

Spirit of South Africa

400
300
200
100



As South Africa increasingly recognises the investment potential offered by clinical trials, Frans van Wyk and Paul Hunt, at Pharm-Olam, examine the challenges and advantages of conducting research in such a diverse country

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Paul Hunt joined Pharm-Olam International in 1999. He was Managing Director of its European subsidiary for five years before being promoted to his current position of Executive Vice-President (Global Offices) in 2004. Before joining POI, Hunt held a senior position with UK CRO, Pharmakopius International, for five years. He also worked for Innovex as Financial Director and spent eight years as Commercial Director with Bosch-Siemens Hausgeräte GmbH.

Since the first human heart transplant was performed in 1967 in Cape Town by Dr Christiaan Barnard, a heart surgeon whose international renown turned the world's attention to medical advances being made in the Republic, South Africa has enhanced its reputation within the medical research arena, including high quality personnel and a sound medical infrastructure. These factors make it a strong, and yet often overlooked, candidate for outsourcing clinical research presenting a number of advantages compared to some emerging markets, as well as some of the well developed and highly competitive traditional sectors.

In 2001, there were an estimated 400 clinical studies performed in South Africa, accounting for an expenditure of US\$150 million (1). Clinical trial activity has increased due to local investment by pharmaceutical companies who see the potential for growth and the availability of experienced investigators working to international ICH-GCP standards. Larger sponsors, including Pfizer, Sanofi-Aventis and GSK, are including South Africa in research and the country seems particularly favoured for, but not limited to, Phase III studies, due to large patient numbers in lifestyle and infectious diseases. This allows for faster patient recruitment compared to established markets in the US and Western European countries.

South Africa is a diverse country of 1.2 million square kilometres, 11 official languages, although English is the most commonly used and, in terms of clinical research, it is acceptable for protocols, CRFs and IDBs. Translations are generally required for the informed consent and patient information brochures. Its population includes black Africans 79 per cent, white 9.6 per cent, coloured 8.9 per cent, and a significant Asian (mostly Indian) 2.5 per cent community. The continued growth of clinical trials in South Africa comes from recent legislative changes, competitive costs, increased public awareness about clinical trials, and the need for doctors to find alternative revenue streams.

HIV/AIDS: THE BIG KILLER

It is not surprising that the focus in South Africa is on HIV/AIDS. An estimated 5.5 million people (approximately 10.8 per cent of

the population over the age of two), are now living with HIV/AIDS, including 240,000 children under 15 years old. Among those between 15 and 49 years old, the estimated HIV prevalence was 16.2 per cent in 2005. However, the estimated HIV prevalence among antenatal clinic attendees in 2005 was 30.2 per cent. The highest prevalence was in the age group 25-29 at 39.5 per cent (2).

According to recent estimates, AIDS killed around 336,000 South Africans between mid-2005 and mid-2006 (3). UNAIDS/WHO is more conservative with an estimate that AIDS claimed 320,000 lives in 2005 – but it is still more than 800 every day (4). This means that 47 per cent of all deaths are AIDS related. Among adults aged 15 to 49 years, it is estimated that 71 per cent of all deaths was due to AIDS and recent predictions indicate that the number will exceed six million by 2015, by which time around 5.4 million South Africans will have died of AIDS (5).

At the end of 2004 there were over one million maternal orphans under the age of 18 in the country (6). The projections for 2015 shows that while broadly speaking the adult population continues to grow, the middle-aged population hardly develops at all, something that is not surprising considering the high level of HIV prevalence and the number of AIDS-related deaths in that age group. Combined with a declining trend in fertility, HIV/AIDS is expected to lead to a significant fall in the number of children born over the next 10 years (7).

TB: THE OTHER BIG KILLER

While HIV/AIDS impacts most publicly on the lives of South Africans, the burden of disease is not exclusively limited to it. In 2006, the WHO ranked South Africa fifth highest TB burdened nation in the world and had nearly 340,000 new TB cases in 2004, with an incidence rate of 718 cases per 100,000 people – a major increase from 338 per 100,000 in 1998 (8).

The TB epidemic in South Africa is likely to be further exacerbated over the next few years due to HIV/AIDS, as is the trend globally. TB-HIV co-infection rates are high, with as many as 60 per cent of adult TB patients being HIV-positive. Multidrug-resistant TB (MDRTB), largely caused by non-adherence to drug



risk factors such as obesity, hyperlipidaemias, hypertension, diabetes and tobacco addiction (10).

These risk factors contribute to a range of disorders like atherosclerosis, end-organ damage, tobacco and nutrition-induced cancers, stroke, ischaemic heart disease, chronic obstructive pulmonary disease (COPD), emphysema, renal disease, cardiac failure, osteoporosis and liver cirrhoses. In 2002, chronic disease mortality statistics indicated that 18 per cent of deaths, of all ages, and 20 per cent of the 35-64 age group were a result of CDL (11).

regimens or inappropriate drug regimens, is further exacerbating the epidemic. National studies of MDRTB conducted by the Medical Research Council of South Africa in 2002 found that 1.6 per cent of new TB cases and 6.7 per cent of re-treatment cases had MDR-TB.

TB places a significant financial burden on the government of South Africa because the cost per patient for treatment averages US\$800 for outpatient care when directly observed therapy (DOT) is provided at health facilities, US\$500-800 for outpatient care when both clinic and community-based DOT are available, and US\$2,200 when the first two months of treatment are provided in hospital. In each case, all costs were financed from government budgets estimated at US\$250 million per year (8), so the country has an active interest in researching new MDRTB drugs.

**CHRONIC DISEASES OF LIFESTYLE (CDL):
THE SILENT KILLERS**

Cardiovascular disease, diabetes, respiratory disease and cancers are a growing cause of death and disability in South Africa's diverse racial and social class groupings. In South Africa, one in three men and 50 per cent of women are overweight. Cardiovascular disease is the most common cause of death for those aged 45 and older (9). Public health services, already under pressure providing acute care for infectious diseases, are struggling to cope with the early detection and effective drug treatment regimes of cardiovascular disease, diabetes and cancer due to financial and resource constraints combined with the fact that, due to limited public awareness, these diseases often go unnoticed by the population. Clinical trials play an active and valuable role in raising public awareness, as well as providing a means of early detection and potentially effective drug treatment. Increasing urbanisation and unhealthy lifestyles contribute to the emergence of a range of CDL



Diabetes mortality rates have increased and the prevalence level is on the rise. According to the WHO, the total estimated cases of diabetes in 2000 was 814,000 and is predicted to increase by 58 per cent in 2030 to 1,286,000.

Like many emerging countries, South Africa has seen increasing numbers of newly diagnosed cancer cases every year, although this is also a result of increased testing. High tobacco use leads to high rates of lung and esophageal cancer.

DOING BUSINESS IN SOUTH AFRICA

Recent surveys by The Economist Intelligence Unit and the World Bank in 2005 ranked South Africa as highly cost-effective (10th out of 31 countries surveyed, 28th out of 155 nations respectively), the highest out of all of Africa. South Africa's exchange rate makes it one of the least expensive countries in which to do business – particularly due to its modern infrastructure.

More than US\$1 billion worth of pharmaceuticals are sold in South Africa annually, and the market is expected to grow substantially. Dispensing occurs via private channels, dispensing doctors, retail pharmacies, retail chains, private and public institutions, industrial clinics, and private and government hospitals.

UNIQUE PUBLIC AND PRIVATE SECTORS

South Africa's health system consists of a large public sector and a smaller but fast-growing private sector. Healthcare varies

South Africa facts	
Population:	47.5 million
Life expectancy:	males 47, females 49
Infant mortality:	67 per 1000
GDP per capita:	\$12,200
Total health expenditure as a per cent of GDP:	8.4 per cent
Sources: WHO World Health Statistics 2006, The World Health Report 2006 Edition	

from the most basic primary healthcare, offered free by the state, to highly specialised hi-tech health services available in the private sector.

Although the state assigns about 40 per cent of all expenditure on health, the public health sector is under pressure to deliver services to about 80 per cent of the population. Despite this, most resources are concentrated in the private health sector, which is dedicated to the health needs of the remaining 20 per cent of the population (12).

Drug expenditure per person varies widely between the sectors. In 2000, about US\$1.15 billion was spent on drugs in South Africa, with the state accounting for only 24 per cent of this amount. Thus, US\$8.30 was spent on drugs per person in the state sector, as opposed to US\$111.80 on drugs per person in the private sector.

The number of private hospitals and clinics continues to grow. In 2000, there were 161 private hospitals; this has now increased to over 200. Most health professionals, except nurses, work in private hospitals. With the public sector's shift in emphasis from acute to primary healthcare in recent years, private hospitals have begun to take over many tertiary and specialist health services.

Chris Hani Baragwanath Hospital in Soweto, one of the largest in the world, has a perinatal HIV research unit which occupies several floors of the hospital and employs 200 staff members. The hospital as a whole has over 3,200 beds and 6,700 staff members, and conducts research programmes across several therapeutic areas, positioning it as an international player in the field of HIV/AIDS research.

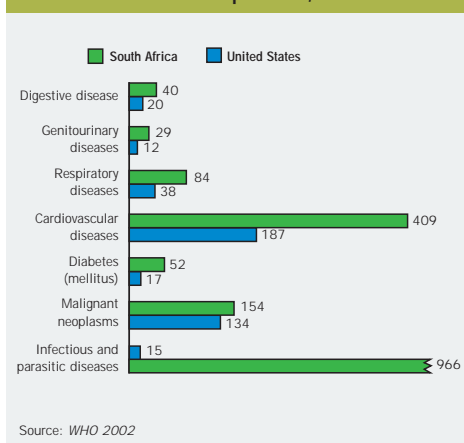
South Africa provides research sites such as Witwatersrand's Donald Gordon Medical Centre, modelled after the renowned Mayo Clinics in the US, which trains medical specialists to advance within their field. South Africa's medical schools have produced some of the world's top specialists in a variety of fields. These opinion leaders provide valuable clinical knowledge and, in cooperation with local clinical trials outsourcing experts, outstanding clinical trials.

CLINICAL TRIALS – DEFEATING THE KILLERS

New medications are needed to combat the burden of disease and the value of clinical trials are well recognised within the research community. Public and private research sites with modern infrastructure and medical expertise are available. The racial/cultural diversity provides an opportunity to investigate racially specific disease traits, whilst the shift from rural to urban areas provides a wealth of patients to investigate emerging and re-emerging diseases caused by urban deprivation.

As in Latin America, South Africa is ideal for seasonal studies, speeding up the global study initiation due to seasonal reversal from the US and Europe. The country also has potential for paediatric studies because nearly 30 per cent of the population is less than 15 years old.

Figure 1: Age standardised death rate per 100,000



South Africa's Medicines Control Council (MCC) enforces national GCP regulations, which supplement international GCP standards. A familiarity with the regulatory standards set by the MCC is an absolute must for sponsors seeking to work in South Africa, particularly given media coverage of the pharmaceutical industry's activities in recent years. By working with a local, experienced partner, sponsors can avoid delays in regulatory acceptance due to oversights in the protocol and study design, particularly for placebo-controlled studies. The MCC also does

not accept applications, nor do they communicate directly with international sponsors without a local representative.

CONCLUSION

South Africa recognises the investment that clinical trials provide for the future of its people. The close co-operation between research sites, their dedicated staff, and patients allows for timely execution of clinical trials according to ICH/GCP guidelines. Patients benefit from free treatment that many could otherwise not afford and support future generations by helping to bring more effective products to market. Sponsor's investment interests work in harmony with government healthcare goals, whilst ensuring that ethics are maintained. ♦

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