



**Clinical Trial Logistics in Africa:
Ensuring Quality, Compliance and Control
within the Pharmaceutical Supply Chain**

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WORLD COURIER is the market leader in the handling, transport, storage and distribution of temperature-sensitive pharmaceutical products and biological specimens in Africa and worldwide. It offers a fully-integrated GxP-compliant pharmaceutical supply chain system, strong knowledge of the local regulatory environment, well-trained staff and expert access to key African nations.

Since 2005, WORLD COURIER's breakthrough Clinical Trial Supply Chain Services (CTSCS) division has revolutionized the way clinical trial materials and samples are managed in emerging nations. Operating the world's largest network of GMP-compliant investigational drug storage facilities, global capacity for WORLD COURIER's 13 depots now exceeds 235,000 square feet and includes a facility in Johannesburg (South Africa). WORLD COURIER has operated company-owned offices in South Africa since 1980.

In 2012, WORLD COURIER was acquired by AmerisourceBergen Corporation, one of the world's largest pharmaceutical supply chain service companies.

Africa is the world's second largest and second most populous continent after Asia, covering six percent of the earth's total surface. With over one billion people, it accounts for almost 15 percent of the world's population.

Today's Africa has increasingly become a source of fascination for pharmaceutical researchers drawn to the study and control of both communicable diseases such as malaria, tuberculosis and HIV/AIDS as well as diseases of the developed world like cancer, diabetes, hypertension and chronic respiratory disease.

With its unique geographies of clear therapeutic specializations, a growing presence of accredited labs and qualified CROs especially in South Africa, relative ease of access to large treatment-naïve populations, proximity to Europe and generally favorable exchange rates, Africa offers sponsors great opportunity for conducting competitive low-cost clinical trials – assuming the logistics can be appropriately managed. According to the U.S. National Institutes of Health, more than 2,700 clinical trials are currently underway in Africa ¹, a number that continues to increase.

¹ www.clinicaltrials.gov, (April 2012)

Critical Mass in South and East Central Africa

In terms of drug discovery and development, South Africa leads the way. Of the approximately 2,700 clinical trials now being conducted in Africa, 1,441 or 53 percent take place in South Africa². Boasting a first-class research infrastructure that meets FDA and ICH (International Conference on Harmonization) standards, experienced investigators trained to EU/U.S. standards, a rapidly growing number of accredited labs and qualified CROs, a strong IT infrastructure that produces consistent quality data, wide public awareness of clinical trials, ease of patient recruitment, predominance of the English language and the country's geographical position as a major gateway to the rest of Africa, South Africa leads the industry continent-wide.

Over 700 more studies are currently hosted in the 13 countries that extend northward from South Africa through east central Africa – Uganda (183 studies), Kenya (162), Tanzania (133), Malawi (86), Zambia (73), Zimbabwe (46), Ethiopia (38), Botswana (38), Mozambique (28), Rwanda (28), Madagascar (8), Burundi (3), Swaziland (1) and Lesotho (1). Together with South Africa, these countries account for over 83 percent of the continent's clinical trial market³.

What should you, as a pharmaceutical professional, know about the logistics of managing clinical trials in Africa?

A Land of Contradictions

Despite the obvious attractions, today's Africa can present a bewildering paradox to those who are unfamiliar with its history and culture, and an unforgiving operating environment for the uninitiated.

Images of emerging democracies, an abundance of natural resources, World Cup fever, a thriving drug discovery environment and modern, cosmopolitan cities like Johannesburg, Nairobi, Cairo and Casablanca are countered by large under-developed rural areas and developing social and regulatory systems. *Opportunity*, on one hand, wrestles with *challenge* on the other, making Africa a true testing ground for pharmaceutical companies and clinical trial professionals endeavoring to do business here. Given the structure and multi-site design of today's typical study along with an increasingly stringent call for regulatory compliance, success in Africa effectively requires bio-practitioners to bridge both worlds without slipping into the void.

But how can this be accomplished when clinical products and samples must routinely travel thousands of miles over extended periods of time between the production floor, central labs and individual investigator sites? Ultimately the answer lies in creating a solid logistics plan in

² Ibid.

³ Ibid.

conjunction with a responsible local partner who is able to successfully manage all non-laboratory and non-clinical aspects of the trial.

Here, then, are the key transport and logistical challenges to be faced when undertaking clinical trials in Africa – challenges that can significantly drive up the cost of a study if not managed effectively in terms of out-of-spec temperature ranges, limited product stability, potential for missed dosings, unnecessary regulatory review, misuse of researchers' time and questionable research results:

- *Infrastructure & Expertise*

Unlike other continents where infrastructure and human capital capabilities remain fairly consistent across most countries, there is a huge range in local facilities, experience, expertise and aptitude across Africa – and even within individual countries – which can make doing business here all the more challenging. A clear understanding of the local infrastructure, resources and service capabilities in critical countries and site locations can help lessen uncertainty before the trial begins.

- *Developing Regulatory Environment*

Like most emerging areas throughout the world, the regulatory environment in Africa is evolving. With this evolution comes complexity, lack of clarity and import and regulatory procedures that can vary significantly from country to country. With 52 distinct nations, Africa is no exception and shippers should understand the regulatory requirements of each country that will host any part of the study and factor in lengthy permit and importation timelines into patient dosing schedules.

In South Africa, for instance, there are four different regulatory agencies that may weigh in on shipments entering and leaving the country: the Medicines Control Council (MCC), the Ministry of Health, the South African Pharmacy Council and the South African Veterinary Council. Pharmaceutical shippers will require MCC import permits, customs invoices, health certificates, VAT-exempt certificates and veterinary import certificates for IPs containing animal material. The need for extensive paperwork creates a somewhat cumbersome import process that, without a strong local presence, can be slowed down by potential documentation errors.

- *Variability of Local Service Providers*

The complexity of the clinical supply chain presents a challenging distribution environment for researchers who must ship large volumes of temperature-sensitive patient kits worldwide, juggling their need to safeguard product quality and chain of custody with a continuous stream of arms-length exchanges between local service providers. If the primary logistics supplier does not

have a well established network and a broad continental reach, shippers may experience an undesirable variability among third-party contractors that can quickly compromise the in-country handling of product and lab samples.

- *Climate*

Almost perfectly centered over the equator, Africa's climate is classified as tropical, with Celsius temperatures typically ranging in the 20s to 30s or higher. Temperatures can vary dramatically from country to country depending on the season and can include searing heat, monsoon-type rain, arid dryness and even snow in the mountain regions of Morocco and South Africa. Given the limited number of direct flights from major international points to secondary African cities and the often lengthy transit times from origin to destination, ensuring the stability of delicate temperature-sensitive consignments can represent an enormous undertaking.

- *Cold Chain Management*

Managing temperature-controlled shipments effectively presents a key challenge in Africa. Extreme temperatures combined with long transit times require the availability of refrigeration facilities and supplies as well as trained personnel to handle them at all key junctures en route. The availability of refrigeration units, the potential for power failures and the local unavailability of appropriate packaging and dry ice in some locations – both for the inbound replenishment of product refrigerants and the outbound temperature control of samples – demand sufficient volumes, adequate oversight and innovative solutions from transport suppliers if quality is to be maintained.

- *Under-developed Geography*

Once a clinical trial gets under way and patient recruitment begins in earnest, the primary concern of the clinical team is ensuring that the correct medications are supplied to each site and each patient on time and within specification. Multiple sites, hundreds of patients and months of testing add a complexity and risk for error that are intensified in emerging markets like Africa. With road and transportation systems that may not be well developed outside of main cities, consideration must be given to the reliability of in-country distribution capabilities for multi-site studies and, if necessary, other solutions sought.

Choose a Qualified Logistics Provider

Generally speaking, the success of a logistics provider over the life of a clinical trial in Africa can be measured by its consistent ability deliver expertise, strong internal controls and required infrastructure when and where it is needed. The crucial first step for the pharmaceutical practitioner lies in selecting, whenever possible, a single, fully-integrated, GxP-compliant service provider with demonstrated effectiveness in the chosen market(s).

By employing the services of such an organization, on-the-ground responsibility is effectively transferred to an experienced and trusted partner with the knowledge and internal operation to support the clinical trial. By choosing a single provider and reducing the number of third-party suppliers, the potential for miscommunication, misstep and error is also reduced.

• *Service Provider Checklist*

In order to optimize the chance for success, the following questions should be asked of any prospective service provider:

- does the company exhibit expert knowledge of the regulatory environments of all countries involved with the study, not just in selected geographies?
- does it keep abreast of current industry happenings? is it a member of relevant industry associations such as the South Africa Clinical Research Association (SACRA) and the South African Pharmaceutical Research Association (SAPRA), for instance?
- how long has the company operated in the specific study locations?
- does the company have a firm understanding of the realities of operating in Africa (i.e. work environment, standards, challenges, pace)? does it have a proven track record?
- are staff and operatives appropriately trained to manage DG Class 6.2 (infectious specimens), Class 9 (dry ice) and other types of cold chain shipments as required?
- what types of physical facilities (offices, warehousing, refrigeration, etc.) are available in key site locations? how will study requirements be met if specific facilities are not available?
- is every shipment routed with the primary goal of minimizing transit time or are they consolidated in company hubs to minimize expense?

- how is operational guidance, technical assistance and quality oversight handled at the local level?
- is a system in place to effectively manage communications between site personnel, sponsor and research partners, the service provider and his local representatives?
- how confident are you that the organization can deliver what it promises, consistently and without fail?

Utilize a Local Distribution Solution

In challenging locations like Africa, a local distribution solution can offer many benefits to both sponsors and site personnel.

To reduce risk and maximize the control of delicate, temperature-sensitive IMPs, pharmaceutical shippers should consider consolidating smaller international shipments into larger batch shipments and utilizing an in-country warehousing solution. Once the bulk shipment has arrived in-country, the distribution of patient kits to local investigator sites can be undertaken from a secure, temperature-controlled local facility according to a pre-determined schedule and within the confines of a secured timeline.

By utilizing a local warehousing solution, pharmaceutical shippers can reduce the occurrence of – or even remove entirely – many of the “unknowns” that typically occur when shipping to developing markets while realizing many quantifiable benefits:

- consolidated bulk deliveries will significantly reduce clearance costs
- the potential for customs and airline delays are substantially reduced by a decreased import frequency
- a successful one-time in-country customs clearance removes unnecessarily repetitive bureaucratic uncertainty and red tape, and with it, the possibility of regulatory delays
- with a larger clinical supply being maintained in-country, the potential for missed dosings due to lack of supply is reduced or eliminated entirely by slightly overlapping bulk importations
- transport costs will likely be significantly reduced, even while taking into account the related warehousing costs
- product stability is ensured with improved control of the clinical supply in local temperature-controlled purpose-built facilities once the shipment has cleared customs
- the fewer the shipments, the more time that is freed up for the clinical team who must coordinate transport and distribution
- the shipper can benefit from local representation, local language skills and local time zones should interface with local site personnel be required

Conclusion

Transportation and logistics services in Africa, like everywhere else, are fraught with unreliable third-party contractors and untrained domestic service providers. In the area of clinical trials, however, the stakes are particularly high. It is crucial, therefore, that research professionals are able to rely fully on their local service provider to manage temperature-sensitive shipments according to international regulatory standards and at the same operational level found elsewhere in the world.

Choosing the right partner and taking advantage of alternate solutions such as local warehousing and distribution will reduce uncertainty and bring knowledge, clarity, stability and international standards to a complex situation. At the same time, it will help sponsors better manage risk and improve their confidence and expectation levels.

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