

Preparing for the Journey

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How do you ensure in-time clinical site deliveries during unexpected events? By treating the supply chain as an expedition – reviewing every known and potential risk, then putting a mitigation plan in place – you stand the best chance of being ready for your worst-case scenario

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Just as there are many risks involved in climbing a mountain – whether expected or unexpected – there are also challenges at every point in the clinical supply chain process, in particular related to clinical site supply. This article reviews the risks associated during planning and execution of a clinical site supply strategy.

Balanced Control

To simplify decision making in clinical supply chain management, various risks must be evaluated in order to mitigate them, thereby assuring a degree of increased control.

Figure 1 illustrates the three major areas of risk: direct control, indirect control and no control. Each supply

chain manager, like every mountaineer, has an area of direct control, such as knowledge of his particular fitness level. However, a single climber is more likely to reach the top safely by using the support of a powerful team. This involves the large area referred to as indirect control – for example, team members can train together and be monitored during the journey. However, there is still an unknown element: the no control area. This is the greatest cause for concern during both an expedition and in the clinical supply chain.

To minimise and mitigate hazardous situations, a detailed risk assessment is the ultimate key for success. Guidelines and regulations, such as Good Manufacturing Practice's Annex 13

and Good Distribution Practice, help to evaluate the business and reduce risk.

Assessing Risks

Nearly every known environmental risk can be evaluated, especially with so much industry experience available following recent events. These have included major earthquakes in Chile and Haiti, tsunamis in Thailand, Indonesia and Japan and, more recently, Hurricane Sandy, which impacted a large area of the US East Coast. While supply chains are typically designed to deliver maximum value – even in the event of several high probability operational risks occurring simultaneously – it is most often the low probability, high impact disaster that causes a supply chain failure. For example, the eruption

of the Eyjafjallajökull volcano in Iceland in 2010 forced the closure of European airspace and caused considerable commercial disruption.

Cold chain drug supply in clinical trials is often perceived as the biopharmaceutical industry's most critical supply chain challenge. This does not come as a surprise, considering the results of a recent customer survey by PAREXEL that showed product integrity has been ranked as the highest risk. Therefore, clinical trial supply chain industry experts play close attention to securing the stability of investigational medicinal products and non-investigational medicinal products, such as rescue or add-on therapy. Nevertheless, the ultimate goal is always patient safety, particularly for those treated with new products in clinical trials.

Industry sectors in which regulatory restrictions make it difficult to quickly respond to incidents tend to have a more effective, risk-mapping approach. Table 1 lists a standard risk assessment approach and indicates the critical stages of the clinical supply chain, highlighting various risks and how they may be mitigated.

To make a complete and accurate assessment, it is essential to bring different specialists together, since its complexity requires various levels of

Critical stages of the supply chain	Risk	Score	Mitigation
Planning	Unclear list of drug demand	High	Sourcing of small initial batch
Sourcing	Unavailability in local market	Medium	Balanced sourcing (central/local)
Manufacturing	Limited production slots	Medium	Predefine in work order timelines
Storage	Facility reaches capacity	Medium	Qualify and subcontract to third party
Distribution	Transport time and outside temperature	Medium	Use appropriate transport box
Site management	Patient safety due to delivery delay	Low	Patient may be treated with standard of care
Return	Limited space at site	Medium	Frequent returns to a local depot
Destruction/recycling	Site cannot destroy	High	Destruction at local or central depot

Source: Mattuschka, Cadman; PAREXEL International

expertise. At a minimum, an assessment team should include a risk management expert, quality person, legal adviser and, of course, operational experts as needed, depending upon which critical stages need to be evaluated. Such an exercise has several advantages, including diversified thinking, clear methodology, balanced scoring, candid fact-based discussion and mutual agreements on mitigation actions.

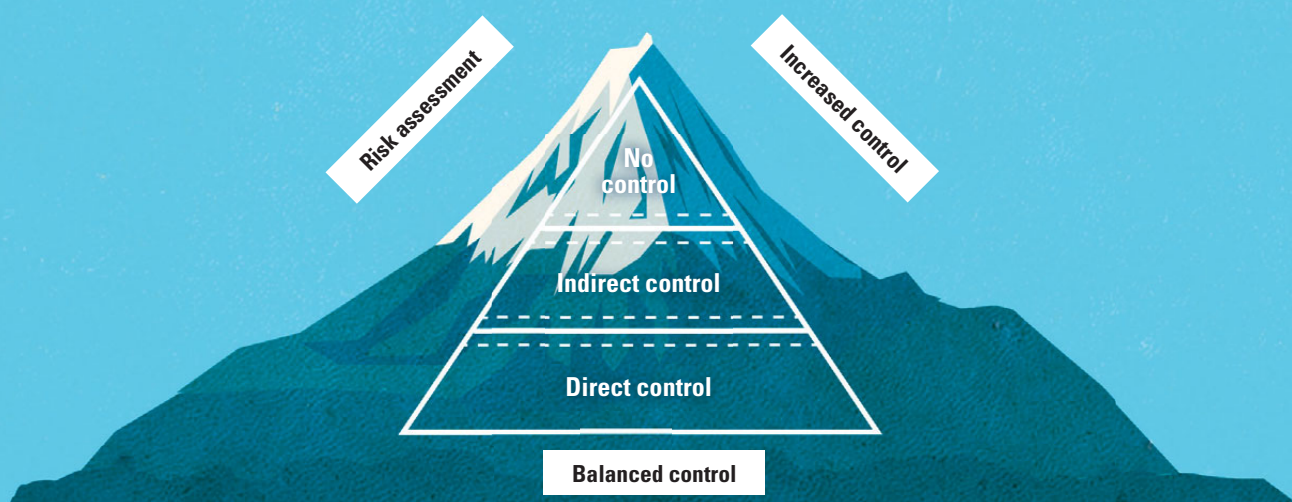
Scoring a Risk

There are various methods used to score a risk, but the most common in the

biopharma industry is the failure modes and effects analysis. One adapted version of this safety management approach was developed by GF Kinney and AD Wiruth in 1976, and is frequently used today within the military.

It is important to set clear definitions of risk categories at the onset. We have identified five categories: patient safety, regulatory aspects, operational aspects, commercial, and environmental issues. Each category must then be precisely described before scores (such as 1 = low, 2 = medium, 3 = high) are implemented for probability, occurrence and severity,

Figure 1: Risk versus control pyramid



as well as potential implication per risk category. This method provides a multitude of results.

With a simple, yet very powerful, bi-dimensional analysis, a rapid extraction of key outliers can be achieved. As an example, Figure 2 compares total severity scores for each identified risk with total probability scores.

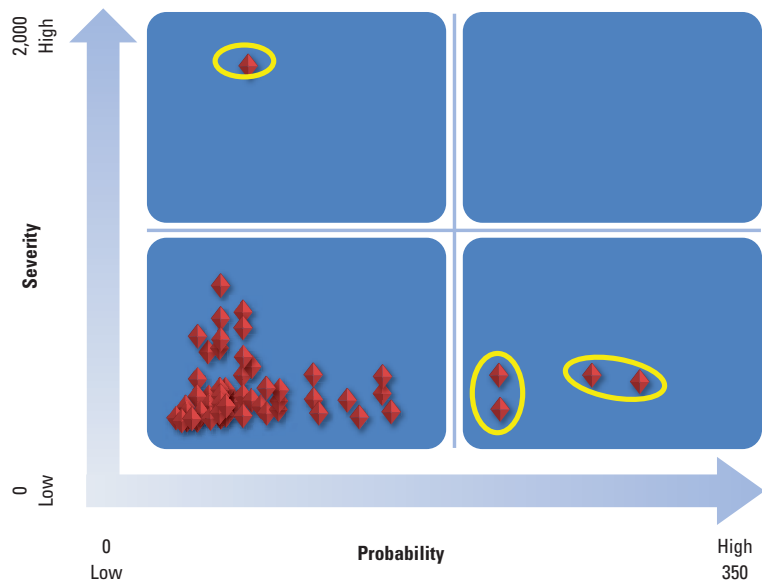
For instance, a cold chamber power outage is rare (as part of the mitigation process, back-up systems should be in place), but in the worst case, the severity can be very high as all stored products may be lost. To take a second example, a customs delay has a higher probability of occurrence, although its severity may be considered relatively low.

Various bi-dimensional evaluations are possible between the five categories. This helps detect and cluster risks efficiently, while also assisting in identifying and implementing required mitigating actions.

Risk Mitigation

Assessing risks and implementing risk mitigation requires discipline. Therefore, it is important to manage and control the full clinical supply chain as much as possible and put appropriate actions in place. As illustrated in Figure 3, this can be seen as a constant cycle, with the assessment being completed before every expedition. Such an assessment should be performed in the clinical supply chain at least twice per year. After all mitigating factors are identified, appropriate actions must be established. It is advised to frequently (perhaps quarterly) monitor any issues. This can be done by utilising key performance indicators and quality metrics, as well

Figure 2: Example of bi-dimensional risk evaluation



Source: Mattuschka, Norris, Eudarc; PAREXEL International

as performing rolling checks of key risk areas. There is certainly a need to refine mitigations, traditionally driven by a process of corrective and preventive action.

While many companies utilise multiple manufacturers and distributors, it is important to remember that outsourcing services does not absolve an organisation of its responsibility to ensure product quality.

Supply chains typically lack resilience due to a reliance on a large range of variables, with room for little to no margin of error. There is a greater need to focus on risk mitigation, including the consideration of business interruption strategies and supplier networks, and ensuring that business continuity plans clearly identify actions to be taken. To come back to the analogy of the

expedition, the business continuity plan is the map that can be referenced if an unexpected diversion or event arises.

In many cases involving the clinical supply chain, manufacturing and distribution phases can present the greatest risks and challenges due to natural and man-made disasters. While alternative suppliers can always be sourced, different transportation options may be more restricted due to an inability to reach the product’s final destination. The need for specialised storage locations may also further complicate the problem.

Business Contingency

It is important to consider that plan activation does not necessarily need to wait until an incident has occurred; rather, the plan and relevant teams

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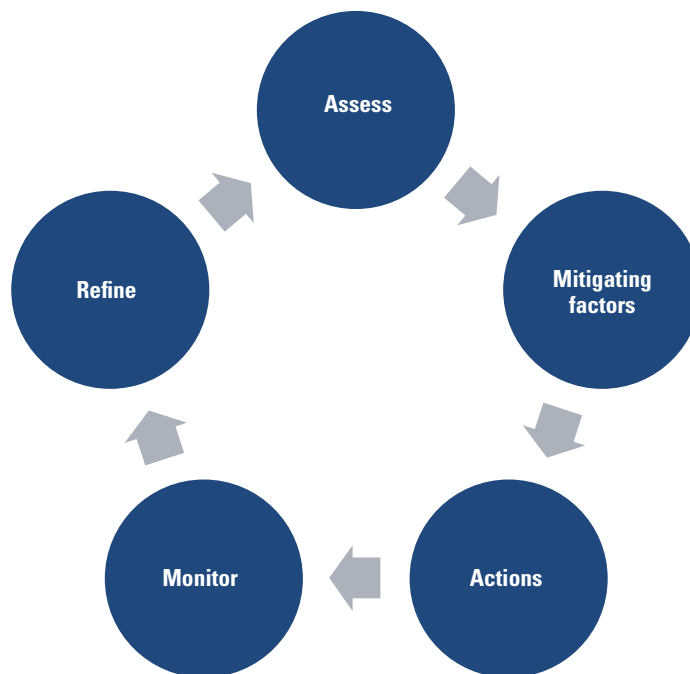
can be invoked so that it is possible to make key decisions ahead of time. During Hurricane Sandy, although the storm's progression off the US East Coast was tracked over several days, many organisations and experts incorrectly assumed it would follow predictions and steer directly into the Atlantic Ocean, where it would dissipate. Unfortunately, the storm headed west and reached land, causing devastation across multiple states.

Companies that had invoked plans and teams in advance made key decisions ahead of time, with additional consideration and potential mitigating actions identified in case the storm did something unexpected. As a result, these organisations fared better in the recovery and continuity of their business operations than those companies that waited until the storm hit. At PAREXEL, we monitored developments during the storm, focusing specifically on how our investigational clinical trial sites had been impacted in order to secure patients' safety. With a robust plan implemented, we could systematically track any incidents and resupply products as needed in a short turnaround time. We followed our map, even when internet access was unavailable, simply by calling pre-defined emergency numbers. In some cases, our local network of Clinical Research Associates made direct visits. Ultimately, we could maintain an overall view of the status of our sites.

Business continuity plans can also outline actions to take if an unknown risk were to suddenly occur, such as the eruption of the Eyjafjallajökull volcano. These plans should outline alternative methods of transport if the transportation of goods via air traffic is restricted, including via the rail network, shipping or road transport. They should also contain details of alternative suppliers that can be easily and quickly referenced, minimising any delay in reacting to an incident. However, such plans must also have a clear structure as to who should be contacted and what priority actions must be taken.

Figure 3: Risk mitigation cycle

Source: Mattuschka; PAREXEL International



Remember that those who are following the plan may not necessarily be the key personnel who would normally deal with such a situation, so instructions should be clear and concise.

Also consider your employees: will they be available to assist in recovery or caught up in the incident? Finally, consider your electronic systems: will these be available during the disaster?

About the authors



Mark Cadman, Senior Business Continuity Manager, joined PAREXEL International in 1997 as a technician in the IT department. This was followed by a number of managerial promotions within IT, encompassing quality management and security. In 2009, he moved to the Business Continuity department, taking responsibility for providing support related to incident management and business continuity to all PAREXEL offices and departments. Mark was instrumental in establishing PAREXEL's current business continuity management programme. He obtained his Certificate of the Business Continuity Institute (BCI) in September 2012 and was awarded MBCI membership in January 2013.
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