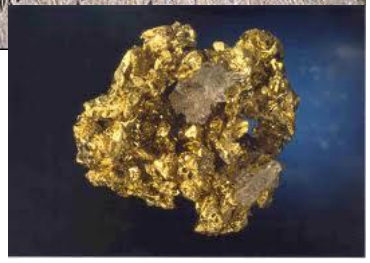
TRICLINIUM

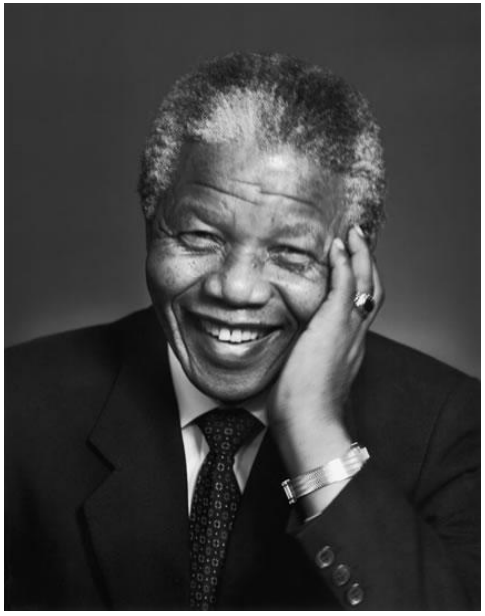
CLINICAL TRIAL PROJECT MANAGEMENT (PTY) LTD

Vaccine Research in South Africa: The VPM1002 Experience

Hannover, 6 September 2012

South Africa





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Triclinium: A South African CRO

- Established February 2000
- Sandton, Johannesburg
- Core competencies in clinical trial conduct:
  - project set-up (feasibilities & site assessment, protocol input, investigator meetings)
  - regulatory submissions
  - project management (sites & third-party *vendors* at *national and regional* levels)
  - site and data monitoring
  - QA audits of sites & vendors (global)
  - Setting up in-house DM

Triclinium: A South African CRO

- Full CRO service via established network of specialised service providers (biometry, laboratory, IP etc.)
- 12 year record: 192 contracts, >80% repeat business
- Phase I – IV trials
- 43427 participants at 676 sites
  - largest single site: phase IIb 2800 subjects
  - multicentre phase III up to 40 sites
- Sponsors: PDPs, Biotech, Pharma, Academia, Global CROs
- GHCC (Gates Foundation preferred CRO)
- Experience across numerous therapeutic areas

Africa: Countries of Activity

South Africa and 12 other countries in SSA

- Senegal
- Tanzania
- Kenya
- Uganda
- Rwanda
- Mozambique
- Malawi
- Zambia
- Botswana
- Zimbabwe
- Nigeria
- Cameroon
- Lesotho

South Africa: Provinces & Capital Cities

Why South Africa?

- Established research culture
- First trials mid-60s, post-thalidomide
- Major Early-Phase presence since the early 1970s
- Steady growth since the 1980s with extension from academic to private sector
- Large database of experienced investigators & well-equipped sites
- Medical expertise & Key Opinion Leaders in many disciplines
- Stringent ICH-compliant health regulatory and ethical review policies

Why South Africa?

- Clinical Research spending approximately US$3bn*
- Clinical practices & training most resemble UK/USA
- Internationally relevant public health issues
- Frequently among highest-recruiting countries in multi-national studies
- Inverse seasons (year-round enrolment)
- Fiscally competitive
- Gateway to the rest of Africa
- Government R&D incentives

** Time-extrapolated data, Wits University survey*

Why South Africa?

Leading 4 trial indications (48%):

- CNS
- Oncology
- Cardiovascular
- Diabetes

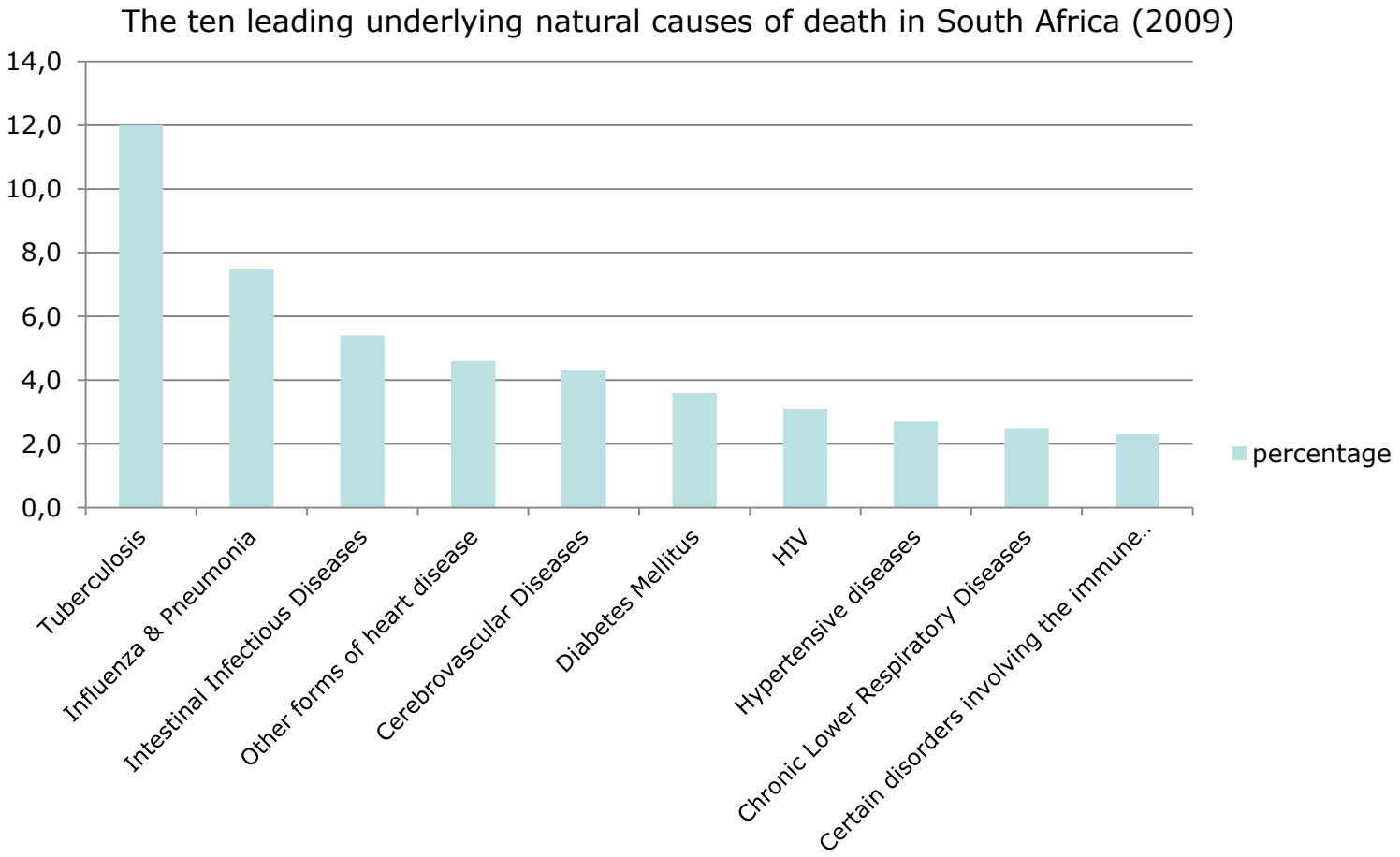
Infectious diseases including HIV and TB (18%)

Of the 1630 trials registered:

- 76% regional contributions to multinational trials
- 9% multicentre trials in SA only
- 15% single-centre (early-phase /BE)

Ref: Survey of SANCTR data July 2005 – October 2010

South Africa: Leading Causes of Death



South Africa: Demographics

- 2011 mid-year population estimate is 50.59 million
- 52% ♀
- Gauteng 11.3 mill; KZN 10.8 mill
- 31.3% younger than 15yrs & 7.7% older than 60yrs
- Life expectancy at birth 54.9yrs (males) & 59.1yrs (females)
- Infant mortality rate 37.9
- Multiple ethnicity
- English language of business & research

Race	% total population
African	79.5
Mixed race	9
Indian/Asian	2.5
Caucasian	9

South Africa: HIV Statistics (2011)

- HIV prevalence 10.6%*
- For the period 2001-2011: HIV prevalence ↑ from 9.4 – 10.6; incidence ↓ from 1.72 – 1.38
- total # of people living with HIV ± 5.38 mill
- ~ 16.6% of the adult population (15–49yrs) HIV+
- ~ 20% ♀ in productive age are HIV+

** Based on antenatal survey adjusted for relative ANC attendance rates & differences in prevalence between pregnant women & the general population. Ref: www.statssa.gov.za*

South Africa: HIV Statistics (2011)

- Approx # new HIV infections (2011) for population aged > 15yrs was estimated at 316 900; 0-14yrs 63 600
- Ratio of new infections in adults ♀:♂ is 1.5:1
- 1.16mill receiving ART (2010) vs 1.33mill requiring Rx; estimated # requiring ART (2011) 1.49mill
- Estimate AIDS orphans 2011: 2.01mill
- % AIDS deaths vs total (2011) 43.6%

South Africa: TB Statistics (2010)

- HIV burden has led to a 3-fold increase in the # of TB cases observed over the past decade
- TB leading cause of death, increasing from 6.5% in 1997 to 12.6% in 2008
- Recent study revealed that approx 20% of persons with HIV-associated TB in SA are infected with MDR strains.
- KZN epicentre of the HIV and TB co-epidemic
- 2006 well-documented outbreak of MDR and XDR at Tugela Ferry

South Africa: TB Statistics (2010)

Estimates of Burden 2010	Number (thousands)	Rate (per 100 000 pop)
Mortality (excl HIV)	25 (16-38)	50 (31-75)
Prevalence (incl HIV)	400 (180-630)	795 (364-1264)
Incidence (incl HIV)	490 (400-590)	981 (806-1173)
Incidence (HIV-positive)	300 (240-350)	591 (488-704)
Case detection, all forms (%)	72 (60-88)	

Ref: www.who.int/tb/data (South Africa 2010)

South Africa: TB Statistics (2010)

Tuberculosis deaths in South Africa by age group

	Age group							
TB	0-14		15-49		50-64		65+	
	Rank	%	Rank	%	Rank	%	Rank	%
	5	3.4	1	19.6	1	11.4	8	3.3

Ref: Stats SA Release P0309.3 Mortality and causes of death in South Africa, 2009: Findings from death notification. Published 30 November 2011

South Africa: TB Statistics

Tuberculosis deaths in South Africa by age group

	Age group			
TB	Post-neonatal		1-4	
	Rank	%	Rank	%
	6	2.2	4	5.2

Ref: Stats SA Release P0309.3 Mortality and causes of death in South Africa, 2009: Findings from death notification. Published 30 November 2011

Vaccine Trials conducted in SA

Search criteria	www.clinicaltrials.gov	Triclinium Projects Database
'vaccine AND South Africa'	73	42
'Phase 1, 2 & 3'	57	36
'Tuberculosis'	16	21

Vaccine Trials contracted to Triclinium

- 47 vaccine trials, 42 trials in SA to date (3 just contracted)
- Phases: I - IV (mostly I & II, including First in Human) and Epidemiology
- Variety of services: Regulatory, PM, Monitoring, Audit as well as protocol writing, contracted vendor services
- Sponsors: Biotech, PDPs, Pharma, Academia
- Origin: All but 1 are international (Europe/US)
- Investigational Products: HIV, TB, Measles, Influenza, Polyvalent paediatric, Hepatitis, Polio

SA Clinical Trial Regulatory Processes

National Regulatory Authority: Medicines Control Council (MCC)

- 6-7 review cycles per annum
- Process: Application – CTC – Council
- Triclinium median approval time: 1 cycle

SA National Health Research Ethics Committee (NHREC)

- registration and inspection role for SA IECs
- 33 ECs registered with NHREC (20 OHRP-registered)

SA National Clinical Trials Register (SANCTR)

- applicants register IEC-approved trials with the DOH and obtain a unique SANCTR trial number prior to trial initiation

SA Clinical Trial Regulatory Processes

Department of Agriculture, Forests & Fisheries (DAFF) for GMO

- Biosafety Directorate
- Cartagena Protocol: environmental impact
- LMO
- 6 review cycles annually (16-20 weeks)
- Public notice
- Dual application & risk assessment
- Conditional approval

SA Clinical Trial Regulatory Processes

- IECs and MCC enforce a high standard of clinical research and ensure strict adherence to GCP and GLP
- High priority given to participant safety and protecting the rights of vulnerable groups (education, HIV, etc.)
- Trial Sites and CROs in South Africa are subject to inspection by MCC, IECs and Biosafety Directorate (for LMOs)
- SA GCP guidelines follow ICH GCP & FDA Guidelines for IND trials
- ALL preparatory activities run in parallel

Recipe for success?

Communication & consultation

- Integral part of the VPM team almost from the point of conceptualisation of the project
- Protocol input