, regulatory framework, weather conditions, customs and duties—was chosen. This region, NCEE (Nordics, Central and Eastern Europe) includes all countries listed in chart figure 1 (page 6).

Patient access and healthcare characteristics, together with stabilized start-up rules and regulations, make the CEE (Central and Eastern Europe) region attractive for patient recruitment in clinical studies. The Nordic countries are well known for advanced and innovative medical research.

Recent data on the increase in clinical sites has shown significant attention being paid to NCEE in recent years, with a reported growth rate in the region of over 12% in 5 years* not solely on hard parameters, such as geography, population size or costs, but involving other “soft” factors, such as the supportive environments and qualified local staff.

The online survey consisted of 14 questions addressing different areas within the pharmaceutical supply chain, from clinical to commercial. To ensure impartial analysis, the survey respondents remained anonymous. The demographic breakdown and external stakeholder analysis is listed below.

Limitations of the Research

The pharmaceutical market is highly regulated with confidentiality an important aspect from both a business and patient viewpoint. As a result, no specific company trends are traceable within this report. All survey questions were structured as multiple choice in order to facilitate data analysis and thus, may not capture all specificities of the complex pharmaceutical environment.

The geographic region represents a relevant starting point for the research on pharmaceutical supply chain challenges.
Q1. Which country are you located in?

This survey focused primarily on the NCEE region, and as such the majority of respondents are from the Nordics, Central and Eastern Europe. This region was chosen because of the diversity of countries, languages, cultures, status of infrastructure and inclusion (or not) within EU regulations.

Q2. In what type of company do you work?

77% of the respondents are from pharmaceutical or biotechnology companies or Contract Research Organization’s (CROs). This analysis therefore provides insight from both sponsors and suppliers.
Q3. Company size of respondents?

The survey is representative of all company sizes providing a balanced market overview. Almost half of survey respondents are employed by large companies, followed by 28% from small companies and 26% from medium-sized companies.

Q4. What department do you work in?

The respondents are highly representative of key major involvement areas within supply chains giving a robust perspective of the challenges. These departments include research, logistics, quality departments and management.
Q5. What is your job title?
The survey primarily focused on company decision makers such as managers, directors and senior executives, who equate to over 65% of respondents.

Q6. Do you work with clinical or commercial supply chains?
The answer to this question indicates that approximately one third of the respondents (37%) cover the entire supply chain in their role.
Q7. Do you deal with domestic or international shipments?

78% of respondents handle both domestic and international shipments. This reflects the set up of the region where countries can be involved in both local and across border shipments, which requires transport via air or road to cross borders. This is in addition to the need for seamlessly precompiled customs documentation to avoid delays.
The top three logistics challenges rated in this survey illustrate the spectrum of the commercial and clinical supply chain well, and are in line with World Courier’s experience based on our daily discussions with customers. As a company we also see a clear trend towards personalization within the pharmaceutical supply chain, which is being driven by innovations such as cell and gene therapies, better patient access to medications and therapies with patient-centric models gaining importance. World Courier expects to see a continual rise in demand for personalized specialty logistics in the future.

Specifically in NCEE, pharmaceutical storage and distribution for clinical trials form part of the critical path to logistical success. In this region—where winter temperatures can drop way below freezing and summer temperatures well above 30°C—temperature control is crucial. Clinical products undergo stability studies to define the range of chemical stability for each specific substance (drug substance and drug product). The defined product range of stability ensures that the product remains safe and effective for use, and must not be stored outside of that range. That same range needs to be applied when distributing the product.

Jens Mattuschka
Regional Vice President
Nordics, Central and Eastern Europe
World Courier
The temperature sensitivity of pharmaceutical products and their appropriate packaging remain key challenges in the pharmaceutical industry. Today 60% of respondents regarded these as major challenges, which is in line with what we hear from customers. This is because delivering to remote or complicated locations, with unavoidable weather conditions, customs inspections and other unexpected delays can make it difficult to maintain product integrity.

In the pharmaceutical industry patient safety is the ultimate goal. To ensure this, regulatory authorities require complete traceability and quality standards to be applied across the entire supply chain of a pharmaceutical product. This means that all containers for shipments need to be validated and qualified accordingly. It is therefore vital to use a validated shipper that is qualified to maintain the required temperature conditions in case of delays in transit. When crossing borders, a success factor for time-critical shipments is the correct preparation of customs documentation. This must be built into the supply chain strategy with a robust risk management plan.

Jens Mattuschka
Regional Vice President
Nordics, Central and Eastern Europe
World Courier
Q10. Where do you see a current knowledge gap in the industry?

Direct-to-Patient services and cell and gene therapies are relatively new, innovative solutions to the industry. Because of this, many pharmaceutical companies seek additional consulting when such shipments arise. This is because clinical trials are becoming more complex, and only successful when a product-specific logistics strategy is clearly defined, ideally as early as possible in the process. Every clinical study design is unique, meaning the successful launch of one pharmaceutical product does not imply success of the next when following the same itinerary. This requires constant learning and updates to be provided on any and all changes in customs in the patient recruitment countries.

Material logistics includes all physical movements at the correct temperature, from storage and distribution through to patient sample collection and shipment to specialized labs. Specific or specialized testing may take place in a limited number of labs, meaning it may also be necessary to send that sample to a laboratory in another country to perform analysis, which requires customs clearance. Every patient sample is unique and a delay at customs can easily compromise the integrity of the sample, which could mean the loss of study-critical information. Therefore, it is crucial to be aware of current requirements and fill any knowledge gap.

Jens Mattuschka
Regional Vice President
Nordics, Central and Eastern Europe
World Courier
LOGISTICS CHALLENGES BY AREA:

CELL AND GENE THERAPY

Q11. In your opinion, how challenging is daily logistics in cell and gene therapy?

![Figure 11](image)

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Extremely challenging 20%
Q12. In your opinion, what are the biggest challenges in logistics in cell and gene therapy currently?

Survey respondents indicated that managing time and temperature are key parameters that therapy developers are focused on now. This is driving a trend within logistics and is why World Courier remains focused on completing documentation in advance of transport, to be able to start and monitor shipments vein-to-vein.

Cell and gene therapies often involve the transport of live cells and therefore operate under time-sensitive and temperature-critical parameters, and need to be exempt from x-ray. This creates the issue of maintaining temperature by utilizing the right packaging system and quickly transitioning customs challenges. These are challenges that therapy developers need to work on with their logistics partners early in the process.

The way to address these issues is to create a vision of the commercial scale supply chain, defining the critical parameters and risk points. This vision can then be used to build, test and optimize a logistics platform through the clinical trial process and ensure that there is a system ready for commercial.

Simon Ellison
Cell and Gene Therapy Service Director
World Courier
Q13. In your opinion, how challenging is daily logistics in clinical trial logistics?

Q14. In your opinion, what are the biggest challenges in clinical trial logistics currently?

- Temperature control, packaging
- Import-export documentation, customs clearance
- Risk management, contingency planning
- Quality Assurance, regulatory
- Visibility of the supply chain
- Changes in demand
- Other
With 77% of respondents from pharmaceutical or biotechnology companies, or CRO’s, it is not surprising that clinical trial logistics are the primary challenge for survey respondents. This is because the material flow of a drug product—from distribution to patient sample collection—remains the critical aspect in determining the success of a trial and ultimately its product launch.

Temperature control and correct documentation for customs clearance are the top challenges to meet according to the NCEE survey. This is in line with the geographic and political landscape of this region; consisting of countries with several languages, specific EU/ non-EU import/export requirements where expert knowledge is needed to seamlessly manage clinical shipments. The key to success is to partner with an experienced logistics provider with global expertise, yet local customs knowledge. This ensures there are no delays as a result of correctly prepared clearance paperwork and constant dialogue with local customs officials.


Raffaele Laciti, MBA
Product Manager, Clinical Trial Supply
Nordics, Central and Eastern Europe
World Courier
Q15. In your opinion, how challenging is daily logistics in commercialization?

Q16. In your opinion, what are the biggest logistics challenges in commercialization?
The majority of drugs on the market today are still classic active substances made of small, chemically-manufactured molecules. However, biologics—made of large molecules that require administration via injections—are on the rise. It is not surprising then, that temperature-controlled packaging is regarded as the number one challenge related to drug commercialization.

Launching a new medication—especially when it is a first-in-class drug—also raises risk in terms of undefined potential demands and inaccurate forecasts. As pharmaceutical product portfolios in general become more diversified and complex, this will create additional complexity for commercialization and in managing the supply chain of those rapidly changing portfolios.

Import-export documentation and customs clearance are further key challenges relating to drug commercialization. With extensive research and development cycles this raises the importance of speed to market to be able to satisfy the given demand. Each delay in transport e.g. at customs, is often caused by incorrect documentation. However within this industry, every day and hour counts, as there are patients desperately waiting for the particular treatment.

Christopher Engel
Product Manager - Commercial Supply Chain
Nordics, Central and Eastern Europe
World Courier
**Q17. In your opinion, how challenging is daily logistics in Direct-to-Patient trials?**

![Figure 17: Not challenging 2%](image)

**Q18. In your opinion, what are the biggest challenges in logistics regarding Direct-to-Patient trials?**

![Figure 18: Temperature control, packaging 57%, Import-export documentation, customs clearance 38%, Risk management, contingency planning 32%, Quality Assurance, regulatory 30%, Visibility of the supply chain 32%, Changes in demand 21%](image)
Planning and running Direct-to-Patient models, especially clinical, whilst ensuring a robust quality management system is in place around the program, can be quite complex. Most respondents noted temperature control and packaging as a major challenge in this respect, which makes sense given the challenges around verifying temperature results on delivery to a patient’s home. The drug is often administered a short time after arrival, however quality—meaning no temperature deviations—must be verified prior to this.

It is also no surprise that few respondents noted import-export customs as a logistics challenge for Direct-to-Patient. Logistics for Direct-to-Patient generally occurs domestically or within the regions around investigator sites or clinics/hospitals.

Mike Sweeney
Senior Director, Patient Centric Logistics
World Courier
Q19. In your opinion, how challenging is daily logistics regarding market access?

Q20. In your opinion, what are the biggest challenges in logistics regarding market access?
In asking respondents to rate their logistics challenges as they apply to market access, it is not surprising that ‘regulations and quality assurance’ scores highest. In all other survey areas—clinical trials, Direct-to-Patient etc.—this topic ranks much lower, as temperature control and packaging are considered more critical to the shipment.

This reflects what we as market access consultants see in our daily work, especially in relation to the effort we spend on regulatory topics and paperwork, including the submission for benefit assessment to HTA authorities.

In terms of temperature control, I see key challenges arise when ensuring and maintaining the right temperature for particular distribution channels. Manufacturers have the responsibility to secure the quality and control of the product. If they can’t deliver e.g. due to a temperature deviation during transport, this may cause bad publicity and more importantly, a temporary shortage of the product and potential loss of income. New cell and gene therapies put further pressure on the manufacturer with the combination of a high-value product and increasing packaging requirements, as they require liquid nitrogen containers.

Dr. Ulrike Kuchenbecker
Director, Health Economics
Xcenda
Q21. In your opinion, how challenging is daily logistics of orphan and rare disease drugs?

Q22. In your opinion, what are the biggest challenges in logistics of orphan and rare disease drugs?

- Temperature control, packaging
- Import-export documentation, customs clearance
- Risk management, contingency planning
- Quality Assurance, regulatory
- Visibility of the supply chain
- Changes in demand
- Other

figure 21

figure 22
Specialty drugs, orphan drugs and biologics have seen significant growth over the last ten years. Orphan drug sales have almost doubled since 2008, with this growth rate expected to continue until 2022 and sales forecast to reach $216 billion*. It is not surprising then that one of the major challenges for orphan drugs is temperature-controlled packaging, as it is in commercialization. The changes in demand, due to a low target patient population, are one of the main reasons why an agile and flexible supply chain solution is essential.

The average orphan drug treatment in the USA is $100k per patient per year. These costs can easily exceed $700k for specialized and life-saving medications. Therefore it is no surprise that regulatory and quality assurance remains a key challenge to ensure logistics is not the reason for losing a high-value drug product or, in worst cases, a patient’s life.

Christopher Engel
Product Manager - Commercial Supply Chain
Nordics, Central and Eastern Europe
World Courier

Q23. In your opinion, how challenging is daily logistics in pharmaceutical storage?

Q24. In your opinion, what are the biggest challenges in pharmaceutical storage?

- Temperature control, packaging
- Import-export documentation, customs clearance
- Risk management, contingency planning
- Quality Assurance, regulatory
- Visibility of the supply chain
- Changes in demand
- Other
The results collected in this survey reflect what we recognize in the industry as the pharmaceutical market evolution. While the 20th Century was noted as the period of ethical advances with the registration of more than 90 synthetic drugs, the 21st Century begins with the complete sequences of human genomes, which has unlocked the biological era with the advent of modern molecular biology methods.

These new trends raise new challenges for temperature control and regulatory and quality assurance. By switching from synthetic to biological products, the operational complexity of running clinical trials and transporting these products have increased dramatically.

A complex operational environment can be summarized as:

1) **Molecules that are less thermo-elastic.** Wider temperature ranges do not work anymore. Now bio-pharmaceuticals require storage and transport within strict and specific temperature ranges. This means storage areas and packaging solutions must be designed and qualified for their specific purpose.

2) **Extra care.** Biological products are huge molecules that are sensitive to brusque movements and excess of light. Therefore their primary and secondary packaging must safeguard the product.

3) **Personalized treatment.** Biological treatments are specific and also patient-specific. As a result, their logistics often involves several stages (i.e. patient – lab – depot – clinic – patient). Logistics operational procedures must reflect this new flow and be formed with the understanding that this shipment is irreplaceable and must be treated as such, all of the time.

Erika Rabak  
Global Project Manager - CSS  
World Courier
The findings from the data analysis lead to the following conclusions:

- Temperature control and packaging remain the biggest challenge in the pharmaceutical supply chain.

- New trends in the market such as personalized medication (e.g. cell and gene therapies) and patient-centric models (Direct-to-Patient) are evolving the pharmaceutical supply chain and shifting the focus towards specialized logistics platforms.

- There is a clear shift in the pharmaceutical industry from synthesized products to biological products.

- Quality and regulatory requirements need to be built into the pharmaceutical supply chain strategy from the very beginning. Being able to partner with a specialized logistics partner is often the key to success.

- There is significant education needed with regards to clinical trials, especially within Direct-to-Patient trials and cell and gene therapy.

**Acronym Legend**

ATMP - Advanced therapy medicinal product  
CEE - Central and Eastern Europe  
CGT - Cell & gene therapy  
CTS - Clinical trial supply  
CSS - Clinical Supply Solution  
Dtp - Direct-to-Patient  
HTA - Health technology assessment  
NCEE - Nordics, Central and Eastern Europe
World Courier is dedicated to knowledge sharing among pharmaceutical professionals. Follow the links below for further content on the key topics of the report.

**E-book:**
Packaging for the Most Challenging Shipments

**Infographic:**
Packaging for the Most Challenging Shipments

**Webinar on-Demand:**
Lessons for the Commercial Supply Chain Taken From the Clinical Trials Model

**Webinar on-Demand:**
How to Reduce Temperature Deviations Through Thermal Container Assessment

**White Paper:**
The Cost of Quality in the Specialty Pharmaceutical Supply Chain

**E-book:**
Direct-to-Patient Services for Clinical Trials and Commercial Distribution

If you have questions or you would like to discuss your supply chain with one of our experts, please get in touch with us at contactus@worldcourier.com or contact the office closest to you.
About World Courier

World Courier provides unparalleled specialty logistics services to drive the commercial success of our partners around the globe. For 50 years, we’ve delivered peace of mind through world-class supply chain programs, transportation services, storage of time- and temperature-sensitive products, and innovative, cutting-edge medicines including cell and gene therapies. Through our daily work – and powered by our 2,500 associates – we are united in our responsibility to create healthier futures. With a presence in 50+ countries, World Courier is driven by a commitment to excellence, and provides customized solutions with global reach to increase access to care; making us the most trusted specialty logistics company in the world. Learn more at www.worldcourier.com.

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AmerisourceBergen provides pharmaceutical products, value-driving services and business solutions that improve access to care. Tens of thousands of healthcare providers, veterinary practices and livestock producers trust us as their partner in the pharmaceutical supply chain. Global manufacturers depend on us for services that drive commercial success for their products. Through our daily work—and powered by our 21,000 associates—we are united in our responsibility to create healthier futures. AmerisourceBergen is ranked #11 on the Fortune 500, with more than $150 billion in annual revenue. The company is headquartered in Valley Forge, Pa. and has a presence in 50+ countries. Learn more at amerisourcebergen.com.