Blog

Ensuring supply continuation when sourcing comparators – what are the risks and how to avoid them!

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Sourcing comparator drug supply for clinical trials can be difficult to navigate, even with an established procurement team. When surveying respondents at the GCSG US Conference 2022, we found that 75% of respondents experienced a challenge when sourcing comparators or ancillaries, proving that you are certainly not alone in experiencing difficulties with sourcing activities. When using the terminology 'comparator', we are including co-medication, non-investigational medicines, and the obvious, comparator drugs themselves. Within this article we will discuss some of the risks when sourcing comparators and how to avoid the risks wherever possible.

What are the risks to supply you might face when sourcing?

When planning a clinical trial, there is so much to navigate that often the comparator sourcing strategy can be an afterthought. Consequently, when it is time to purchase the comparator, the market may not be favourable, and the options are limited. Common challenges that can be faced include:

- Lead time is too long
- Expiry date is too short
- Limited availability of the product and/or shortage/discontinuation risk
- Regulatory roadblocks through lack of documentation

It is important to consider that the sourcing market often moves quickly, therefore delaying decisions on whether to purchase stock or wait for the next batch can impact your strategy. The chances are you are competing with other clinical trials for the same stock.

Plan, Plan, Plan!

If you take one piece of advice from this article, then I would recommend it be this…take the time to plan your supply route well in advance of recruitment starting. By allowing time to plan, it affords you time if the primary sourcing route does not work out as planned, gives you more time to accumulate stock and significantly increases the chances of establishing a robust supply route.

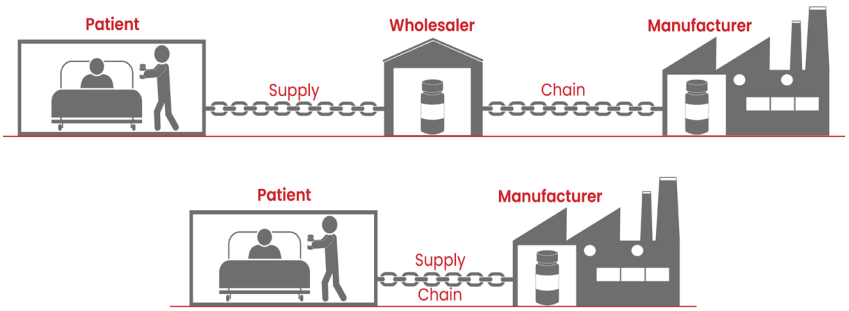
One of the first decisions you will likely need to make is whether you outsource your comparator sourcing or keep it in-house. By outsourcing, it is likely your vendor will have a larger reach in the market (multiple vendors), more knowledge of supply availability and often can get information and products faster. Although you will pay a margin to an outsourcing partner and may incur higher freight costs than keeping it in-house, the right outsourcing partner will be more cost effective overall. However, if a direct supply agreement is being established then outsourcing may add complexity in some cases.

If the decision is made to outsource, then share as much information as possible with the vendor. For example, study countries (so they can advise on what documentation may be required), predicted enrolment rates (so together you can establish resupply plans), and plans for regulatory submission (I will come back to this point).

An alternative method would be to delegate sourcing to the clinical sites or patient. Although this reduces the sponsor burden it increases the burden on the site or patient, they may not be willing to source or may request compensation. Furthermore, there may be inconsistency between product type or batches. However, if this is not a concern, this could be a faster route as it is going direct to site or patient (rather than through a vendor). This option will not be possible within the EU, UK, or Israel where repackaging and QP release is required.

How Much Are You Willing to Share?

Regardless of whether you use a vendor or your in-house team, when planning your supply route there will need to be consideration as to whether you will go directly to the manufacturer or through wholesalers (also known as the open market). How you classify the product in your protocol can help shape this decision. Whilst it is possible to go direct to the manufacturer to purchase their product for use as a comparator, it is generally easier if you are using their product as a co-medicine (combination therapy).



Direct sourcing reduces the links in the supply chain, will generally enable you to get the documents you require (e.g., a certificate of analysis) and more control over the number of batches received and even the possibility of a dedicated manufacturing run which will get you the best possible expiry date. Despite these positives, it is important to be aware that it is very likely you will be expected to provide data disclosure. This is of course dependent on the manufacturer, but we have experienced sponsors being asked for trial details (EudraCT or IND number), study design, planned locations of clinical sites, agreement to share trial data.

Furthermore, the manufacturer may insist on changes to, or reject, the study design, although, they have an ethical responsibility to support clinical trials some make the process laborious.

If data disclosure is not a concern, approaching the manufacturer to establish a supply agreement could result in free drug supply. If exploring this route, ensure you factor in the time for legal review of the agreement, drug manufacturing (if it is a dedicate run) and the fact that you may lose control over the drug livery (e.g., insistence on supply from Germany).

At some stage information on your trial will be in the public domain such as clinicaltrials.gov, it is unavoidable. However, by that point, you could already have an established route of supply without any data disclosure. This can be achieved through the open market. There are wholesalers throughout the traditional sourcing markets (USA and Europe) that have relationships with manufacturers where they can get drug product without data disclosure and/or they have permission to sell any excess stock they hold.

Utilising the open market offers more flexibility – there are several wholesalers to select from, particularly in Europe, which increases competition and drives down prices (compared to direct sourcing). Additionally, we often see shorter lead-times when sourcing through the open market compared to going direct. This can be a very appealing option if lead time is a driver for your study.

When sourcing drug product in the EU, some markets are more competitive than others when it comes to pricing but also consider the market size. For example, the Baltics region is usually competitively priced and will often provide a certificate of analysis (CoA), but the market is far smaller than countries in Western Europe. Smaller markets can result in multiple batches or challenges with the continuation of supply.

Planning your supply route in advance and working with your vendor, if applicable, can help navigate this. Most vendors will supply you with a market assessment and a supply plan which gives a snapshot of the market and trends. Together you can establish a plan. For example, if you are running a global study that includes China, and sourcing within China is not an option, a route that comes with a CoA will likely be needed such as the Baltics. However, the market may not be large enough to support the whole trial so a second or third market could be introduced for ex-China supply. Sometimes wholesalers can offer stock with or without a CoA – often non-CoA stock is cheaper, so consider if you really need one for every country.

Think outside of the box...

It is very easy when comparator sourcing to rely wholly on established routes. This can be very successful when it comes to supplying your clinical trial with comparator products. The market in the USA for example is very well established and excluding a shortage occurring, resupply is consistent. Sometimes though it is pertinent to challenge the status quo.

It is common practice when managing a global clinical trial to supply European sites from the EU and North American sites from the USA, the Asia-Pacific region is sometimes supplied locally or from the EU or USA. This is a well-established method; however, it is often not the most economical. It is common knowledge that US drug prices are amongst the highest in the World – sometimes up to 10 times the price of the EU. Therefore, if you are working with a limited budget, it would be worth exploring a central source of supply for the whole study from Europe. So long as you have approval from the FDA and your regulatory team is on board this could be a very cost-effective route. Furthermore, your vendor may be able to obtain a statement confirming equivalence between EU and US products which is helpful for importation.

Similarly, consider sourcing market from outside of the traditional USA, EU, and UK – especially if products are in high demand and there is inconsistent supply in the major markets. Markets such as Australia, Canada and the MENA region are genuine alternatives and a way to get consistent supply at a competitive price. Clearly, when sourcing outside of the EU and USA, where there are established anti-counterfeit programs it is important to conduct due diligence on the supply chain. At RxSource, we have vast experience providing Canadian products for global studies with significant cost savings for our partners (visit our website for case study).

An additional consideration when working on a limited budget or even if trying to reduce waste is to work with a vendor that can provide supply chain optimisation solutions. RxSource partners with such a vendor who will review the study design and introduce an algorithm that can significantly reduce the amount of comparator needed and ensure the clinical sites do not hold excessive stock. Utilising this approach, alongside demand-led packaging has enabled us to reduce the financial burden on the sponsors we work with.

Don't paint yourself into a corner!

Ultimately when sourcing comparators it is more likely than not you will experience a supply challenge. The key is to be ready for it and to always have alternative plans. Whenever I speak to sponsors, I suggest they not paint themselves into a corner by being too specific on their clinical trial application. If, when listing your comparator, you include a specific market authorisation number, if that product goes on shortage and you lose supply then a protocol amendment would be required and there is a risk of an interruption to patient dosing. The same risk applies if sourcing directly, even with a supply agreement, shortages or acquisitions can have a devasting impact on resupply.

If on your submission you do not specify the market authorisation number, this gives you a much better opportunity to manage resupply in the event of an interruption. For example, if a product goes on shortage or is even discontinued in the USA, you could look to Canada or

Europe to continue supply. Additionally, you may want to consider a generic, just be cognisant that they are more prone to discontinuation than innovators.

Similarly, if you source your comparator and then request documentation for shipping to the clinical sites you may find the documents you require are unavailable. It is rare to obtain a CoA from the USA so if you are running a study in China you may need to pivot to another market.

Comparator sourcing is about experience, knowing markets and planning appropriately. Try to think ahead as to what roadblocks or challenges you may face. Research the drug you are using to see if there have been previous shortages or challenges. Consider whether you want to use an innovator product or a generic – perhaps the generic is your back up option.

Finally, don't try and face the challenge alone, rely on vendors or if keeping it in-house, speak to colleagues or industry peers to understand their experience. At RxSource, we have over 18 years of sourcing experience (and over 150 years across the team) and are always willing to offer our advice and support.

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10 years+ Industry Experience

3 years+ with RxSource

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