



Hello SOUTH AFRICA:

A Diverse and Sophisticated Market

With a diverse population, a thriving research environment, strong infrastructure along with geographic reach into the rest of Africa, South Africa has many advantages for the global pharma industry.

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ith its population of more than 50 million people from diverse ethnic backgrounds, South Africa offers excellent opportunities

for both local product launches and global research, experts say.

Currently, the South African pharmaceutical market makes up less than 1% of the world market, with pharmaceuticals estimated to constitute about 1.5% of the country's GDP, according to the Pharmaceutical Industry Association of South Africa (PIASA).

According to Espicom, the South African pharmaceutical market is set to grow at a constant rate over the coming years.

The South African healthcare market is made up of a private sector and a public sector. South Africa's regulations favor the use of generic medicines with substitution required

FAST FACT

- » Population: 50.1 million
- » Total expenditure on health per capita: \$862 (\$U.S.)
- » Total expenditure on health as % of GDP (2009): 8.5%
- » Gross national income (PPP): \$10,050

Source: The World Health Organization.
For more information, visit who.int.

in private sector pharmacies, PIASA notes. Generic medicines constitute 60% of medical usage in the private sector and although a figure is not available, the major share of medicines used in the public sector are EDL (essential drug list) products, which indicates a high level of use of generic medicines.

"The state sector market is subject to an intensively competitive monopsonistic tender system," says Ashley Pearce, managing director of MSD, a Merck subsidiary, and president of the PIASA executive council. "EDL products play a large role in the public sector. Antiretrovirals are a big growth area as South Africa carries the largest burden of HIV/AIDS of any country."

Mr. Pearce adds that the private sector had a free pricing system until 2004.

"Since then prices are regulated under a 'Single Exit Price system' (SEP), and increases in medicine prices are regulated with an annual review based on CPI and exchange rate," he says.

In 2009, the Department of Health increased pharmaceutical prices by 13.2%, a move that was welcomed by PIASA. This increase helped combat increasing margin pressures experienced three years ago mainly due to

imported raw materials against a weakening local currency, according to Espicom.

However, Linda Reid, senior manager, commercial effectiveness services, South Africa, IMS Health, says prices were frozen in 2011 and will likely also be frozen in 2012. She notes also that proposed legislation from the Department of Health for the introduction of international reference pricing to control prices of initially branded products could create market constraints.

"The draft proposal is likely to be revised, but if implemented in its current form it would result in greater than 10% suppression of market value over the next five years," Ms. Reid says. "In addition, the population is expected to shrink relative to the last five years — predominantly driven by the high burden of HIV/AIDS and associated diseases — resulting in a negative impact on market value."

Pharma R&D

Local research, on an academic level, is thriving and has the full support of the Department of Science and Technology and the Department of Health, as well as novel tax incentive plans through the revenue service to facilitate the growth of research and development in South Africa, says Catherine Lund, managing director, OnQ Research.

Cost of healthcare, cost of living, disease burden, unemployment, and education are some of the biggest drivers for market growth in South Africa, says Lisa Artruc, project manager, South Africa, Criterium.

"South African researchers embrace all manner of research conducted in many different fields, including but not limited to phytomedicine, complementary medicines, tradi-

tional medicines, as well as the more conventional medicine approaches," Ms. Lund says.

Mr. Pearce adds that South Africa offers a gateway to the rest of Africa.

"Locally based companies have been active in immediately surrounding territories and are now starting to expand to the rest of the continent," he says.

In addition, South Africa is a signatory to TRIPS and as such has a robust patent system, Mr. Pearce says.

"This has attracted investment by multinational companies over the years," he says.

Merck, through MSD, has a large portfolio of products in South Africa targeting a broad range of conditions, ranging from infectious disease, with both medicines and vaccines, to cardiovascular, respiratory, oncology, diabetes, and dermatology indications, Mr. Pearce says.

"For MSD, the emerging markets are a critical part of the company's strategy for future growth, and our vision is to enhance ac-

cess by providing affordable medicines and vaccines," he says. "The strategy is to apply innovation and growth across the business, from introducing novel compounds to broadening our focus on innovative, branded generics."

One potential hurdle for global developers, experts say, is the country's industrial policy that favors local manufacture. For example, data from IMS Health show the leading two companies in South Africa are local companies: Aspen and Adcock Ingram.

An estimated 90% of the research being done in South Africa is driven by local companies. However, experts say this number is hard to quantify because much of the R&D driven by local companies may be supported by global funding.

One global company working locally is MSD, which entered into a five-year strategic collaboration with Adcock Ingram, South Africa's second-largest pharmaceutical company.

"MSD and Adcock Ingram have agreed to copromote and distribute a number of established MSD products, including over-the-counter products and selected prescription medicines currently registered in South Africa by MSD and Schering-Plough," Mr. Pearce says. "This collaboration was extended late last year to include additional regions in sub-Saharan Africa, namely in Botswana, Namibia, Swaziland, Lesotho, Kenya, and Ghana."

"By reputation, South African clinical researchers are highly experienced and consistently deliver data of an exceptionally high standard."

CATHERINE LUND / OnQ Research



Therapeutic Landscape

Ms. Artruc says local research concentrates more on the local disease burden,



"The clinical research community in South Africa is an active one, always striving to improve the quality of research."

LISA ARTRUC / Criterium

South Africa: Key 2012 issues

- » There is increased funding for disease treatment and prevention, and greater access to low-cost antiretroviral therapies intensifies through government-directed efforts, but HIV/AIDS continues to be a burden on healthcare financing.
- » A new international reference pricing system for originators and pricing benchmarking system for generic players is in a draft legislation stage.
- » New pharmacy dispensing fee further encourages generic uptake.

Source: IMS Health, Market Prognosis, April 2011. For more information, visit imshealth.com.

for example TB and HIV, whereas global research tends to concentrate more on other therapeutic areas, such as CNS, diabetes, infection, respiratory, allergy, gastrointestinal, lipidology, cardiovascular, angina, acute MI, cardiac failure, rheumatology, neurology, and oncology.

Ms. Lund notes that while the focus of research has traditionally been in the arena of HIV — South Africa has one of the highest rates of HIV and AIDS infections in the world, equivalent to just more than 10% of the entire population, according to Espicom — TB, malaria, lifestyle diseases, CNS, and cardiovascular are also being researched.

For patients, the dual system of private/public healthcare facilities ensures a standard of care that is comparable with that of most European countries, says Bronwen Muir, senior director of clinical operations at ICON Clinical Research in Johannesburg.

“The public facilities are often affiliated

with the universities and provide medical care to about 80% to 90% of the population,” she says. “Much of this care is provided either free or at a nominal cost to the patient.”

The ruling political party is in the process of outlining the move toward a national health insurance system, which would provide broader-based and higher-quality access to healthcare for all South African citizens, Ms. Reid says.

“Implementation and rollout will take several years, and product prices will likely be suppressed, but broader access will drive volume sales of pharmaceuticals,” she says.

From the point of view of pharmaceutical companies, reimbursement can be a challenge, Ms. Reid says.

“The South African pharmaceutical market is divided into public and private, with 17% of patients subscribing to public medical insurance called Medical Aid,” she says. “Medical Aid covers 17% of lives, but the private sector

Clinical Trials in South Africa by Therapeutic Area:

Oncology	20%
HIV and HIV-related	19%
Rheumatology	9.8%
CNS	9.4%
Infectious diseases	7%
Cardiovascular	6%
Diabetes	6%
Respiratory	4.4%
Tuberculosis	4.3%
Hemophilia	3.1%
Circulatory	2.7%
Gastroenterology	1.2%
General	8.5%

Source: IMS MIDAS, MAT Dec 2010, Rx+OTC. For more information, visit imshealth.com.

Top 10 Therapeutic Classes in South Africa

HIV Antivirals	7.9%
Non-narcotic analgesics	5.2%
Oncology drugs	4.1%
Respiratory agents	3.1%
Antidiabetics	3.1%
Anti-ulcerants	2.8%
Antidepressants	2.6%
Vaccines	2.6%
Vitamins & Minerals	2.6%
Anti-epileptics	2.4%
All others	63.7

Source: IMS MIDAS, MAT Dec 2010, Rx+OTC. For more information, visit imshealth.com.

makes up a disproportionate 83% of the value of the total pharmaceutical market.”

A Clinical Outlook

Experts say the conditions for clinical research in South Africa have never been better.

Firstly, clinical trials are conducted in accordance with ICH GCP Guidelines for Good Clinical Practice in the Conduct of Clinical Trials in Human Participants in South Africa, generally known as SA GCP Guidelines, Ms. Muir says.

“All personnel involved in clinical trial work in South Africa are required to be in possession of a valid GCP certificate issued by an accredited institution, which is valid for a period of three years,” she says. “The South



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LINDA REID / IMS Health



“ South Africa offers a gateway to the rest of Africa. ”

ASHLEY PEARCE / MSD/Merck

Africa Ministry of Health requires adherence to ICH GCP guidelines, and the Medicines Control Council (MCC) enforces National GCP regulations as well.”

Ms. Artruc notes that medical practitioners are continually engaging in GCP courses to equip themselves for a career in research.

“Medical schools are actively participating in research, and investigators are keen to do research,” she says. “In addition, there is a huge patient base with a wide spectrum of diseases often yielding treatment-naïve patients.”

South Africa has developed a reputation for being able to recruit patients quickly and appropriately for clinical trials, Ms. Lund says.

“The value of clinical trials to both patients and the medical institutions is recognized by the medical fraternity,” Ms Muir says. “An increasing number of the specialist departments within the public hospitals are participating and benefiting from involvement in the opportunities and advancements presented by clinical trials.”

One clear advantage South Africa offers in clinical research is that more than 50% of the population is concentrated in urban areas, providing sponsors with easy access to large numbers of potential subjects for clinical studies, Ms. Muir says.

“Patients are accessed through the large state hospital sites or private sites,” she adds.

There has been a steady increase in the number of applications to conduct clinical research trials over the last few years, and it has become an important source of revenue for the country, Ms. Artruc says.

She says while South Africa is on an underdeveloped continent, it has developed world-class medical technology.

Ms. Muir adds that there is still a perception that South Africa operates at a third-world level and is only suitable to conduct studies in diseases such as HIV/AIDS, despite the fact that it has a developed economy with established infrastructures and political stability.

“Frequently South Africa is not considered for trials at the start, but rather is included at a later stage as a backup or rescue country,” Ms. Lund notes. “This perception needs to change, as it would be far more effective to include South Africa from the onset of a study. South Africa remains the gateway to other African countries, which allows more

“The standard of healthcare is comparable with that of most European countries; there is a dual system of public and private facilities.”

BRONWEN MUIR / ICON Clinical Research



opportunity to include additional countries in clinical trials.”

In addition, late-phase studies account for only 5% of applications with the main focus on Phase I to Phase III clinical trials, Ms. Artruc says.

UNDERSTANDING THE BIG PICTURE



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Merck/MSD is currently participating in 35 different clinical trials in South Africa, with just under 4,000 participants enrolled in these trials, Mr. Pearce says. Therapeutic areas in which MSD is conducting clinical trials include: cardiovascular and atherosclerosis, infectious diseases, vaccines, RID (respiratory, immunology), diabetes, neurology and ophthalmology, oncology, and women's health.

"MSD has been increasingly investing in clinical research in South Africa since the 1980s," Mr. Pearce says. "This is due to the consistent delivery on recruitment targets by local clinical research teams, as well as clinical research sites providing quality data in the development of new medications."

In an effort to raise South Africa's profile as a premier location for conducting clinical re-

search, the PIASA has, in collaboration with the South African Clinical Research Association (SACRA), recently launched a campaign to promote South Africa as a destination of choice for clinical trials.

The campaign targets government, clinical research organizations within the pharmaceutical sector, and clinical investigators to create or enhance awareness of South Africa's globally competitive clinical trial capabilities. Additionally, it encourages local pharmaceutical firms and CROs to pitch for clinical trials internationally; provide materials that support local CROs in boosting their global competitiveness; positively influence state policymakers to streamline regulatory processes by MCC infrastructure, staffing, and capacity; and encourage and support the recruitment of doctors as clinical investigators, promote GCP training and skills development, and strengthen academic clinical leadership.

Regulatory Oversight

Clinical trials are carefully managed and overseen through independent ethics committees, and in addition, each of the major academic teaching hospitals has its own ethics committee, Ms. Artruc notes.

"The ethics committees are very stringent in their review of protocols and always ensure the safety of trial participants," she says. "Turnaround from submission to approval is about six weeks."

Protocols are submitted to the MCC, whose main goal is to ensure that protocols are scientifically sound, that participation in clinical trials is to the benefit of the country and its people, and that vulnerable communities are protected.

Ms. Lund notes that the MCC is extremely vigilant on ensuring all clinical researchers are appropriately GCP trained.

Ms. Artruc says through the support of the private sector, the MCC has continued to improve its timelines and today the time to approval of a protocol is three months.

This is a significant improvement over the six to 12 months it took the MCC to either reject or approve an application for a clinical trial just three to four years ago, Ms. Muir points out.

When it comes to product registration, there can be challenges due to the unpredictability of the amount of time required to register a product through the regulatory authority, Ms. Lund says.

"Regulatory systems in South Africa are very stringent and are world-class in terms of ensuring ethics, patient protection, and scientific merit," Mr. Pearce says. "Systems are largely paper-based and therefore long review and approval times can be expected for clinical trials as well as the registration of medicines. Furthermore, the MCC faces severe resource constraints, which exacerbate the long timelines. Delays in registration of medicines are of particular concern with registration taking upward of 31 months." PV

11 Reasons to Conduct Clinical Trials in South Africa

1. High-quality medical infrastructure with a mixture of academic (public) and private institutions situated throughout the country.
2. Eager, experienced investigators who are trained to U.K. or U.S. qualifications alongside South African qualifications and who are familiar with ICH and SA GCP requirements.
3. A well-established clinical research industry that has been conducting and managing clinical trials for about 30 years. Many of the large pharma companies have had established and growing clinical research departments in South Africa since the late 1980s.
4. Regulatory agency and ethics committees that adhere to FDA and ICH GCP requirements.
5. English is the primary language of business.
6. A combination of first-world and third-world diseases and diverse patient populations: Caucasian, African, Indian, Asian.
7. First-world IT infrastructure and standards.
8. Large population of treatment and clinical trial naive patients.
9. Easy access to principal investigators.
10. Modern medical facilities with an increasing number of dedicated clinical research centers.
11. Standards of healthcare comparable with most European countries.

Source: Bronwen Muir, Senior Director Clinical Operations, ICON Clinical Research Johannesburg. For more information, visit iconplc.com.

EXPERTS



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and markets a broad range of medicines, in more than 20 therapeutic areas. For more information, visit msd.co.za. PIASA (the Pharmaceutical Industry Association of South Africa) is a trade association of companies involved in the manufacture and/or marketing of prescription medicines in South Africa. For more information, visit piasa.co.za.



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