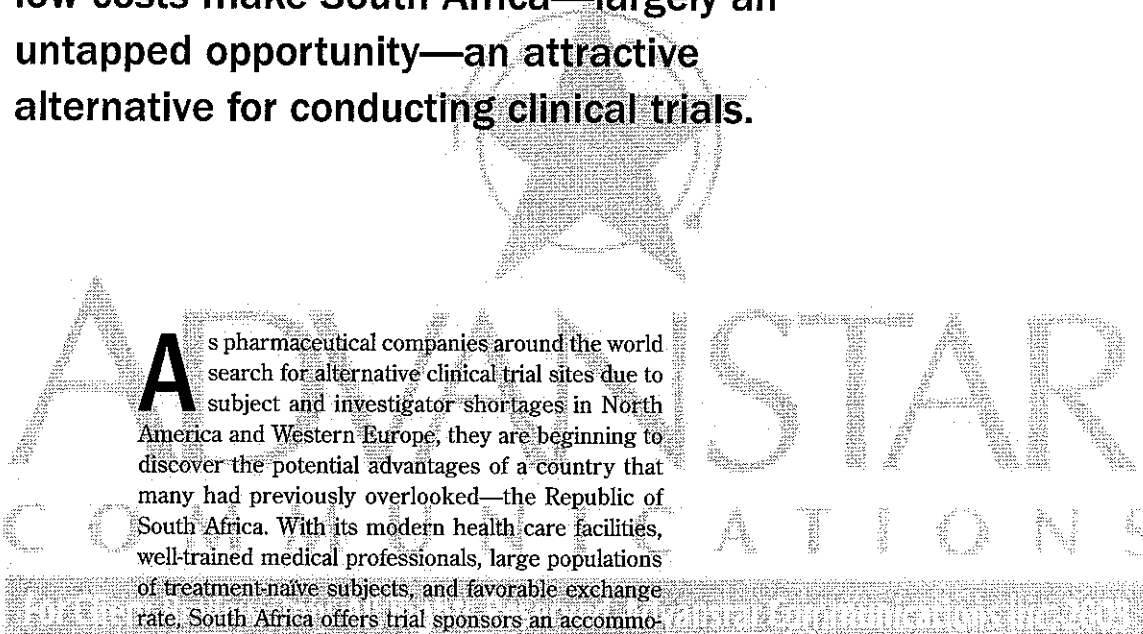


# Discovering South Africa

Herman Scholtz and Sybrand G. Pretorius

**A high-quality medical infrastructure and low costs make South Africa—largely an untapped opportunity—an attractive alternative for conducting clinical trials.**



**A**s pharmaceutical companies around the world search for alternative clinical trial sites due to subject and investigator shortages in North America and Western Europe, they are beginning to discover the potential advantages of a country that many had previously overlooked—the Republic of South Africa. With its modern health care facilities, well-trained medical professionals, large populations of treatment-naïve subjects, and favorable exchange rate, South Africa offers trial sponsors an accommodating environment for cost-effective, high-quality clinical studies.

Misconceptions about South Africa persist from the past despite the dramatic changes that have occurred throughout the country in recent years. Located at the southern tip of Africa, South Africa today is the richest and most economically developed country on the continent. Although it contains only 4% of Africa's land mass and just 5% of its population—about 44 million people—South Africa accounts for approximately 25% of Africa's total goods and services by dollar value.<sup>1</sup>

The current atmosphere in South Africa is demonstrated by its commemoration in 2004 of the tenth anniversary of the country's first democratic elections, celebrating a decade of remarkable achievements and peaceful transformation. At the same time, South Africa still faces some significant economic and social issues, as well as health care problems such as HIV/AIDS.

Despite these challenges, South Africa continues to move forward—supporting the optimism expressed in the nation's slogan: "Alive With Possibility." It is this steady progress, combined with an impressive array of clinical resources, which is fueling the growth of South Africa's clinical research industry and prompting pharmaceutical companies to take a fresh look at the advantages South Africa has to offer.

### The clinical research environment

**Medical infrastructure.** One of the most important advantages of South Africa's clinical research environment is the high quality of its medical infrastructure—both personnel and facilities. The standard of health care is comparable to that of most European countries, with a similar system of public and private facilities. South Africa's rapidly growing private health care sector, with more than 200 hospitals and clinics,<sup>2</sup> offers a standard of care that is competitive with the best in Europe and North America. The quality of South Africa's health care system is highlighted by the fact that more than 100,000 tourists from around the world traveled to the country in 2003 for medical procedures,<sup>3</sup> making South Africa one of the world's leading destinations for the growing phenomenon of "medical tourism." In addition, South Africa's long history of Western medicine and excellent academic medical centers provide a strong foundation for the first-rate training received by physicians, nurses, and other medical personnel there. This medical training is generally accepted in both Europe and North America.

**Access to subjects.** More than 50% of South Africa's population is concentrated in urban areas, providing sponsors with ready access to large numbers of potential subjects for clinical studies. A significant portion of this population is treatment naïve—a key benefit at a time when shortages of available and qualified subjects constitute a major source of delays in the clinical development process. South Africa's sizeable population of steroid-naïve asthma subjects could be of particular interest to sponsors in North America and Europe, where such subjects are increasingly rare. In addition, this subject population is available for studies of seasonal conditions during the North American and European winter months—a factor that could significantly reduce the time needed for studies of such conditions.

Equally important for some sponsors is the availability of large numbers of healthy, reliable volunteers to participate in Phase I trials in South Africa—unlike the situation in many other parts of the world.

**Cost advantages.** As a result of the country's lower labor costs and a favorable exchange rate, South African clinical trials typically provide substantial cost savings compared with those conducted in North America or Western Europe. This economic advantage is a major reason why clinical studies for generic drugs are already common in South Africa. Cost effectiveness is particularly important to generic manufacturers due to the high level of competition in their segment of the pharmaceutical industry. The industry also benefits from the availability of local expertise in bioequivalence testing and other Phase-I-related services that have evolved rapidly in recent years to meet the needs of generic drug sponsors. The availability of healthy volunteers and naïve subjects provides additional savings of time and money for clinical trials conducted in South Africa.



**Experienced resources.** Although South Africa's clinical research industry is still relatively small, it is by no means in its infancy. All of the major global pharmaceutical companies have conducted clinical studies in South Africa for a number of years, and the quantity of trials is increasing rapidly. Currently, about 400 studies are conducted each year in South Africa, across a wide spectrum of therapeutic areas. These trials account for direct annual expenditures of approximately \$150 million<sup>4</sup>—a figure that is projected to triple in the foreseeable future.<sup>5</sup> Serving this growing market are numerous contract research organizations (CROs), laboratories, and other support providers with extensive experience in clinical research. Some of these organizations offer specialized expertise in therapeutic areas such as respiratory diseases, HIV, diabetes, and cardiovascular disease. With South Africa's tradition of Western medicine, qualified investigators and other medical professionals are also readily available.

Experience with good clinical practice (GCP) and International Conference on Harmonisation (ICH) guidelines is widespread in South Africa. The country's Ministry of Health requires adherence to ICH GCP guidelines for the conduct of clinical trials, and the Ministry's Medicines Control Council (MCC)—the regulatory agency that oversees clinical trials in South Africa—enforces national GCP regulations as well. Data from studies conducted in South Africa have been widely accepted by both the U.S. Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMA).

#### **Other benefits**

**Location.** South Africa's Southern Hemisphere location, with seasons that are the opposite of those in Europe and North America, can also provide a significant benefit to trial sponsors. It is particularly valuable for sponsors studying certain respiratory diseases or other seasonal conditions, allowing them to conduct trials continuously throughout the year and potentially reduce time to market.

**Common language.** There are 11 official languages in South Africa, but English is the common language of government, business, and the scientific communities. The only local translation typically required for trials in South Africa would be the informed consent form for subjects whose first language is not English.

#### **Meeting the regulatory challenge**

While there are many advantages to conducting clinical trials in South Africa, there is also an acknowledged challenge that must be understood and addressed—the time required to gain regulatory approval to begin trials in the country. The fact that South Africa has a well-established regulatory process based on ICH and GCP guidelines for clinical studies is beneficial for sponsors. However, the review and approval process is relatively lengthy—currently averaging 10 to 12 weeks from the time an application is submitted to the MCC until a decision is rendered. From the submission deadline, there is also a one-week validation process when the MCC can request information omitted from the original submission. Four to five weeks after the original submission deadline, the clinical trials committee (CTC)

meets to discuss the application and may provide feedback to the applicant. Another five weeks after this, the MCC meets to discuss the application and responses. The results of the assessment are delivered to the applicant soon after the MCC meeting.

All clinical trials for nonregistered biopharmaceutical products or new indications for registered products must be reviewed by the MCC. The lengthy application form must be accompanied by the investigator brochure, the completed trial protocol, and the informed consent form, together with a variety of other documentation such as proof of GCP training for the investigators and trial insurance details. There is a fee for each application, which is currently about \$900. An approval letter from the MCC allows the study to commence and also permits the importation of the study drug.

For generic drugs, however, there is an expedited process. Bioequivalence studies using a product that is registered in South Africa are typically approved by the MCC within about three weeks after an application is submitted.

In addition to MCC approval, all clinical trials must be approved by an accredited ethics committee (EC). In South Africa, an EC is typically associated with the particular hospital, clinic, or academic center where a study is to be conducted, but there is also an alternative, centralized EC process. The application requirements are similar to those required by the MCC, and a small application fee is typical. The average turnaround time for EC reviews is about two weeks. The MCC and EC application processes can take place in parallel.

Given the complexities and timeframe of the clinical trial application process in South Africa, it is essential for sponsors to work with a local partner experienced in preparing applications for the MCC and local ECs. An organization that is familiar with the many complex requirements can help draft the regulatory submission to expedite the process and avoid undue delays.

### Choosing a partner

Expertise in regulatory requirements is just one of many reasons why a sponsor should choose a well-qualified local partner when planning clinical trials in South Africa. Whether that partner is a CRO, a local affiliate, or another type of service provider, selecting the right one is probably the most important success factor for a sponsor conducting trials in any foreign country.

What are the essential characteristics of a good clinical partner in South Africa? Experience should be the primary selection criterion. A potential partner should have a proven track record of successfully conducting studies in South Africa, with a demonstrated ability to recruit investigators and subjects, meet deadlines, and produce solid data—as well as the capability to obtain regulatory approval for new trials without undue delays. In short, an experienced partner helps a sponsor minimize risks and avoid pitfalls that could increase time to market, jeopardize completion of a study or compromise the integrity of study results.

Other key attributes a sponsor should seek in a South African partner include:

- Strong relationships with experienced investigators and qualified sites
- Access to extensive databases of potential subjects in various therapeutic areas and healthy volunteers for Phase I studies

- Adequate resources in South Africa to perform the functions required, including management resources, trained monitors or other personnel, and validated facilities
- Thorough knowledge of, and commitment to comply with, ICH and GCP guidelines during every phase of a trial
- Well-established quality assurance systems, standard operating procedures (SOPs), and other internal controls, processes, and procedures to maintain quality and ensure compliance with all regulations and study requirements
- Adequate infrastructure to support the trial, including communications and information technology systems
- Ability to work closely with the sponsor by maintaining strong lines of communication and supplying continuous oversight and feedback throughout the trial process.

By selecting the right local partner and understanding the specific challenges of the South African regulatory process, global pharmaceutical companies can reap the benefits of the many advantages offered by the clinical research environment in South Africa and successfully conduct cost-efficient, high-quality trials with the potential to reduce the time and cost of bringing new pharmaceutical products to market.

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**Herman Scholtz**,\* MBChB, MMed, FCA (SA), is corporate vice president and worldwide head of clinical pharmacology, PAREXEL International, 200 West Street, Waltham, MA 02451, (781) 434-5305; fax (781) 768-5512; email: [herman.scholtz@parexel.com](mailto:herman.scholtz@parexel.com). **Sybrand G. Pretorius**, MBChB, MBA, is senior director of clinical pharmacology, PAREXEL International.

\*To whom all correspondence should be addressed.

