Sourcing innovator products in the age of biosimilar research

Michael Cohen, BSc, MBA

Sourcing innovator drugs is a critical and complex component of biosimilar research. Understanding the challenges and conducting thorough upfront planning are crucial in ensuring success.

Keywords: Innovator drug sourcing challenges

Sourcing innovator drugs for clinical trials is a crucial component of pharmaceutical research. Today, well over half of phase III trials utilize an innovator drug as a comparator to help prove the new drug being developed is superior to the product currently on the market.

Biosimilar research presents more complexities than traditional clinical trials, as an innovator product is used throughout all phases of research, not just in phase III. This article will address what is required throughout each phase, and the associated challenges.

Reference Library construction

Unlike traditional drug development, preclinical work is essential in the development of biosimilars, and is much more involved. The goal of the analytical research is to prove that the biosimilar manufactured has the same biological content as the original innovator product to which it is being compared.

In the construction of a Reference Library, small quantities of the innovator drug are acquired from a large number of lots over the course of months or sometimes years. Depending on the product and the company developing the biosimilar, there are varying requirements regarding amounts sourced and the expiration date spacing between lots. Some companies ask that each lot be a different expiration date, and others ask that there are two and sometimes three months between each sample that is purchased. Unlike other phases, it may be possible to purchase the innovator drug in smaller quantities for the Reference Library, working around potential restrictions from the product manufacturers.

In gathering these lots for the preliminary research, it is important to work with multiple suppliers who will have access to a variety of markets and supply sources to ensure the best selection of manufacturer lots. Clear communication is paramount in ensuring the correct product is purchased, as even a small quantity will cost tens of thousands of dollars, and, over time, could exceed one million dollars in product cost.

Phase I studies

The goal of phase I research is to test both the biosimilar under development and the innovator drug on healthy volunteers to ensure the safety of the new product. In some ways, sourcing product for this phase can be less complex than in building a Reference Library, because the product is sourced only once, and from a single lot. Quantities typically range between 100 and 400 vials or syringes depending on the drug and preferences of the biosimilar developer.

The biggest challenges arise in sourcing products that are subject to manufacturer restrictions. In some cases, the products will not be available without providing trial information. In other cases, the products are available in the open market, but a Certificate of Analysis (COA) will not be available. In best case scenarios, there will not be any issues, although this most often is not the case. The market in which the study is being conducted also determines whether product will be available with a COA. For example, the US tends to have more restricted products, and it is not possible to obtain a COA for most drugs, even if sourced direct from the manufacturer.

Phase III studies

Sourcing for phase III studies presents the greatest challenges, and requires considerable upfront planning in order to successfully secure the innovator products needed and to mitigate potential risks to the trial. Without proper planning, delays or even cancellations could occur, jeopardizing an investment of hundreds of millions of dollars. These potential delays or cancellations could ultimately affect the timing of the new product launch, which could have an implication of billions of dollars for the biosimilar developer.

In this phase, required volumes could range from 2,000 to 10,000 vials or syringes, sourced over a two- to four-year period. Because most biologicals have relatively short shelf lives, and because enrolment in trials can vary, it would not be prudent or even possible to acquire all products from a single lot.

Approximately six to 12 months prior to sourcing the product needed for phase III, an extensive market intelligence process should take place. An experienced supply partner or CRO (Contract Research Organization) should be able to gather the necessary information to address the following:

- Can the innovator product be sourced direct from the manufacturer? If so, what information around the study do they require? If purchased from the manufacturer, what are their standard lead times to fill the required orders?
- What volume of product can be sourced on the open market? This often proves to be a valuable alternative to sourcing from the manufacturer, or can be used to supplement product supply when manufacturer lead times are lengthy.
- What is the pricing difference between that of the manufacturer and sourcing on the open market? If sourcing on the open market, are there price variances by region (US versus EU) or by country within the EU?

- Are there alternate markets from which product can be sourced with a COA or other batch release information to allow for QP (Qualified Person) release or approval from the US Food and Drug Administration? This would provide an option if supply is limited in the target markets from which it was originally intended to source.
- What is the shelf life of the innovator drug that is being sourced? If it is longer, such as in the cases of Herceptin and Remicade, product can be accumulated prior to the start of the study to work around future market or manufacturer limitations. If the expiration dating is shorter, as in Humira and Avastin, then more frequent sourcing of smaller quantities will be required. In this situation, a greater amount of retention samples and packaging runs will need to be considered, which will increase the overall study cost.

The importance of this supply research in phase III is imperative, and should be re-evaluated multiple times prior to sourcing, as well as throughout the duration of the trial. A qualified sourcing partner should be more than willing and able to support this critical research, and if not, a partner that is should be identified.

For more information, please contact Michael Cohen, Managing Director, Myoderm, 48 East Main Street, Norristown, PA 19401, USA, email: mikec@myoderm.com, telephone: +1 610 233 3300

Funding sources

This paper was prepared and sponsored by Myoderm.

PHASE III INNOVATOR MARKET AVAILABILITY

US PRODUCT	EU PRODUCT
Humira	
AbbVie must approve all trial supply requests. It is likely that they will reject requests for biosimiliar studies. Product can be purchased on the secondary market, however, it may not be possible to acquire more than 100–200 syringes per month. Expiration dating is typically 12–15 months from time of purchase.	AbbVie will not supply for trials. Product can be purchased on the secondary market, however, it may not be possible to acquire more than 1,000 syringes per month. Expiration dating is typically 12–15 months from time of purchase.
Rituxan/Mabthera	
Genentech will consider supplying for trials, but will require the sponsor name and some general trial/protocol information. Up to 1,000 vials per month of either strength may be available on the secondary market. Expiration dating is typically 21–24 months from time of purchase.	Roche will supply for trials but will require the EudraCT number and a list of countries. Some product is available on the secondary market, however, it may only be possible to acquire a few hundred vials per month of either strength. Expiration dating is typically 18–24 months from time of purchase.
Remicade	
Janssen will supply for trials and does not require study information. Expiration dating is typically 24–36 months from time of purchase.	Merck will supply for trials but will require the EudraCT number or other trial information in some markets. There is a substantial amount of product available on the secondary market. Expiration dating is typically 24–36 months from time of purchase.
Herceptin	
Genentech will consider supplying for trials, but will require the sponsor name and some general trial/protocol information. Up to 1,000 vials per month may be available on the secondary market. Expiration dating is typically 18–24 months from time of purchase.	Roche will supply for trials but will require the EudraCT number and a list of countries. Up to 1,000 vials per month may be available on the secondary market. Expiration dating is typically 30–36 months from time of purchase.
Avastin	
Genentech will consider supplying for trials, but will require the sponsor name and some general trial/protocol information. Up to 1,000 vials per month of either strength may be available on the secondary market. Expiration dating is typically 12–18 months from time of purchase.	Roche will supply for trials but will require the EudraCT number and a list of countries. Some product is available on the secondary market, however, it may not be possible to acquire more than a few hundred vials per month of either strength. Expiration dating is typically 10–15 months from time of purchase.
Neulasta	
Amgen will not supply for trials. 300–500 syringes per month may be available on the secondary market. Expiration dating is typically 21–27 months from time of purchase.	Amgen may support trials when purchasing from specific EU markets. Several hundred syringes per month may be available on the secondary market. Expiration dating is typically 21–24 months from time of purchase.
Neupogen	
Amgen will not supply for trials. 200–300 packs of 10 syringes per month may be available on the secondary market. Expiration dating is typically 18–24 months from time of purchase.	Amgen may support trials when purchasing from specific EU markets. Several hundred syringes per month may be available on the secondary market. The presence of biosimilars of this product has limited supply in some markets. Expiration dating is typically 18–24 months from time of purchase.
Enbrel	
Amgen will not supply for trials. 300–500 packs of 4 syringes per month may be available on the secondary market. Expiration dating is typically 18–24 months from time of purchase.	Pfizer will supply for trials but will require the EudraCT number and a list of countries in some markets. Several hundred packs of four per month may be available on the secondary market. Expiration dating is typically 18–24 months from time of purchase.