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Your Clinical Supply Solutions

White Paper

Why Comparator Strategy Starts at Protocol Design

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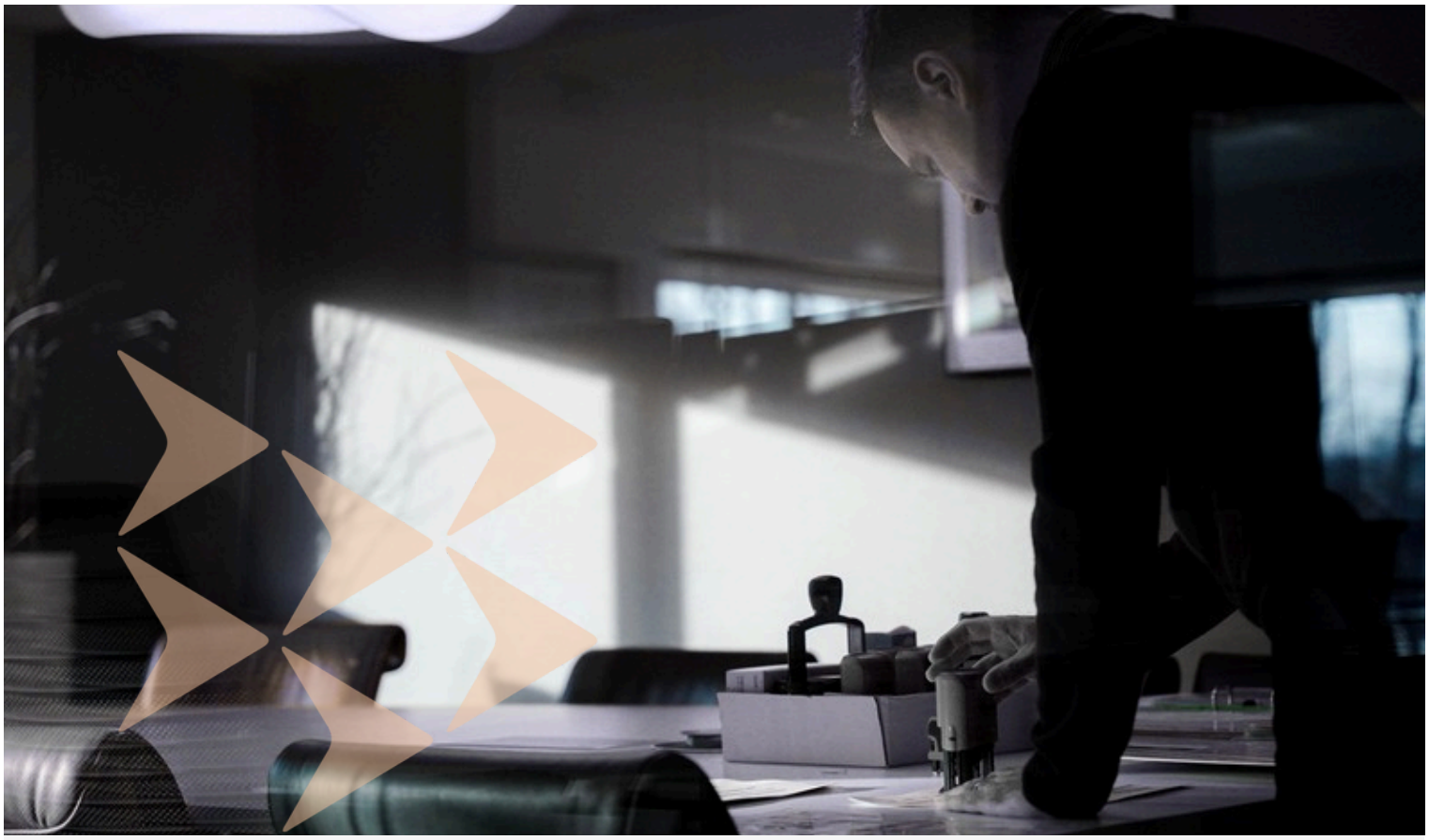


Contents

A clinical trial protocol has to take many things into consideration, and the way that the comparator drug is listed is perhaps one of the simpler (or at least shorter) parts of a very detailed and involved document. As a result, the importance of it can be overlooked.

This White Paper aims to share insights into how 'getting it right from the get-go' can help to avoid shortages, delays and unnecessary costs. Most issues related to disruption in the supply of comparator drugs happen when the supply chain is already up and running, and they are often unavoidable, but your ability to manage this disruption and to switch over to 'Plan B' can most often be traced back to how well that eventuality was prepared for. This inevitably leads us all the way back to Protocol Design.

How ‘Specificity’ Impacts ‘Flexibility’

By definition, ‘specificity’ and ‘flexibility’ are far from kindred spirits. What might seem like a robust and conscientious approach to detail in a planning stage can, even with our best intentions, turn into supply chain handcuffs if things don’t go to plan.

When planning for the use of a commercially licensed drug (comparator) in a clinical trial it pays to be as flexible with your wording as regulatory guidelines allow. Whilst those guidelines may vary from territory to territory, the approach remains the same.
If you build in as much wiggle room as you can for your comparator description, then you will have more options at your disposal if your desired comparator is delayed, disrupted, or even discontinued.

Key examples of over specifying could be:

- Specifying a brand name when a generic name will suffice
- Quoting a specific strength, pack size or presentation when there are many
- Naming a particular manufacturer when there are several, or where more may come to market
- Listing a drug license number or particular country of origin
- Using language that limits the ability to switch to a biosimilar or generic, should one be launched during your study
- Stating that certain documentation will be provided, if it goes beyond the level needed for compliance

Many poor comparator strategies are borne from a supplier putting forward a drug that happens to be in stock and available when a trial is first supplied. Commercial markets are fluid, and the best option today may not be viable in 2 years' time, and whilst no comparator vendor can look into the future with absolute clarity, sponsors rightly rely on vendors to provide strategies based on experience, data and market insights, and not just snapshots of current stock levels.

However, even the best approach can hit a hurdle, and this is where the well-prepared sponsor can protect *themselves* by not over *specifying during* the protocol design.

How Might Specificity Hurt Me In Practice?

Picture it. Your first supply went perfectly. Everything has been packed, labelled and distributed. Sites are well stocked and life is good. But in clinical supplies we are only ever a few months away from the next round of supplies, so you reach out to your vendor (the one that based your supply strategy around what happened to be on the shelf at the time).

"Bad news, I'm afraid. The drug is now on back order and there is no re-supply date – the manufacturer has said it's going to be at least 9 months before more stock can be available".

Just when everything was going so well! Plan B is never as good as Plan A, but having a Plan B feels very good in this scenario.

In practice, the person who only has Plan A will scurry around looking for any supply of the very specific drug they started with and will be keeping everything crossed that someone can come up with a miracle.

Those miracles can and do happen, but very rarely, and the reality of a back order without a very imminent re-stock date is that the drug is not in a position to come to market. If it isn't actively being manufactured and released then anyone operating on a commercial/wholesale level can't access it, beyond accessing the last few packs that may be hiding on a shelf within their network.

The best-case scenario here is a protocol amendment, delays, and in the worst case there is significant risk to trial continuity.

The person with Plan B will still be inconvenienced. They would likely need to spend time changing label text and designs amongst other things, and they would incur costs. But importantly, they would not need to amend protocols or wait for approvals from regulators, saving a lot of valuable time and expense. They would be able to move on with confidence that the commercial drug they switch to would still fall within the scope of their protocol.

Early Vendor Input Can Help Reduce Disruption

Within Clinical Supply Chains, especially where comparator drug is required, we walk a path that straddles the Clinical and Commercial spheres, and even though these two spaces share some common ground, there are times when we rely on our counterparts for their insights and expertise.

As a Vendor, the conversations we have with Sponsors are invaluable. I hold my hands up; more than once I have gone into a Teams Call with my own idea of the problem at hand and what I think is the right answer, only to find out that the Sponsor is working with goals, pressures and constraints that could not have been apparent without that conversation taking place. It's an old adage, but communication is key.

These conversations must take place, and they should be as early as possible in the planning process. The ideal time is when the trial itself is simply a concept; an idea being floated around by management that may or may not crystallize. This is when early input can set the protocol design off down the right path, and vendor input into comparator selection can be meaningfully adopted.

A thorough vendor overview should, at the very least, include the kind of information that the sponsor could not reasonably be expected to access themselves,
for example: whether the product has a history of shortages, how collaborative the manufacturer is when directly approached for clinical trial supply, and what level of disclosure would be required.

This type of Vendor insight can be taken a step further. For example, not all commercial pharmaceutical products are created equal, even if they are the same molecule, and the type of variance that occurs when we start looking beyond the outer carton, can impact how a drug is utilized in a study.

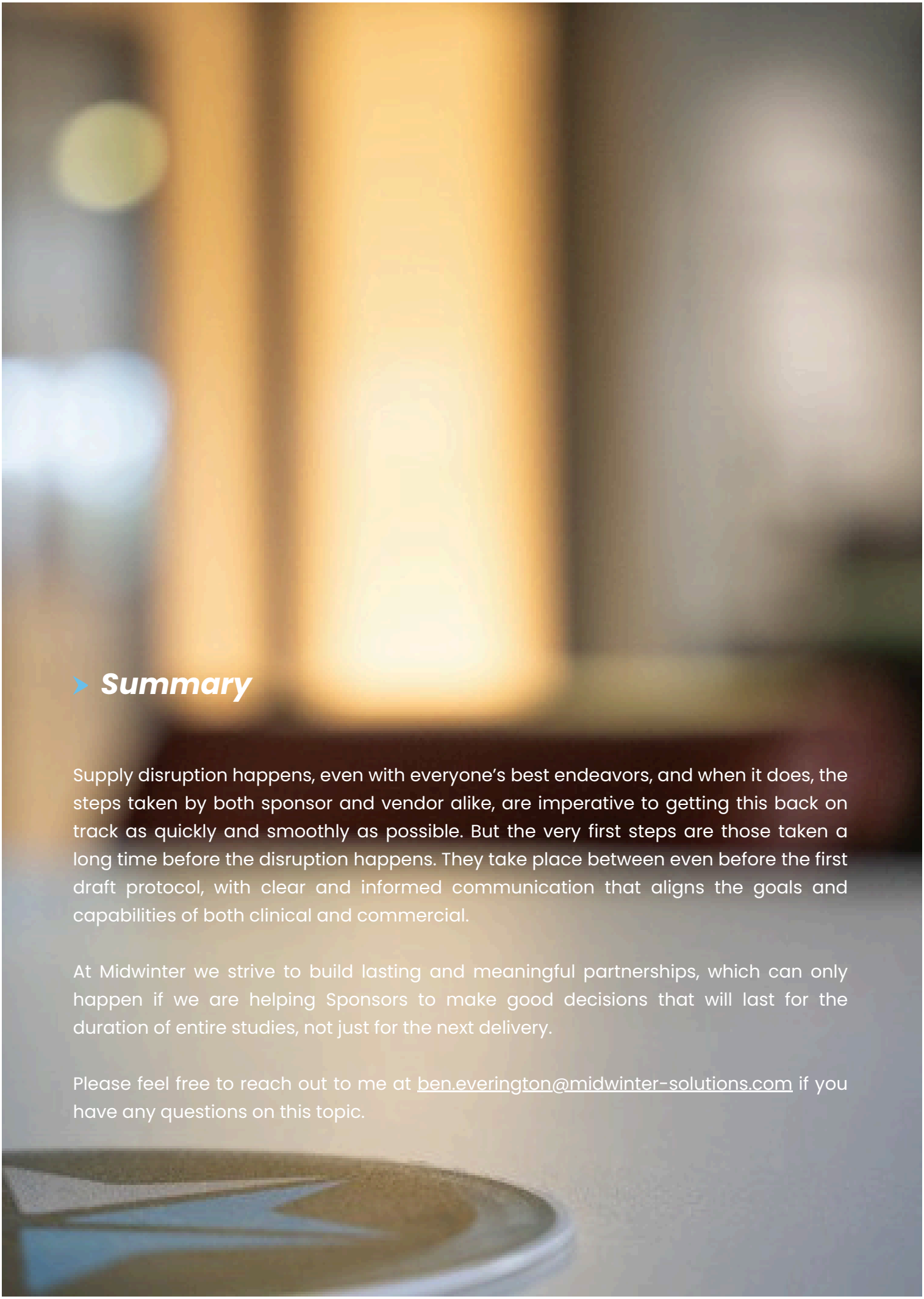
Shelf life can vary between presentations and between manufacturers, one product may be easier to blind than another, and one may have more market share than another making it more accessible.

Questions Sponsors Can Ask to Understand Their Commercial Supply Chain

Vendors should (without Sponsors having to ask), provide the type of insight that enables you to plan for flexibility from the outset.

But in the event that a Sponsor isn't getting the type of information that is needed, they could consider the following questions to help them allow for comparator flexibility during the early planning stages:

- Does this product have a history of shortages or supply disruption?
- Clinical have specified their preferred presentation/dose, but what are the other options?
- This drug is generic; can you provide the details of two back-up manufacturers in case our first-choice encounters disruption?
- Do the back-up options come at a different pack price?
- Is it possible that we see different pack origins throughout the study?



Summary

Supply disruption happens, even with everyone's best endeavors, and when it does, the steps taken by both sponsor and vendor alike, are imperative to getting this back on track as quickly and smoothly as possible. But the very first steps are those taken a long time before the disruption happens. They take place between even before the first draft protocol, with clear and informed communication that aligns the goals and capabilities of both clinical and commercial.

At Midwinter we strive to build lasting and meaningful partnerships, which can only happen if we are helping Sponsors to make good decisions that will last for the duration of entire studies, not just for the next delivery.

Please feel free to reach out to me at ben.everington@midwinter-solutions.com if you have any questions on this topic.

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