White paper

Cerba Research

10 Best Practices in Logistical Management of Kits and Samples for Virology and Cell & Gene Studies

With the number of unique procedures and their frequency per protocol rising annually by 6.5% and 8.7% respectively, kit building and sample collections have become increasingly complex, underscoring the need for streamlined processes and tailored solutions in clinical trials.[1]

Although the external and economic conditions seem very favorable, there are many challenges, especially from a logistical point of view.
The increase in demand will put more pressure on the internal processes of the entire pharmaceutical supply chain. As a result clinical trial managers are challenged to come up with creative solutions, based on an efficient and effective logistics strategy.

Cerba Research has supported many clinical trials and is used to working with several supply chain strategies. With more than 80,000 processed samples and 500 studies, the company has established a solid logistical track record.

This record was built by overcoming many hurdles and logistical challenges throughout the years. Cerba Research's Laboratory Logistic solutions team has summarized these experiences in ten critical lessons.

The views and knowledge discussed in the ten lessons all apply to Virology as well as Cell and Gene study settings. Study directors, clinical trial managers, scientists, research and development professionals and business development specialists can benefit from the pragmatic insights and models discussed in this white paper.

"With more pressure on internal processes, clinical trial managers are challenged to integrate creative and efficient logistic strategies."

Best practices:

- Risk management
- ROI and clinical trial operations management
- Clinical trial operations KPIs
- Differences in capacity and demand
- Training and knowledge sharing in the supply chain
- Specialized quality assurance
- Data management in clinical trials
- Integrating sustainability in the supply chain
- Process optimization
- Making the best use of an expert network model

Lesson 1: Risk management

According to the FDA[2], risk management consists of: identifying and characterizing the nature, frequency and severity of the risk. It occurs throughout a product life cycle from early identification to post marketing approval.

So, in essence risk management occurs through all stages of pharmaceutical product development.

Furthermore, the management of risks is based on four consecutive processes:

- Assessing a product's benefit-risk balance.
- Developing and implementing tools to minimize its risks while preserving benefits.
- Evaluating tool effectiveness and re-assessing the benefit-risk balance.
- Making adjustments in order to support risk minimization (FDA).[3]

"Involving strategic partners will result in additional risk minimization insights."

Based on years of experience, we have found that the second process in particular tends to cause headaches for many clinical trial specialists. Legislative authorities and advisory bodies tend to share very broad directives when it comes to risk minimization tools. Phase 3 is of special importance for clinical trial managers. It is in this phase that the volume of samples and complexity of logistical processes tend to be very high.

Risk management should be based on both an outside-in and inside-out perspective. Most risk assessments start with an internal process chart based on the entire supply chain. On these charts, risks are typically plotted in terms of impact and whether it is likely that certain unforeseen events can happen. Although necessary as a starting point, internal risk assessments are not sufficient. It is necessary to extend them with an external perspective.

The impact of external risks can be high for any clinical trial operational department.

They can be diverse and may include political, economic, legislative and regional risks. Global political uncertainty for instance may directly affect costs in the clinical supply chain. Especially when alternative longer routes have to be taken. Another major external occurrence is bad weather. Extreme weather has the potential to cause severe clinical trial delays.

It is impossible to stay ahead of these uncertain events. However clinical trial managers can anticipate uncertainty by using scenario analyses in combination with back-up plans.

A measured approach to risk analysis

- Performing a stakeholder analysis will help you to gain additional insights into the entire supply chain. Every company is part of a complex network of organizations in a turbulent environment. Potential risks can be found outside the scope of the organization. Do not forget to look into external suppliers. Allocate enough time and resources in preparation of back-up plans.
- Even if you have to work against tight deadlines, always allocate additional time for unforeseen events.
- Use the experience of your suppliers and partners. Contract Research Organizations, laboratories, specialist courier companies and healthcare professionals working on clinical sites, have their own specialties. You can save time and gain more experience by using their advice and knowledge.
- Do not fall into the pitfall of paying too much attention to risks that are not manageable. Involve your strategic partners and suppliers to create back-up plans.
- It can be a time-consuming exercise, but reviewing or re-aligning your primary and secondary processes will pay off eventually.

A practical risk minimization tool

A proven tool that can be used for managing risks is the impact chart as described below.

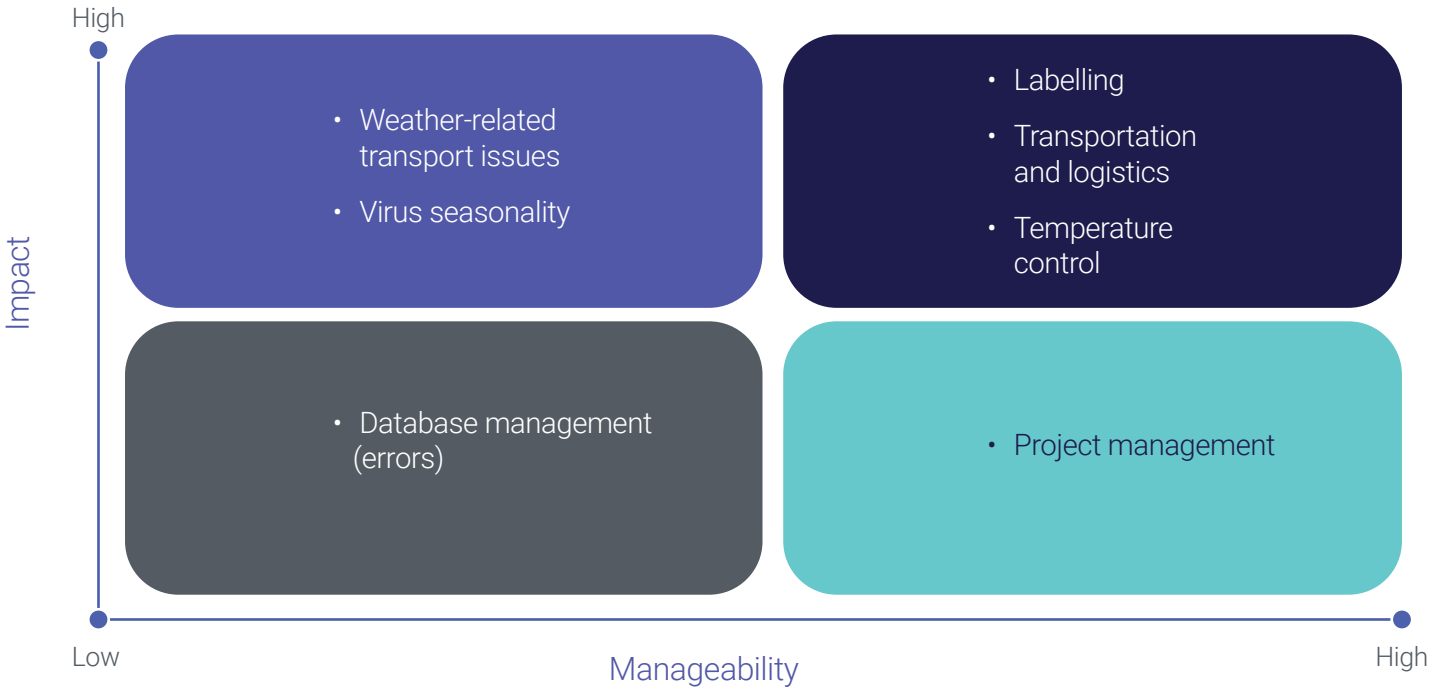


Figure 1.1: Risk minimization tool

The model can be used for prioritization purposes, as part of a risk management analysis. It is recommended to use a structured approach by:

- Establishing the primary and secondary processes of the operational side of the clinical trial
- Plotting the risks on the impact chart
- Identifying all relevant internal and external stakeholders
- Focus on risks with a high impact and high manageability
- Anticipating risk with a high impact and low manageability
- Integrate relevant FDA (and/or other legislative bodies) regulations and directives

When identifying risks, the following questions should be dealt with:

1. Is this risk manageable?
2. Is it possible to anticipate on this risk?
3. On a scale of 1–10, what is the impact on the clinical trial?
4. How does this risk affect the clinical trial distribution chain?
5. Which other stakeholders (i.e. suppliers, sub-contractors, processing labs) are affected by this risk?
6. If we calculate/estimate the possible cost of the concerning risk, what would the value be?
7. If this risk happens, how does this affect the clinical trial (Validity, costs, study delay, etc.)?
8. If applicable, how could this risk affect our corporate image/business reputation?

The above structured approach can be used as a guideline, in order to support clinical trial managers with their day-today queries. It will help them to allocate the right amount of time and resources to risks that are manageable and have a high impact. The key here is to find the right balance when allocating resources, between risks that are manageable and risks that cannot be managed. A common pitfall for clinical trial managers is to focus too much attention on resources that have a high impact and a low manageability.

Primary processes

Process	Risks	RC	RI
Site training	Language barriers may cause difficulties, when training contractor site staff	2	3
	Last minute site trainings may cause delays in the clinical trial process	4	3
Sample collection	Variations in sample collection equipment may influence study results	3	9
	In-house logistical bottlenecks	2	3
Laboratory analysis	Data interpretation errors	4	5
	Staffing/capacities issues in laboratories	6	5
Reporting	Database errors may be carried over to the reporting stage	4	9
	A lack of database standardization in the industry	8	7

Secondary processes

Process	Risks	RC	RI
Purchasing trial items	If bought in different regions or from different suppliers, purchased items may influence studies	4	8
	Quality issues of sampling materials	4	9
Transportation	Delays due to bad weather conditions	8	9
	Regional strikes within the transportation sector	5	9
Logistics	Temperature control failure	5	9
	Sample loss during internal distribution	3	5

Supporting processes

Process	Risks	RC	RI
QA & QC	Different QA/QC systems in the value chain	4	6
	Compliancy issues for contractors/ sub contractors	3	4

Figure 1.2: Process Risk Identification

- It is advisable to perform risk analyses for any separatelogistics project. Risks may differ per study, project type, region and time period. Furthermore, the economic and legislative situation may evolve over time.
- Being compliant is not enough. Use the guidelines of legislative authorities, such as the FDA, to improve your clinical trial processes. Other advisory guidelines such as Good Distribution Practices can be used as an additional source to identify risks in your clinical trial process.
- It is inevitable that potential risk-related events will happen. As a result, problems and bottlenecks are likely to occur in the clinical supply chain. It is therefore recommended that clinical trial managers acquire the competence to carry out a thorough root cause analysis. The retrospective nature of defining root causes might be in conflict with the usual way of thinking in a clinical trial setting. Preventing high risk related events seem to be the focus. Any clinical operations expert should accept that any actor in the supply chain may put a spanner in the works of a study. A root cause analysis is a valuable instrument in the toolbox of the clinical trial manager.
- Lastly a contingency plan should be made in advance. In this way the continuity of the clinical trial in question is guaranteed, even in the occurrence of a worst case scenario.

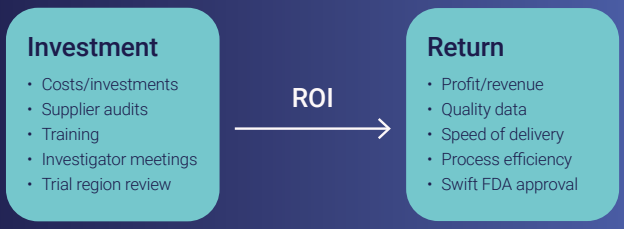
Lesson 2:
ROI and clinical trial operations

One of the first topics that springs to mind with ROI (return on investment) is financial metrics.

However, it must be stressed here that return should not be solely expressed as financial output.

There is more to a successful clinical trial outcome.

Crucial factors that correlate with a high return on investment are: speed of delivery, quality and efficiency.



Speed of sample delivery

Quick turnaround times at clinical sites will contribute to the ability to meet ambitious trial goals. The question is: how can a CRO increase the speed of delivery of the trial?

In order to answer this vital question, one has to look at the pre-trial phase. During the initiation phase, decisions are made about the regions, investigator sites, suppliers and budgets. There are numerous sub-processes that have a positive effect on speed of delivery such as the training of site staff, efficient sample kits and best-in-class courier service.

The factor that has the highest positive impact on the trial is regional choice. It can be challenging to carry out clinical trials in developing regions, especially for Virology as well as Cell and Gene studies or trials with a high rate of perishable samples. Many unforeseen hurdles may appear during a trial, such as delays caused by customs clearance, weather and poor transportation conditions in certain regions. CROs with an established international track record will be able to advise on the best clinical trial regions.

Quality

Taking a balanced approach to quality pays off in the long run. A focal point from a quality perspective is sample integrity. In this sense quality is expressed as a high return of usable samples. In order to achieve low sample waste rates, it is important to integrate quality throughout the logistical cold chain. Sooner or later, a low cost logistics strategy will backfire on the clinical trial operations.

So it is not advisable to save costs on the logistics side of the trial. A detailed approach to quality will have a positive effect.

The quality of the items in sample kits for instance has a positive effect on sample integrity. High quality materials such as vials and swabs also have a positive effect on the sample integrity. Quality contributing factors are also found with suppliers of sub processes, such as couriers.

Depending on the study, remote temperature logging devices, sample containers and innovative packaging solutions make a difference when it comes to sample integrity quality. Measuring quality as a ROI variable will shift the discussion to a more balanced approach, rather than just focusing on the financial metrics.

Efficiency

In contrast to other fields, regional selection for sample collection can have a major effect on project costs. Get it right and an effective trial is guaranteed with lower costs. Get it wrong and region selection will have a disastrous impact on project ROI. Specialized CROs can share best practices on region selection. A higher ROI can be achieved by selecting investigator sites within a certain parameter of the laboratory facilities where the analyses are performed. Virology and Cell and Gene samples are more perishable than other therapeutic fields such as oncology.

On top of this, the physical condition of certain viruses, such as RSV can be very unpredictable during transport. There are ways to extend sample life by using processing laboratories. By doing so, more regions become accessible for the clinical trial in question. Without processing laboratories, the efficiency and ROI of a clinical trial is increased significantly. Specialized CROs with a global track record have experience with different regions and processing laboratories. Using their expert knowledge will provide insights in how to obtain the targeted ROI.

Most clinical trial professionals are tempted to view ROI as a financial metric. The overarching lesson is that there is more to ROI. We have taken the viewpoint/perspective that return can also be expressed as speed of delivery, quality and efficiency. It is tempting for clinical trial managers to adhere to the sponsors' ambitions to perform clinical trials with the lowest possible costs. The challenge is to move away from this discussion by viewing costs as investments. Initial investments in a solid and reliable cold chain will eventually pay off as a higher return. It is our experience that making a compromise on quality, speed of delivery or suppliers, will eventually result in higher costs and therefore lowers the ROI.

It is inevitable that a low cost strategy is associated with higher risks. We do understand that costs cannot be overlooked, since sponsors have to hit their financial targets too. If costs remain an issue we recommend discussing this with suppliers in the clinical trial value chain. They will definitely help clinical trial managers to reduce costs wherever possible while guaranteeing ROI rates based on high quality output.

Lesson 3:
Clinical trial operations KPIs

KPIs (Key Performance Indicators) that can be used to monitor the success of a clinical trial are: turnaround times, sample waste percentage and costs. It is essential to review KPIs in relation to each other.

An isolated view on KPIs will result in information that is less usable. For instance, reviewing trial costs in isolation from context and other KPIs is in essence useless information. In other words interlinkage of KPIs is important to convert KPI metrics in valuable management information.

Apart from being compared to each other, KPIs should also be compared at project level. Historical trial project data that derive from KPI reports may provide a reliable pool for future clinical trials. However, we need to be cautious here, because KPI data may be different per study type. Centralizing the sample type during KPI reviews will support better judgement. Studies may differ due to the perishable nature of samples. For instance, generic study samples differ from Virology and Cell and Gene-related studies. Influenza and viral samples are more perishable and sensitive to ambient temperature. For Virology and Cell and Gene studies, it is likely that the share of courier costs is higher in relation to the total trial costs compared to other fields. KPI metrics will therefore be different. It is recommended to set KPI targets in liaison with all partners involved, including transportation and logistical costs.

In this white paper, we take a different approach to defining KPI by zooming in at the micro level. There are many factors that (in) directly affect sample quality as reflected by Figure 3.1. The success of the clinical operational phase of a study can be assessed by reviewing all KPIs: temperature, sample packaging, laboratory process efficiency, sample turn around and handling times, etc.

Management teams who are responsible at project level are likely to review the success of a clinical trial based on financial KPIs/metrics. By doing so, they are missing out on some essential details that can have a significant impact on the trial outcome. There is an interlinkage between detailed performance indicators and overall financial performance of a trial. For example, minor packaging decisions such as the usage of the right cardboard and insulation of clinical trial sample kits can affect the financial outcome of a clinical trial. For example, minor packaging decisions such as the usage of the right cardboard and insulation of clinical trial sample kits can affect the financial outcome of a clinical trial. Overlooking minor details will have a negative effect on the clinical trial process outcome. When studies are composed of thousands of samples, a minor deviation may cause major clinical trial delays.

Project-level KPIs	Micro-level KPIs
• Financial ROI	• Temperature monitoring
• Profit margins	• No. of Packaging deviations
• Total costs	• Sample kit errors
• Revenue	• % Investigator site training
	• Sample shipping
	• Reconciliations
	• Laboratory process efficiency
	• Sample turn around times

Figure 3.1: Project- and micro-level KPIs

There are regional study related differences that sponsors are not aware of, such as the size of the swab used for influenza studies. Required swab types differ per world region. Getting the product subtleties wrong will not only result in wasting thousands of clinical supply products, it will also have a negative impact on the already tight deadlines of the concerning trial.

The importance of implementing monitoring tools is affirmed by policy makers.[4] This is shown by a recent addendum [E6(R2)] of GLP guidelines.[5] The latest version specifically highlights the importance of establishing a monitoring plan, including performance metrics. It also stipulates that the study sponsor is responsible for selecting sites, processes and on-site monitoring. This supports the notion that there is more to reviewing clinical trials than looking solely at the financials as outlined in lesson 2 of this whitepaper.

In conclusion: monitoring the operational side of clinical trials based on KPIs is an absolute must. It is recommended for study sponsors to distinguish KPIs at project level and at a more detailed level. Liaising with strategic partners and integrating detailed KPIs in master service agreements will pay off. Specialized suppliers will have in-depth knowledge about how to monitor their part of the clinical trial and how to select the right metrics.

"Minor deviations may cause major clinical trial delays. Monitoring KPIs at micro level is essential to prevent project set backs."

Lesson 4: Differences in capacity and demand

Selecting the right strategic partner to carry out contracted research is of vital importance.

Sponsors should zoom in on the type of trial. In mainstream fields, sample analysis can be planned on a linear basis.

For Virology and Cell and Gene studies, the challenge is to adjust capacity to demand. The demand for influenza studies is seasonal. The somewhat unpredictable nature of influenza can cause serious planning issues and can have major negative implications for the concerning study.

This point is illustrated in **Figure 4.1.**

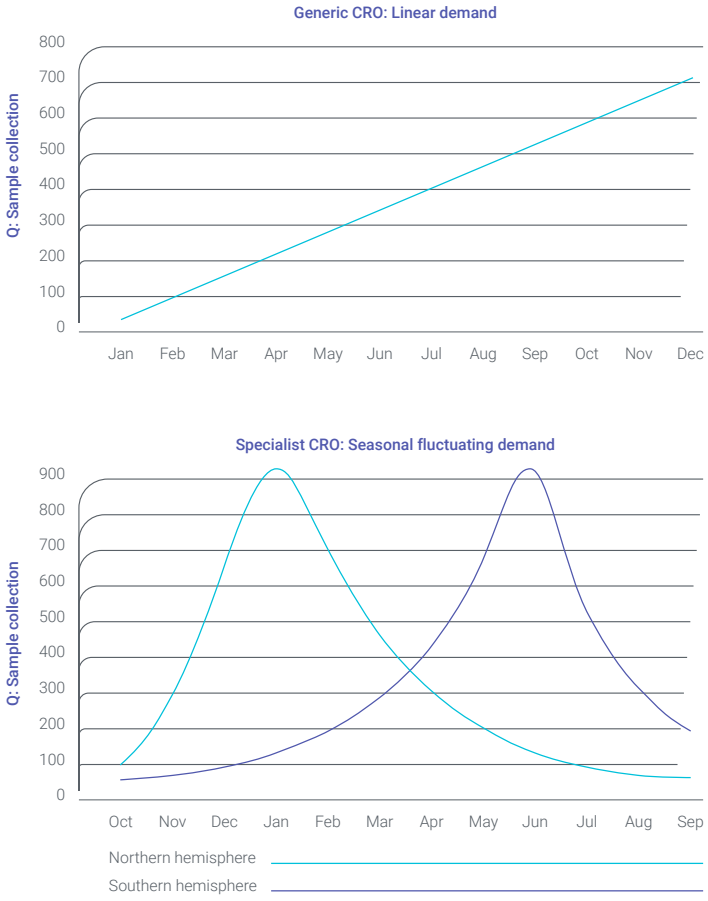


Figure 4.1: Generic CRO vs specialist CRO sample collection

During influenza studies, contract research laboratories need to scale up within a very short time frame, due to peak demands, as illustrated in the above example. A CRO who is used to carrying out generic studies does not have the experience to deal with seasonal demand shifts, whereas specialized industry players are capable of handling these operational bottlenecks.

Apart from the diagnostics side of a clinical trial, the logistical planning is also affected by the non-linear demand pattern. Furthermore, Virology as well as Cell and Gene samples differ from other studies. This notion has significant implications for other partners in the supply chain. A different type of courier is needed who is capable of transferring samples based on just-in-time delivery. The same notion applies to other specialized actors in the supply chain such as packaging and data logger companies. In-depth supply chain and process knowledge is necessary in order to act as a true partner during a clinical trial.

Not every supplier is able to raise the bar to expert level. In order to achieve high-throughput sample ratios it is a must to select the best players in the market. Opting for mediocrity will inevitably correlate with lower results, caused by logistical delays. Operational capacity and demand planning for a Virology and Cell and Gene study is completely different compared to other therapeutic fields. It is advisable to learn from specialized partners in the network who know the ins and outs of cold chain logistics for seasonal studies.

Lesson 5:
Training and knowledge sharing in the supply chain

Training is often overlooked as an essential contributor to the overall quality of a clinical trial. It is assumed that its function is incorporated in the entire supply chain. In reality this is often not the case. Training and knowledge sharing is an easy target when cost-saving activities are enrolled. Most biotech and pharmaceutical companies have outsourced the operational side of their clinical trials. In a way outsourcing equals a loss of knowledge. Specialized expertise is now found in the outsourced network of the drug or vaccine developer.

An integrated approach works best to identify any gaps in terms of training needs. Usually training needs are identified during the initiation stage of the concerning clinical trial. It is of the utmost importance to involve all parties concerned. Even the smallest detail during a clinical trial can have a big impact on the total result of a study. Knowledge sharing also refers to advising on best practices or key learnings. Negative issues tend to be avoided for a number of reasons but they are the most valuable sources of learning. The following real-life example illuminates the usefulness of sharing learnings.

"Investments made in training will eventually pay off."

Practical case: Investigator and site training/third party sample kits

For a global study, the concerning sponsor wanted to limit the total amount of site trainings. The idea was to use a train the trainer principle, which was used in the past for nonviral studies. The rationale behind this limitation was due to cost savings. A very important detail was missed, during the train the trainer principle: the correct usage of the Influenza swab. On top of this, third party sample kits were used with label errors. In the end a certain number of samples had to be discarded from the study.

The cost of the loss was higher than the initial projected cost saving. After the study, a review meeting was held to share feedback and learnings of the entire process. The sponsor and the concerning CRO did not include the minor details, such as kick-off presentations and sample kits in their risk assessment process. This costly learning was shared within the relevant organizations during quality review meetings in order to avoid similar occurrences in the future.

Lesson 6:
Specialized quality assurance

Clinical trials became almost synonymous with quality assurance. Quality is not only of vital importance for the end product but also for the entire set of preceding processes. Logistical operations form a sub process, which has a significant impact on the total clinical trial. Most quality assurance and control activities are dedicated to the core processes of the concerning organization. For a CRO/CLO this means that the focus is on related directives and activities that derive from standards and guidelines such as ISO15189:2012, GCP (Good Clinical Practice), GLP (Good Laboratory Practice) and GCLP (Good Clinical Laboratory Practice).

Clinical trial managers have to be able to read through a clutter of quality assurance rules and regulations. Because of the scope of a clinical trial, there is no one-fits-all solution. Quality directives seem to be scattered through many systems. For instance, for diagnostics services, the backbone of a good quality system is based on ISO15189, which specifically deals with standards for medical laboratories. GLP is applicable to non-clinical studies. So in the Virology and Cell and Gene field, GLP is pre-dominantly applicable to preclinical research. Then there is GCLP, which is dedicated to clinical research. An important reason to launch this directive was to bridge the gaps that existed between GLP and GCP. Besides the clinical side of studies, clinical trial managers also need knowledge about the logistical side of WHO technical reports (WHO Technical Report Series, No.961, 20118), can shed additional light on specific quality requirements for storage and transport of temperature sensitive shipments.

However the issue here is that this report is applicable to pharmaceutical products (finished end product). It does not specify how to deal with samples in a clinical trial setting. Specific distribution-related guidelines can be found in Goods Distribution Practice documentation (GDP Guide, EU, 20138). Again, these directives fail to provide specific insights applicable to clinical trials. On top of the many generic regulations there are specific recommendations for the many sub-areas of a trial.

During logistical activities of a Virology and Cell and Gene clinical trial, the quality assurance focal area can be narrowed down to two major areas: internal and external logistics. Specific areas include temperature-controlled storage, qualification of humidity alarms, perishable cargo regulations published by the IATA (International Air Transport Association), building related requirements including, material handling, stock management, building hygiene and cleanliness.

Summarized, it is hard to pinpoint a normative reference for very specific sub-processes, such as clinical trial operations. It is difficult to extend generic quality management directives to very specific sub-processes and projects like clinical trials. In a clinical trial setting, quality assurance is most often custom-designed. It is up to the project responsible manager to translate all the quality related directives to the concerning clinical trial.

Clinical trial managers may experience all the quality-related regulations as a burden. Their own quality assurance department is focused on the primary processes of their business, which is drug or anti-viral development. This means that the 'average' clinical trial manager is left to his/her own devices when it comes to translating all the complex quality knowledge to the specific study. This is where the supplier network comes into play.

Every strategic partner will have specialized quality assurance knowledge available. CROs are closer to the clinical trial supplier network. Their scope will include quality procedures applicable to very specific technical procedures, such as temperature control and monitoring, logistics and storage of samples and courier services. Clinical trial managers can be relieved of the increasing workload by involving the supplier network of CROs and CLOs. Their strategic partners include refrigeration experts, building-related systems consultants and logistics specialists. It is advisable to use the specialized quality assurance knowledge of these experts.

Their sector specific knowledge will certainly contribute to the overall quality of the clinical trial.

Lesson 7: Data management in clinical trials

The main advantage of outsourcing a clinical trial is that sponsors do not have to worry about any operational issues. On the other hand, outsourcing does not mean that sponsors are fully hassle-free. There is a lot of data to look into, between the start-up phase of a trial and the pre-market authorization phase. The question is: how can a sponsor monitor all the relevant operational data with minimum resources? Suppliers in charge of collecting and distributing (Virology and Cell and Gene) samples can support real-time data monitoring in cooperation with their suppliers. In this respect 3 data types are of special importance: (1) Sample shipment data (2) Distribution data (3) Data deriving from the final database.

Sample integrity data

Arguably, sample integrity data is even more important during Virology and Cell and Gene studies than in other therapeutic fields. Virus samples can become unstable when certain temperature and packaging requirements are not met. 24/7 sample logistics management (including track and tracing kits and correct labeling) is crucial for maintaining sample integrity. Throughout the operational phase of the clinical trial, several focal points may be included for data monitoring purposes. Temperature is controlled via realtime data logging devices. This is done throughout the entire lifecycle of a sample. This process accumulates into a significant amount of data.

Distribution data

With influenza studies, a peak can be expected, right after the start-up phase. When samples are taken from research participants, the logistical supply chain process starts. A peak in data can be expected when samples are scanned and distributed via special courier services. Depending on the type of study, processing laboratories might also be included as a data processing point in the logistics process. Each stage within the distribution process, will generate additional data.

Final study database

The final database is an accumulation of the laboratory analyses, excluding the logistics data. The database forms the end product of the study which may take years to compose. A lot can happen between the kick off and end stage of a study. Progress reports are necessary in order to provide valuable feedback to the sponsor, especially during the laboratory analytical stage of the study. Many clinical trial managers fall into the pitfall of analyzing too many data reports. It makes sense to keep your eye on the ball but paying too much attention to the details might result in a loss of efficiency.

We highly recommend using an approach to centralize data monitoring around preventive and corrective processes, in cohesion with industry guidelines.[6]

Contract Research Organizations can assist with setting up customized data monitoring dashboards. With their experience they are able to support sponsors with all the relevant data they need, such as data monitoring and daily sample receipt reports.

> "We highly recommend to use an approach to centralize data monitoring around preventive and corrective processes."

Lesson 8: Integrating sustainability in the supply chain

Sample integrity, data management and trial efficiency seem to be dominating themes in relation to clinical trial operations. Sustainability is usually not a top of mind theme for the ´average´ clinical trial manager. Nevertheless, we would like to highlight the importance of this global theme for clinical trials. For sponsors like big pharma companies, sustainability is becoming increasingly important. This notion is supported by the fact that 2 of the 5 largest additions on the Dow Jones Sustainability Index[7] consist of pharmaceuticals (Merck & Co, Allergan Inc.).

Clinical trials tend to be conducted either in a consortium or within a strategic supplier partnership model. Therefore it is important to align sustainability goals within the partner network. It is likely that the involved partners have different views on sustainability. On top of this, one partner might have developed itself further in terms of sustainability, while others are still struggling to initiate the first steps. A situation in which different partners are not fully aligned calls for action. It is unlikely that partners are able to synchronize sustainability actions at short notice. It is therefore important to seek sustainability similarities in the partner network. It is our experience that the following sustainability themes are integrated with most clinical trial partners: CO2 footprint, packaging and just-in-time supply management.

Moving forward with smart packaging and logistics

For Virology and Cell and Gene studies, the packaging of samples is of special importance. Sample integrity depends on careful temperature monitored processes and best-in-class packaging solutions. Virus stability may be affected if packaging materials are of inferior quality. However there are solutions available that allow for a sustainable approach without compromising on packaging quality. Specialized CROs have learned that the usage of light materials for sample kits in combination with smart container packaging reduces the amount of pallet space per shipment. Efficiency savings per pallet might be minor. However, if these savings are calculated for several seasons of sample processing for a multi-year study, the accumulated end result will have a positive impact on sustainability figures.

Specialized cold chain couriers are able to service clinical trial stakeholders with customized sustainable packaging solutions. A high rate of sustainability can also be achieved through efficient internal and external logistics. Sustainable shipments can be achieved by selecting couriers and air transport companies that have invested in a sustainable fleet (such as hybrid vans, trucks and energy efficient cargo planes).

Just-in-time supply chain management

Purchasing sufficient clinical trial materials in advance creates piece of mind. This does not mean that this approach is efficient. For seasonal Virology studies like influenza for example, it can be unpredictable whether or when the flu season 'kicks in'. Waste rates can have a devastating negative effect on the operational budgets of trials. It is not unusual that investigator sites are left with a large amount of unused sample kits. This calls for an efficient purchasing strategy. Specialized Virology and Cell and Gene CROs have access to historical seasonal data and know by experience how the demand curve for a clinical study will evolve once the concerning flu season has started.

As explained in lesson 4, the seasonal nature of Virology and Cell and Gene trials dictates the entire operations of a clinical trial, including the selection and management of couriers. We recommend specialized couriers who have the capabilities to deal with seasonality. The golden rule with sustainability is to set realistic goals. Aligned and agreed trial metrics form the basis of a solid sustainability strategy. More interestingly sustainability can also be linked to financial performance. There is a direct link between sustainability performance and lower costs. The lower the CO2 emissions, the lower the costs. Additional lean and green solutions will yield a higher efficiency. In order to assist with establishing a sustainable company we recommend several guidelines and tools on how to reduce CO2 emissions. These tools are available on websites of leading environmental institutions, such as: DEFRA[8], Department for Environment, Food and Rural Affairs, UK, Environmental Protection Agency, US, Department of Energy, World Resource Institute/Greenhouse Gas Protocol.

"Opting for a specialist CRO with a solid supply chain strategy will eventually result in sustainable performance."

Lesson 9:
Process optimization

Process optimization is far more complex for Virology and Cell and Gene studies. This notion is best illustrated with the example below.

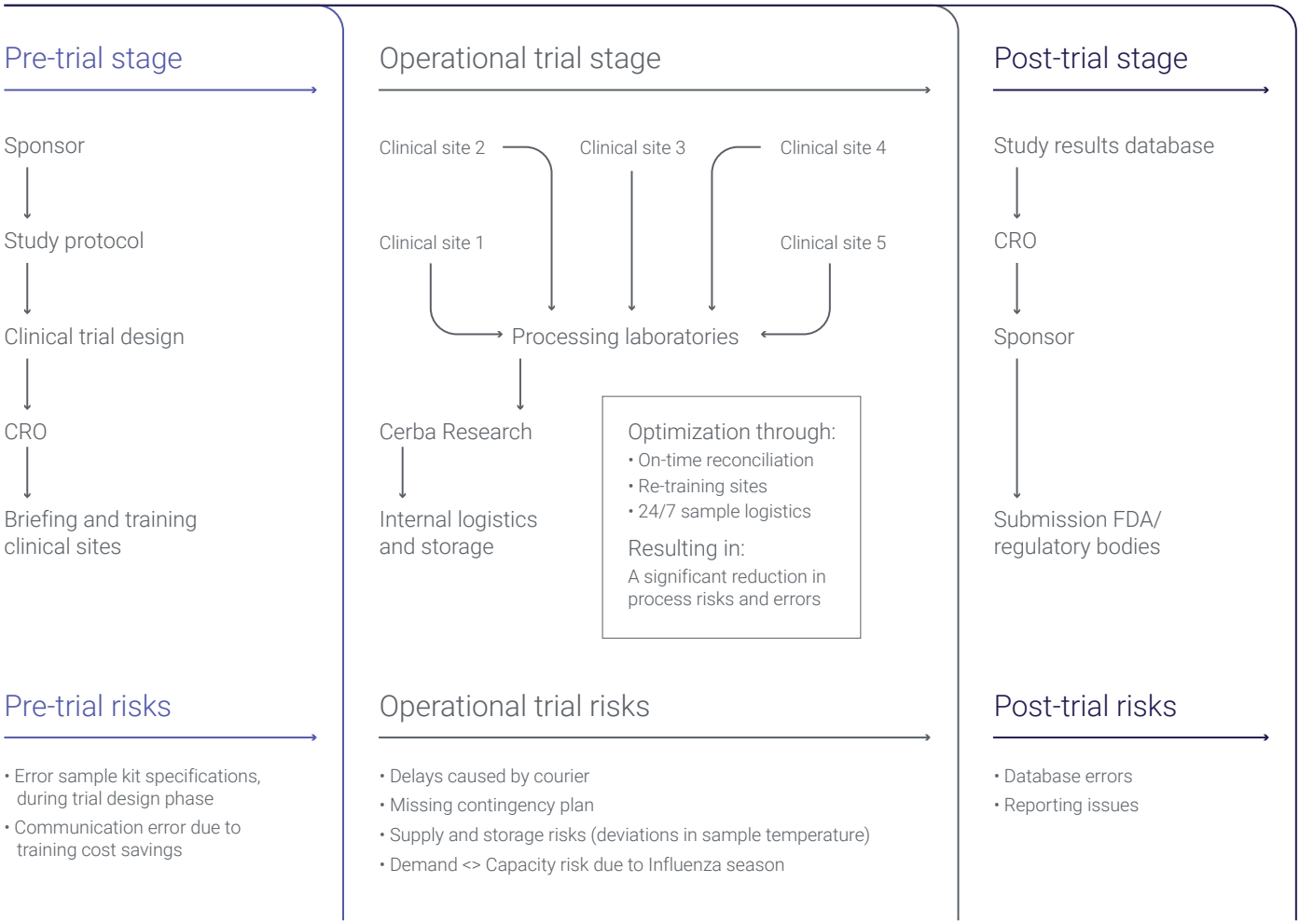


Figure 9.1: Clinical trial process optimization stages

The clinical trial process seems similar compared to other therapeutic fields, however there are major differences. The seasonal nature of Virology and Cell and Gene was illustrated in lesson 4 and highlights why the clinical trial process is so different. In the model above, the risks shed light on the focal points for optimizing clinical trials in a Virology and Cell and Gene setting.

The logistical process for Virology and Cell and Gene-related studies such as influenza are optimized by:

- Selecting the right logistics partner. This is of vital importance, because of the complexity of the samples (live virus). A specialized courier will be able to provide conditioning-monitored boxes, reporting/back logs, contingency planning, live GPS track and tracing and a global network of logistical support offices and warehouses. High quality couriers will have a positive impact on process optimization.
- For every partner in the clinical trial process it is important that they can deliver in a turbulent and unpredictable environment. This means that they need to be able to deliver flexibility, swift response times, adjust their activities to specific client needs and deal with peak demands.

Lesson 10: Making the best use of an expert networking model

The current pharmaceutical market is characterized by a strategic focus on outsourcing. Most biotech and pharmaceutical companies made the strategic shift towards an outsourced networking model. Outsourced secondary processes like manufacturing and clinical research seem to be the norm nowadays. Networking models require a different approach in relation to managing and controlling clinical trials.

The key here is to make the most of your networking partner's key competences and skills. Specialized suppliers, such as couriers, packaging companies and laboratories bring expert knowledge to the table. They can provide valuable insights into potential bottlenecks and operational issues. Successfully applying expert knowledge will most certainly result in operational efficiency.

There is a major difference between a partner and a supplier relationship. A supplier/client relationship is more focused on short-term financial metrics. In other words the relationship is predominantly evaluated based on costs and margins. There is more to a partner/client relationship in the sense that it is strategic in nature. This type of relationship is not only evaluated based on quantitative KPIs. Instead, longterm mutual benefits are evaluated as well. Distinguishing partners from suppliers is a valuable exercise in relation to a clinical trial. Strategic partners can make a significant difference. For instance choosing a specialized courier can have a major impact on the success of a clinical trial. Couriers with cold chain supply knowledge have access to the most optimal routes on a global scale. Listening to their advice can mean the difference between a delayed and a successful study.

This is where experience come into play. Couriers know all about delays that can potentially be caused by weather related circumstances, issues during customs clearance, packaging and handling, etc. Another example of strategic partners are CROs. CROs themselves tend to have their own network of strategic partners, including packaging an labeling companies. Packaging and labelling will not be on the radar of the average study sponsor. Biopharmaceutical companies and vaccine developers have other priorities.

This seems like a very minor process in a clinical study but it is certainly worth mentioning. In fact, making the wrong decision in terms of labeling can have a devastating effect on the end result of a study. The difference in results is clearly visible in **Table 10.1.**

Generic CRO results vs. specialized CRO results

Project	Organization	Sample identification issues*
Study V	Generic contract research organization	11.1%
Study M	Cerba Research	1.0%
Study O	Cerba Research	0.5%

* Analysis based on a total of (12,361 samples). Issues: sample leakage, duplicates, labeling issues

Table 10.1: Clinical trial process optimization stages

In this example, the sample identification issues were significantly higher when using a generic supplier.

The main issues in study V were caused by making the choice for a low cost kit supplier. In the end a significant number of samples had to be discarded from the study. In this case a specialized strategic partner would have certainly advised the use of different/high quality labels.

Figure 10.2 illustrates how a networking model can leverage strengths in the supply chain. What works best is to find 'overarching' key drivers supporting a swift clinical trial process. The model illuminates the interlinkage of these drivers in connection to the specific actors.

Mutual trends such as quality and on-time delivery are differentiated amongst actors. For a sponsor, quality means on-time delivery, before FDA evaluation. For a CRO, the main quality drivers are: swift, safe and efficient clinical trials. For a courier, quality means on-time delivery while maintaining the integrity of samples. In other words, quality is differentiated throughout the clinical trial process.

Sponsors can directly benefit from this model by listing and sharing KPIs and key drivers with other partners in the network. In this way, mutual goals are reinforced and strengths are leveraged. During the initiation phase of a trial, sponsors should not only list quantitative KPIs and drivers. Qualitative drivers are equally important. This focal point ventilates the main dilemma for the initiator of a study: how to balance quality and costs? Table 10.1 revealed that there is a connotation between low cost and quality output of the clinical trial. The lesson learnt here is that low cost will come at a high price. It is essential that drug developers are willing to invest in the partnership network. It pays off to select best-in-class strategic partners rather than opting for low-cost suppliers.

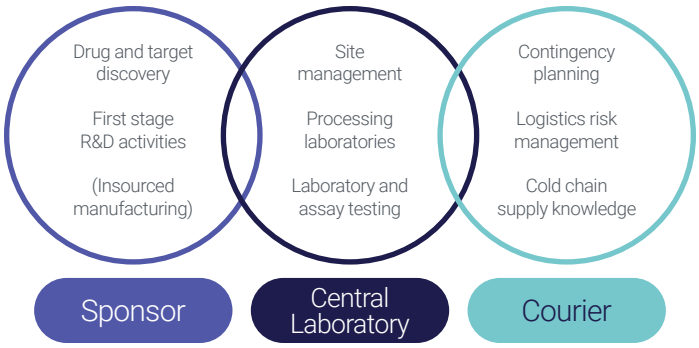


Figure 10.2 Leveraging strengths in the networking model

For sponsors it is also recommended to ask CROs to take on the role of main contractor. In this way the study initiator is released from activities that are not considered as core.

Central Laboratories can utilize their specialist networks. In summary, it is recommended to stay focused on core processes and let every partner in the network excel at their own specialty. This will ultimately benefit the overall efficiency of the concerning study.

Conclusion

The 10 lessons provide useful insights in the specialized field of Virology and Cell and Gene clinical trial operations from a practical point of view. The overarching conclusion can be narrowed down to the following 4 focal points:

There is certainly rationale to invest in clinical trial operations services. Logistical services account for a low percentage of total clinical trial costs and a high risk reduction potential. In fact it is about making a strategic choice: a preventive strategy (low risks/high guarantees/higher costs) or a corrective strategy (high risk/low guarantees/lower costs).

Due to the seasonality of demand, Virology and Cell and Gene studies are different than other fields. This notion calls for last-minute scale up and planning capabilities for all involved suppliers.

Specialized CROs and partners are capable of dealing with these sector-specific characteristics.

Overall, it is advisable to review CROs as strategic partners rather than suppliers. The lesson here is to use the strengths of all industry players in the entire supply chain. Every partner in the network has their own specialized capabilities. Use CROs in the role of contractors for the entire operational side of a clinical trial.

Performance expressed as KPIs (key performance indicators) and ROI (return on investment) is different for Virology and Cell and Gene projects.

The qualitative aspects and operational details are more important than in other therapeutic fields.

Cerba Research

About Cerba Research

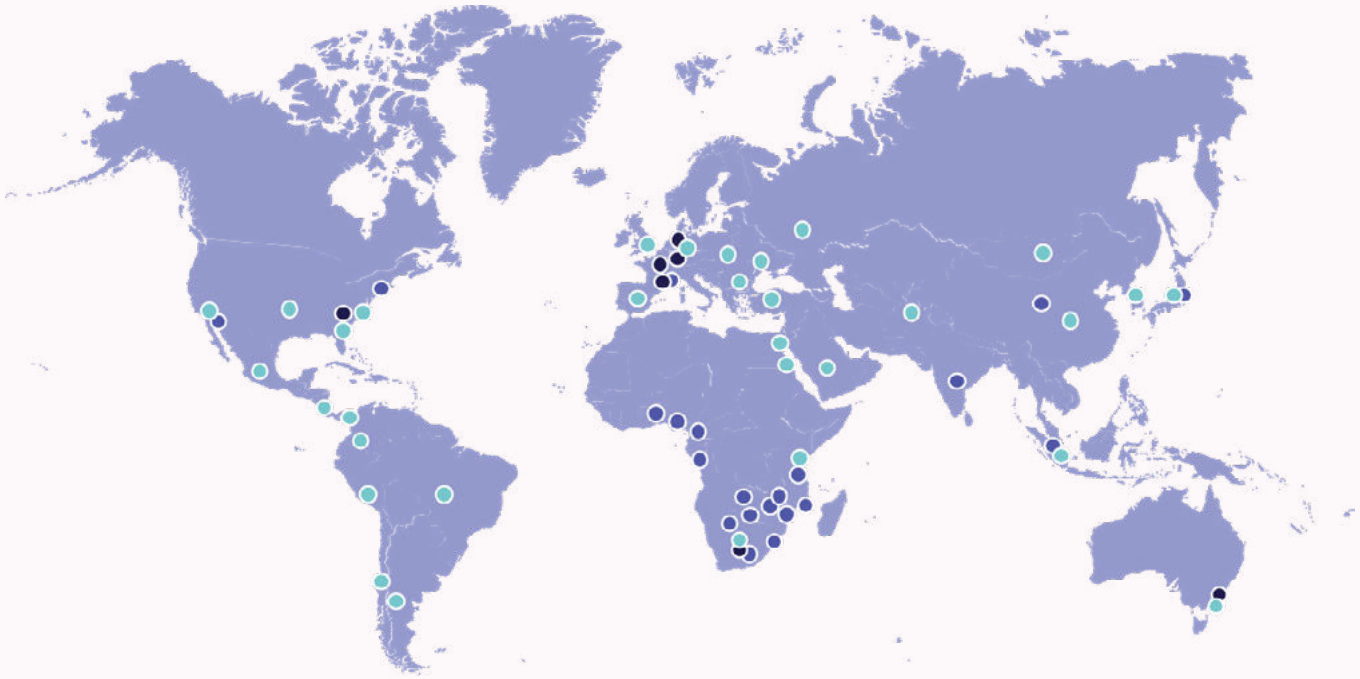
Cerba Research is a leading speciality laboratory services provider across all clinical development phases, to pharmaceutical, biotechnology, medical device, government, and public health organizations.

It combines the deep scientific expertise of specialist services with the capacity and breadth of a global central laboratory network.

Cerba Research develops innovative solutions to unique challenges in research and support logistics management for kits and samples at scale for multiple focus areas, with world recognized expertise in Virology, Oncology and Cell and Gene Therapy.

It is part of the Cerba HealthCare Group with 15,000 employees on five continents, driven to advance health diagnosis.

International network supporting global clinical trials



- Research & Partner Labs
- Pre-Processing Labs
- Office Locations & Technical Platforms

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Belgium, France, Germany, Italy, Netherlands, Russia Serbia, Spain, Turkey, UK, Ukraine

Asia Pacific

Australia, China, India, Japan, Pakistan, Philippines, Singapore, South Korea, Taiwan, Vietnam

Middle East

Israel, Saudi Arabia

Africa

Ghana, Kenya, Malawi, Rwanda, South Africa, Tanzania, Uganda, Zimbabwe

North, South & Central America

Long Island (NY), Montreal (QC), New Jersey (NJ),Richmond (CA), San Diego (CA), Argentina, Brazil, Chile, Colombia, Peru, Costa Rica, Guatemala, Mexico, Panama

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