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COMPARATOR SOLUTIONS

# How to Efficiently Manage Clinical Trial Comparator Sourcing Challenges

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# How to Efficiently Manage Clinical Trial Comparator Sourcing Challenges

Comparator sourcing is a vital component of successful clinical development programs. While in the past studies overwhelmingly compared drugs against placebo, many clinical trials now have active control arms. Companies must master a set of operational, regulatory and financial challenges to efficiently secure reliable supplies of comparator drugs for these trials.

Changes to the design of clinical trials have made comparator sourcing a key enabler of R&D success. During the past 20 years, ethical concerns about the use of placebos when effective treatments are available and a desire to demonstrate the superiority of experimental treatments over approved products have combined to make active control designs popular among regulators, payers and sponsors. Trials that use this design randomize patients to receive an experimental candidate or a product that is approved in the patient population enrolled in the study.

Having an active control arm allows sponsors to tell potential participants that they will receive either the experimental medicine or standard of care, potentially making it easier for the trial to recruit and retain subjects. Also, actively controlled trials gather data that show how experimental candidates compare with drugs used in the real world. If positive, the data can support discussions with regulatory agencies and payers, helping the experimental drug to win approval and secure reimbursement.

Sponsors have responded to these pressures and opportunities by incorporating active control arms into many of their trials, particularly in late-phase development. From 2005 to 2017, almost half of all Phase III clinical trials were comparator controlled.[1] The figure is higher in some indications, notably oncology. In Phase III cancer trials run over the same period, just one third of studies used a placebo. It is far more common in late-phase cancer trials to compare experimental medicines with approved drugs than with placebos.

These changes have enabled sponsors to realize benefits for themselves and the patients they enroll. The shift has also created challenges, though. Clinical trials with

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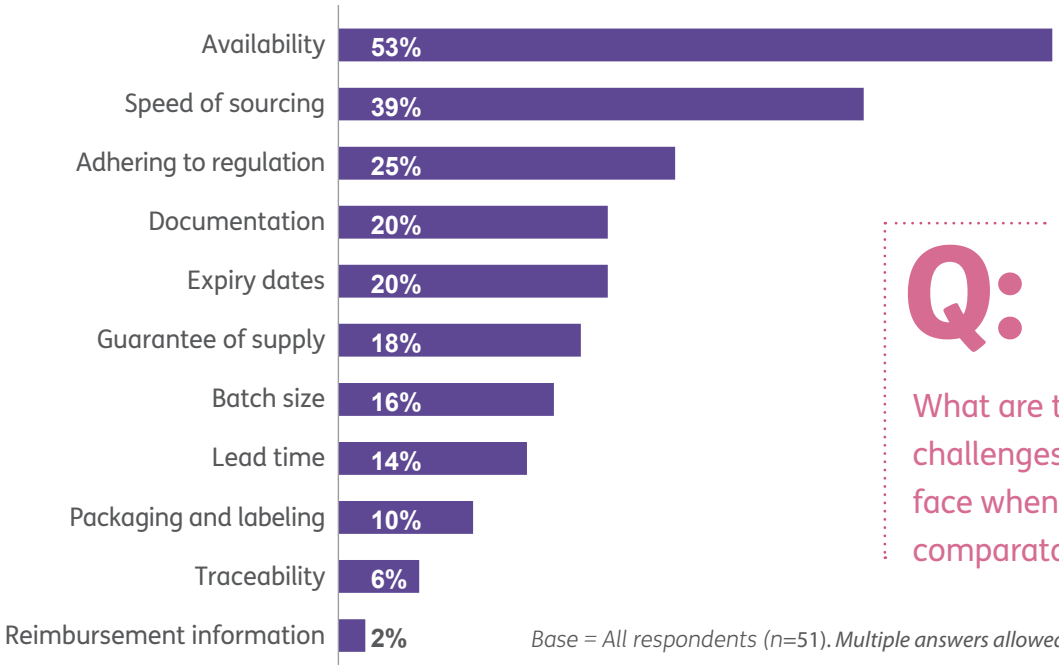


**Q:** What are the top 3 challenges you face when sourcing comparator drugs?

*Base = All respondents (n=51). Multiple answers allowed.*

*Source: Pharma Intelligence & Pilatus Custom Research | June 2018*
*Trends in Comparator Sourcing Survey 2018*

active control arms only proceed efficiently if the sponsor has reliable supplies of the comparator product.

In a globalized clinical trial environment, efficient comparator sourcing requires a detailed knowledge of the regulations covering the practice in different countries and strong relationships with global manufacturers, authorized distributors and verified comparator wholesalers. These are the resources that ensure authentic products are sourced and moved across borders without incident.

## Why Comparator Sourcing Is Challenging

When starting a comparator sourcing project, companies must know their own supply needs and how they are affected by external regulatory issues, quality standards, commercial factors and local procedures and contingencies related to the movement of goods. This entails understanding the volumes manufacturers can supply, how that may change as the trial progresses, what quality and customs documentation is required and a range of other issues outside of the core competencies of drug developers.

Companies must assess and manage these issues while facing resourcing pressures. A 2018 survey conducted by Informa's Pharma Intelligence and Pilatus of professionals involved in sourcing comparators for pharmaceutical companies, biotechs and contract research organizations found cost is their biggest challenge, with around two thirds of respondents citing it as an issue.

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Relatively little data exist on the cost of comparator sourcing but the information that is available, plus anecdotal reports, suggests the outlays for large companies can be significant. In 2012, the Tufts Center for the Study of Drug Development (CSDD) found a large pharma company estimated it spent $120 million a year on comparators.[2] The estimates of other companies were lower but still sizable. The average clinical supply budget across the 11 large pharma companies surveyed by Tufts CSDD was $50 million, half of which went toward comparator sourcing. Biotechs will have smaller, but relative to their size still significant, comparator sourcing budgets and face at least as much pressure to control costs as their larger peers.

The pressure to reduce the cost of comparator sourcing can, however, ultimately exacerbate some of the other challenges companies face. More than half of the polled comparator sourcing professionals cited availability as a challenge, and a significant minority listed speed of sourcing and adherence to regulation as notable issues. Focusing on cost, not value, can exacerbate these challenges by leading companies to take financially motivated decisions that ultimately make it harder to quickly source enough comparator products while complying with regulations and quality requirements.

The survey also uncovered region-to-region differences in the challenges of comparator sourcing. For companies working in North America, cost is the main challenge, reflecting the high prices of drugs in the US. It is cheaper to buy medicines in other parts of the world, but these regions tend to be less homogenous, creating a different set of problems. Respondents cited customs as a challenge in Europe. In Asia, language barriers and doubts about drug quality are among the biggest concerns.

These findings show companies must overcome multiple potentially unforeseen obstacles, which are not necessarily easy to identify, to get comparator drugs to where they need them, when they need them, without running up a big bill or falling foul of regulators. Failure to clear these obstacles can have significant effects on clinical development programs. Two thirds of the polled professionals said compliance challenges have notable impacts on the broader study. Almost as many people pointed to supply to individual sites as a challenge with far-reaching effects for the study.

## How Companies Are Meeting Sourcing Challenges

Faced with the growing need to manage these challenges and access comparator drugs, clinical trial sponsors have developed a range of sourcing strategies and efficiency initiatives. Best practices have emerged from these efforts, leading many companies to adopt strategic, partnered approaches that consider comparator sourcing needs early in the clinical trial process.

The efficiency initiatives discussed by the surveyed comparator sourcing professionals reveal they prioritize value over cost. Although the citing of cost as the main challenge would suggest savings should be the top priority, in fact the survey shows people are focused on creating a smooth-functioning comparator sourcing system that provides them with real value.

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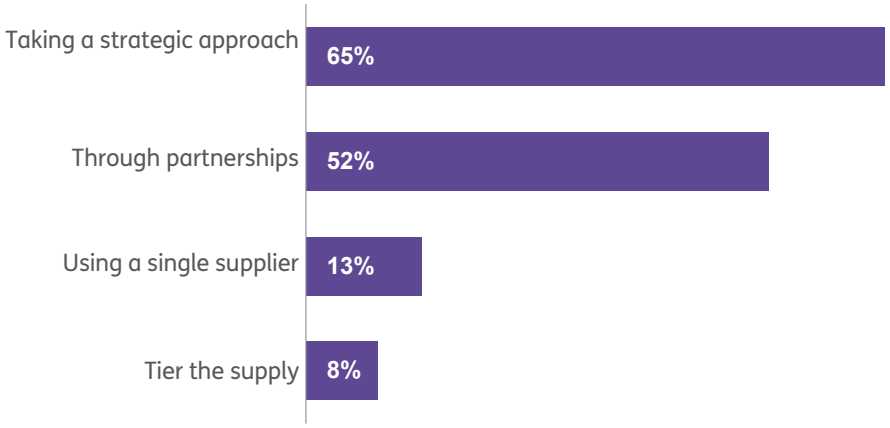
## Q: How are you reducing the risks associated with comparative clinical trials?

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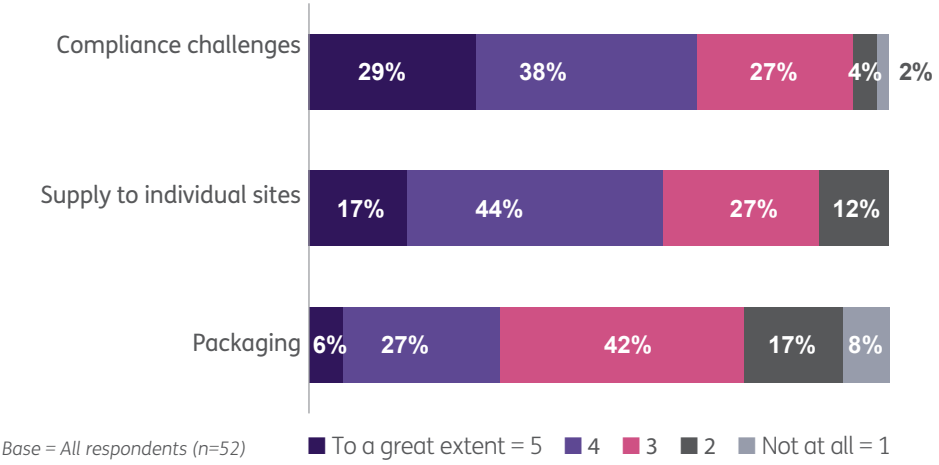
## Q: To what extend do each of the comparator elements impact the broader study?

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Many of the efficiency initiatives discussed by respondents relate to the need to consider comparator sourcing earlier in the clinical development process. These companies are thinking about comparator sourcing as far back as protocol development, ensuring they have time to identify risks, explore a range of options and ultimately secure supplies by the time the study starts.

This requires more work up front but is preferable to failing to prepare. Companies

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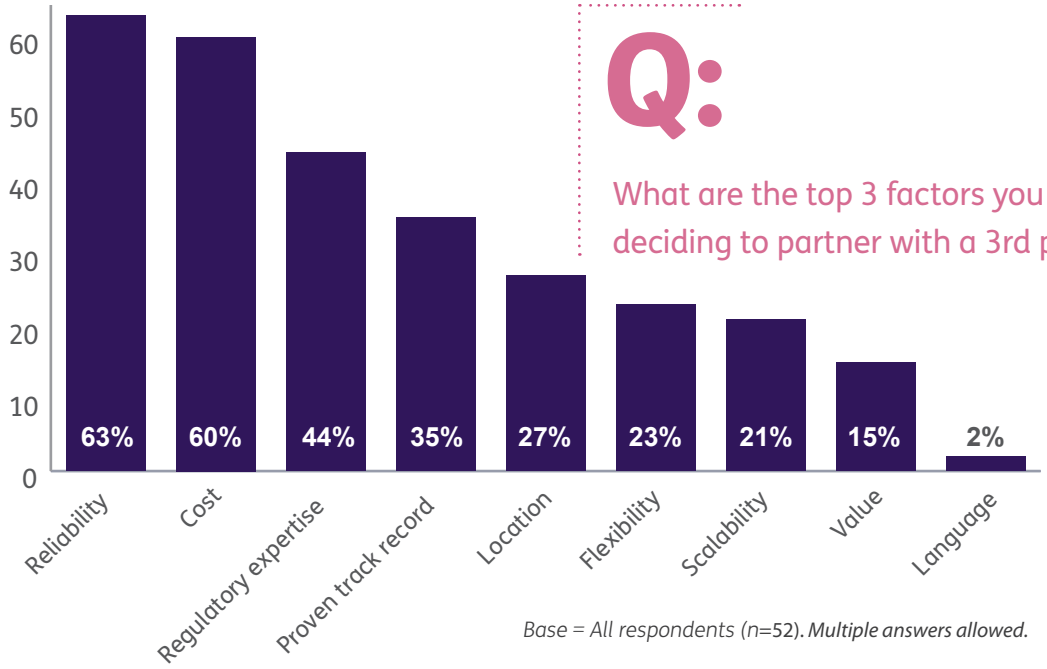


**Q:**

What are the top 3 factors you consider when deciding to partner with a 3rd party?

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that delay their preparations run the risk of encountering problems mid-study, forcing them to rescue the situation in a live project when there is a lot at stake. Widespread understanding of these issues means it is now more common for companies to start planning early. Around two thirds of respondents said they mitigate risks by adopting a strategic approach, which entails taking the time to assess all the options.

There are no hard and fast rules about when to start preparing, though. The market dynamics and product usage vary too much from comparator to comparator for a prescriptive attitude to be effective. Rather, companies are best served by assessing the situation early, defining what drugs they need to source by when and formulating a main plan and multiple fallback options that will deliver what is needed.

Asked about their efficiency initiatives, other survey respondents emphasized related points about the value of forecasting. Comparator sourcing professionals who engage in forecasting talk frequently with manufacturers to ensure the required product volumes will be available when they are needed by the study. This proactive, forward-looking approach enables the identification and mitigation of potential supply bottlenecks. Forewarned, a company can scale up its sourcing effort in anticipation of the extra demand.

## Why Companies Work With Specialist Comparator Sourcing Partners

The value of working with a specialist comparator sourcing partner to access expertise is the other big theme to emerge from the discussion of efficiency initiatives. Respondents to the survey highlighted how partnering with specialist comparator sourcing organizations with expertise in each geographic region makes the process more ef-

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ficient. More than half of respondents listed partnering as a way to reduce the risks associated with comparator-controlled clinical trials.

The preference for partnered approaches is in line with the prioritization of value over cost seen in the other responses. Enlisting the support of external experts can increase up-front costs. However, as companies have learned, that focus on up-front costs obscures the direct and indirect ways an effective specialist comparator sourcing partner can save money.

For example, a specialist may identify opportunities to source products from multiple or lower-cost, markets such as the European Union, where medicines can be as much as 50% cheaper than in the US. However, without the specialists' initial research and ability to obtain the correct quality documentation that can clearly prove product equivalence across the trial countries, such cost saving initiatives may, in fact, place a study in jeopardy. Further savings are possible if the specialist comparator sourcing partner leverages relationships with manufacturers to make bulk purchases.

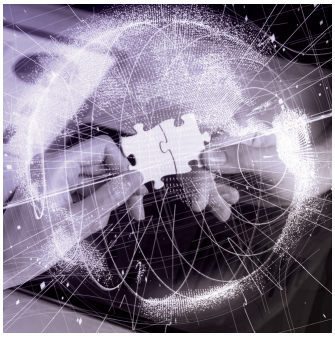
Partnering with specialists also achieves indirect savings by cutting the risk of time-consuming delays. Specialist comparator sourcing partners understand product manufacturing schedules, have insights into market shortages and know in advance about forthcoming formulation changes. This knowledge enables specialist comparator sourcing partners to horizon scan for risks, ensuring the sponsor can make well-informed decisions that secure sustainable supplies for the duration of a clinical trial and minimize the risk of catastrophic delays.

In blockbuster indications, even a short delay to the clinical trial — and, by extension, time to market — can mean missing out on many millions of dollars in sales. If the delay allows a competitor to come to market first, McKinsey calculates the laggard company will have a 6% market share disadvantage 10 years later.[3]

The survey responses show specialist comparator sourcing partners prevent supply-related delays. Multiple respondents pointed to the ability of specialist comparator sourcing partners to obtain the products they need as a key advantage of outsourcing. Specialist service providers have access to multiple potential sources of drugs and as such are more likely to find available comparator supplies than pharma companies. In some cases, this makes the supply of a comparator more reliable. In other cases, it is the difference between a clinical trial having access to a comparator or not.

Other respondents highlighted the knowledge possessed by specialist comparator sourcing partners, their ability to ship to international hubs and the simplicity that comes from working with excellent coordinators and project managers as factors that make outsourcing appealing. Combined, these factors result in a streamlined process that reliably delivers comparator drugs to clinical trial sites.

Exactly how streamlined and effective the supply process is depends on the capabilities of the specialist comparator sourcing partner. It is vital to pick the right partner to



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ensure products are reliably sourced and all opportunities for cost savings are taken.

When the polled comparator sourcing professionals look for a partner, they prioritize reliability and cost. Almost two thirds of respondents said these factors are among their top three considerations when choosing a specialist comparator sourcing partner.

Many of the other factors the respondents prioritize relate to cost and reliability, too. For example, almost half of respondents cited regulatory expertise, particularly in relation to quality, as a top consideration. The value of such expertise to comparator sourcing professionals is that it ensures the supply process is efficient and free from time-consuming delays, which affect cost and reliability. Cost and reliability concerns are also at the heart of respondents' preference for specialist comparator sourcing partners that are scalable, flexible and have a proven track record.

## The Future Of Comparator Sourcing

The survey shows comparator sourcing is hard and is likely to remain so for the foreseeable future. If drug supply chains and the regulations that govern them remain complex, comparator sourcing will continue to be challenging.

Yet, the data also show companies are learning how to manage the challenge. The emergence of a consensus around the best ways to mitigate the myriad supply challenges gives companies a set of best practices to apply to comparator sourcing.

These best practices point to proactive, specialized partnered approaches that consider comparators early in the clinical trial process as being the best way to manage sourcing. Companies that adopt this way of working today will give themselves a long-term advantage as ethical and commercial pressures make comparator-controlled trials ever-more common in the years to come.


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