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Partnering to Advance Human Health

Guide

Expect the unexpected:
A checklist for Comparator Sourcing

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When operating comparative trials, there are several aspects that require careful consideration and where challenges may typically develop.

Initial questions sponsors should consider include:

- Initial demand and long term forecasting
- Regional regulations
- Import / Export requirements
- Financial impact
- Supply route / vendor
- Expiry constraints
- Back-up options
- Substandard and falsified medical products

Initial demand and long term forecasting - the scale and complexity of global clinical trials can make accurately forecasting patient recruitment and retention a seemingly impossible task. Inaccurate forecasts can have a detrimental impact on comparator source and supply activity, risking stockouts or wastage depending upon which way the balance tips. Utilising technology to calculate clinical supply/demand over time, simulating a range of supply/demand scenarios and monitoring patient enrolment data will optimise comparator supply strategy.

Regional regulations - The world may be getting smaller but as sponsors embrace a globalised approach to clinical trials, regulatory requirements intensify. For instance, for comparative studies taking place in the EU, a comparator is considered an IMP, and 'must meet the requirements of the Clinical Trial Directive, including batch certification and release by a Qualified Person according to Annexes 13 and 16 of the EU GMP Guideline [11, 15]. Requirements for batch release may not be described in the equivalent detail in different regions and other country-specific rules may apply related to BSE/TSE requirements.' [i]

Not only does compliance vary from market to market and change frequently but new legislative requirements are often introduced with little notice, especially in emerging markets, making it difficult for sponsors to safeguard compliance. Access to a live database of market-specific regulatory requirements is essential to overcome this challenge and reduce risk.

Import / export requirements - Moving comparator products across borders can be a complex process and where there may be some similarities, no two countries are the same when it comes to import/export requirements. For example, while most of the APAC region requires CofA documentation, China may no longer accept chain of custody documentation when importing comparator products into due to a recent (August 2018) change in approach by NMPA.

To avoid customs chaos and the delay and risk (to both patients and commercial performance) that comes with it, sponsors need to have a firm grasp of import/export requirements across regions and how things like Importer of Record responsibilities, lead times, documentation requirements, airport facilities, broker interactions, product valuation methodology and temperature-controlled shipping solutions can make or break a study.

To safeguard investment, protect the safety and efficacy of comparator products, and keep a trial's wheels in motion, customs requirements cannot be overlooked nor underestimated.

Financial Impact - The cost of delaying the launch of a product by just one day is estimated to be approximately $8 million in lost sales [ii] so it is vital that sponsors have access to reliable market intelligence that enables them to select the most effective sourcing strategies.

Sponsors also need to consider the financial impact of having to pre-pay for comparator trial materials - a cost which maybe be substantial and could prohibit the progress of the trial if the funds are not available in advance.

Supply Route / Vendor - selecting the most effective sourcing strategy can be critical to the success of a comparator trial. Liaising with suppliers or requesting quotes from manufacturers will inform smart decision making but sponsors should be aware that barriers may present themselves in the form of manufactures being unwilling to provide pricing or lead time estimations without assurance that the product is for a genuine study. Working with specialists with established trust and relationships within the marketplace overcomes this barrier.

Expiry Constraints - Well rounded and robust sourcing strategies should take into consideration expiry dates, stability, raw material and packaging material requirements for each country involved in the study. QA involvement and oversight early in the process can help ensure comparators conform to the sponsor's requirements and quality-based regulation, such as GMP.

Back-up options - it is good practice to include a back-up option for comparator trial materials in the Clinical Trial Application in case the primary comparator drug becomes unavailable during the trial period. in case of such an event, this removes the timely and costly need to re-submit a CTA and prevents trial stoppage and negative patient impact.

Substandard and falsified medical products - Counterfeit medications risk patient safety. They may not containthe right amount or quality of active product, or indeed any active product at all. Or, they may contain an agent that could cause harm to a patient [iii].

An estimated 10% of all medicines sold worldwide are counterfeit [iv], with 'higher prevalence in regions where drug regulatory and enforcement systems are weakest' [v].

To mitigate against the risk of substandard and falsified drugs in comparative studies, supply sources need to be trusted, regularly audited and traceability evident. The ability to authenticate comparator products (and provide corresponding documentation), via testing is also a must to prevent counterfeit products entering the supply chain and posing a risk to patients.

References

[i] ISPE Good Practice Guide: Comparator Management

[ii] Lionbridge LIFE SCIENCES; Bairu et al 2014; Metadata Solutions 2013

[iii] ISPE Good Practice Guide: Comparator Management

[vi] Fighting fake drugs: the role of WHO and pharma. Lancet. 2011 May 14; 377(9778):1626.

[v] World Health Organization. Medicines: spurious/falsely-labelled/ falsified/counterfeit (SFFC) medicines 2012. http://www.who.int/mediacentre/factsheets/fs275/en/

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