



CONCISE VERSION OF
REVITALISING CLINICAL
RESEARCH IN SOUTH AFRICA

A STUDY ON CLINICAL RESEARCH AND
RELATED TRAINING IN SOUTH AFRICA



*Applying scientific thinking
in the service of society*

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P O Box 72135, Lynnwood Ridge 0040, Pretoria, South Africa
1st Floor Block A, The Woods, 41 De Havilland Crescent
Persequor Park, Meiring Naudé Road, Lynnwood, 0020, Pretoria, South Africa

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PO Box 72135, Lynnwood Ridge, Pretoria, South Africa, 0040
1st Floor Block A, The Woods, 41 De Havilland Crescent, Persequor Park
Meiring Naudé Road, Lynnwood 0020, Pretoria, South Africa
Phone: +27 (0) 12 349 6600 • Fax: +27 (0) 12 349 5461
Email: admin@assaf.org.za

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The Academy of Science of South Africa (ASSAf) was inaugurated in May 1996 in the presence of then President Nelson Mandela, the patron of the launch of the Academy. It was formed in response to the need for an Academy of Science consonant with the dawn of democracy in South Africa: active in its mission of using science for the benefit of society, with a mandate encompassing all fields of scientific enquiry in a seamless way, and including in its ranks the full diversity of South Africa's distinguished scientists.

The Parliament of South Africa passed the Academy of Science of South Africa Act, Act 67 of 2001, and the Act came into operation on 15 May 2002. This has made ASSAf the official Academy of Science of South Africa, recognised by government and representing South Africa in the international community of science academies.



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NOVEMBER 2009

* Full Report available on www.assaf.org.za

FOREWORD



This report provides a review of the overall state of clinical research in South Africa. At the initiation of the study, the Study Panel's task was to review the existing scientific evidence regarding the current state of clinical research in South Africa. The review focused mainly on key clinical research issues as they were outlined in the brief. Some highlights of the findings include the fact that there has been too little research on the public understanding of science or of public perceptions of clinical trials in South Africa, and that there is currently no national plan to provide coordinated support for the education and development of clinical researchers. More than half of the total expenditure on clinical research is by the private sector. Finally, since the public sector is playing too small role in this domain, it needs to become more actively engaged.

The study was initiated as a result of discussions with the Pharmaceutical Industry Association of South Africa (PIASA), which suggested that the Academy of Science of South Africa (ASSAf) should raise awareness of the value of good scientific clinical research to South Africa at top levels of government and academia. This also included raising awareness of the benefits of having clinical research units at universities, hospitals and research institutions in order to retain research scientists in the country, as part of the agenda of building a larger pool of researchers for the future. Proposers of the study were Prof. Wieland Gevers and Prof. Jimmy Volmink and former ASSAf staff member Ms Rudzani Ramaite. The ASSAf Council approved the study and approved the appointment of a 13-member Study Panel of experts.

The 13-member Study Panel, chaired by Prof. Bongani Mayosi, has completed the study and this report is the product of their work. The report has been peer

reviewed by one national and two international peers who recommended that the report be published. The ASSAf Council also has reviewed both the report and the reviewers' comments, and has approved the report for publication. The Council hopes that this report's recommendations and findings will lead to productive interventions, and the growth of high-quality clinical research in South Africa.

The report recognises that good clinical research is crucial for the development of the country, and thus recommends ways in which it can be revitalised and promoted. It proposes solutions to the challenges highlighted in the report. These recommendations are based on thorough analysis of the evidence obtained by the Study Panel. The report lists the recommendations in detail and further suggests which institutions and individuals can best facilitate the implementation of these recommendations. One of the key recommendations is that the South African Government should invest more money in clinical research.

The Council expresses its appreciation to Prof. Wieland Gevers and Prof Jimmy Volmink for proposing the study and thanks the chair of the Panel, Prof. Bongani Mayosi and all the Panel members for their participation and outstanding contributions to the development of the report. The support staff, Ms Phakamile Mngadi (Study Director), Dr Nthabiseng Taole (Project Manager) and Prof. Roseanne Diab (Executive Officer) are thanked for their contributions and assistance during the course of the study.

PROF. ROBIN CREWE

President: Academy of Science of South Africa

ACKNOWLEDGMENTS



This report is the joint work of a 13-member Study Panel appointed by the Council of the Academy of Science of South Africa (ASSAf). Each panelist has agreed to the specific formulation of the report and to its conclusions, findings and recommendations.

The Study Panel members were: Professor Bongani M Mayosi, MASSAf, University of Cape Town: Chairman; Professor Amaboo (Ames) Dhai, University of the Witwatersrand; Professor Peter Folb, MASSAf, Medical Research Council of South Africa; Professor Wieland Gevers, MASSAf, Academy of Science of South Africa (General Secretary); Professor Gregory D Hussey,

MASSAf, University of Cape Town; Ms Maureen Kirkman, Pharmaceutical Industry Association of South Africa; Dr Edith Nonhlanhla Madela-Mntla, Medical Research Council of South Africa; Professor Letticia Moja, University of the Free State; Professor Jagidesa (Jack) Moodley, University of KwaZulu-Natal; Professor Daniel Ncayiyana, *South African Medical Journal*; Professor William Pick, MASSAf, Council of Medical Schemes; Dr Nandi Siegfried, Medical Research Council of South Africa; and Professor Jimmy A Volmink, MASSAf, Stellenbosch University.

Dr Harriet Deacon served as the Study Researcher, and Ms Phakamile Mngadi was the ASSAf Project Officer for this study.

The Study Panel would like to acknowledge the following individuals for their assistance in compiling this report: Dr Richard Chawana, University of the Witwatersrand; Professor Peter Cleaton-Jones, University of the Witwatersrand; Dr Liesl Grobler, University of Cape Town; Ms Lee Louw, Stellenbosch University; Dr Percival Mahlati, National Department of Health of South Africa; Dr Philemon Mjwara, Department of Science and Technology of South Africa; and Ms Rudzani Ramaitse (former ASSAf staff member). The Panel also wishes to express its gratitude to Professor Roseanne Diab (ASSAf Executive Officer),

Dr Xola Mati (ASSAf Chief Operations Officer), and Dr Nthabiseng Taole (ASSAf Project Manager) for their valuable support during the conduct of the study.

The Study Panel met on eight occasions from September 2007 to May 2009. Panel members were allocated different sections/chapters of the project and at these meetings the different sections were discussed. They deliberated on gaps/omissions, overlaps, possible contradictions/controversies, target audiences/ stakeholders for the different recommendations and aspects of the report. The draft sections were circulated to members prior to these meetings and a number of small sub-group meetings were also held. Internal reviews of the different sections/chapters were also undertaken by some members of the Panel, who were nominated (within the Panel) to do so.

Dr Richard Clark edited the pre-final draft report and Ms Beverlie Davies edited the final draft; the Panel appreciates their input. The three independent peer reviewers were: Professor Adesola Ogunniyi (Nigeria), Dr Mamphela Ramphele (South Africa), and Professor Sir David Weatherall (United Kingdom). The Panel wishes to thank them for their insightful comments that have enriched this report.

The Panel also acknowledges the financial support provided by the United States National Academies (USNA) through the African Science Academies Development Initiative (ASADI) programme, as well as funding provided by the South African National Department of Science and Technology.

PROF. BONGANI MAYOSI

Chairperson: Clinical Research and Related Training in South Africa

CONCISE BRIEF OF THE STUDY

1. What was the brief of the ASSAf Council to the Study Panel?

The brief of the Study Panel that was appointed by the Council of the Academy of Science of South Africa (ASSAf) was to examine and address the most relevant and reliable evidence on the key questions below, especially regarding clinical trials, and to make recommendations that were most appropriate and feasible, based on that evidence:

- (i) How to build a national culture in which clinical research is seen as essential and clinical trials are widely accepted and promoted as the most reliable basis for establishing the efficacy and safety of new therapies, procedures and approaches?
- (ii) How to equip and encourage clinicians-in-training to embrace clinical research and evidence-based practice as indispensable elements in delivering effective health care?
- (iii) How to improve the level of funding and execution of clinical research for investigator-driven clinical research, including clinical trials research?
- (iv) How to ensure that clinical research flourishes in South Africa under conditions that protect the rights and safety of individuals?
- (v) How can government, parastatal institutions, academia and industry interact more constructively in creating a favourable and enabling environment for clinical research to be conducted?

2. Why was the topic addressed by ASSAf and not by another body?

According to its Act, *Act 67 of 2001*, ASSAf is obliged to:

"Provide effective advice and facilitate appropriate action in relation to the collective needs, opportunities and challenges of all South Africans". The Academy may, "at the request of any person or on its own initiative, investigate matters of public interest concerning science and on the strength of the findings act in an opinion-forming and advisory manner".

ASSAf has influence as a high-level, independent and constructive body. This influence can be used more effectively in bringing about policy change to make a contribution in an interlocking area of national importance and opportunity that has resisted resolution and reform over many years, and caused considerable frustration in its participant sectors. ASSAf, through a panel of experts, could examine areas that would lead to significant improvements and influence government perceptions regarding the value of clinical research and related training to the South African economy and health system, by engaging with senior government officials in a number of ministries, e.g. the Presidency, Health, Education, Science and Technology, Finance, and Trade and Industry. Each of these departments has a vested interest in improving the health status of the nation and providing access to adequate, affordable health care in a framework of economic and social prosperity. It would be entirely feasible for ASSAf to examine identified special topics where further focused studies or workshops would be appropriate, including how funding would be sourced.

EXECUTIVE SUMMARY

Clinical research in a developing country like South Africa contributes to health care at all levels by identifying the causes of problems, facilitating diagnosis, improving the efficiency and effectiveness of care, and promoting good policy-making. It also supports the training of competent health professionals of all kinds, and contributes to global knowledge about locally, as well as generally, prevalent diseases in terms of prevention and treatment.

The key narrative of clinical research in South Africa over the last two decades has been that of a largely unplanned, but cumulative, disinvestment in publicly funded programmes, resulting from the withdrawal of the health departments of provincial governments from this sector (academic hospitals are now funded for service functions only), the absence of discounts for research tests from the business model of the National Health Laboratory Service (NHLS), chronic underfunding of the Medical Research Council (MRC) despite its obviously important mandate for maintaining and developing medical/clinical research capacity in the country, and the lack of funding streams to universities that might in principle have been applied to meet the overall shortfall in support.

These intersecting developments are a kind of 'elephant in the room', well known to all participants, but very poorly documented. Tertiary service units struggle to remain active in research, and to translate their expertise into improved health service. As a result, many clinical researchers have been left with no option but to turn to the pharmaceutical industry for the funding of those clinical trials in which the companies concerned have an interest, or to international donors who conduct large-scale, short-to medium-term, projects in South Africa, with local researchers drawn into international teams, often led by outsiders. The pharmaceutical investment is directed predominantly at the profitable areas of chronic diseases of lifestyle, mental illness and allergy, while most of the external donor funding is directed at the serious local HIV and TB pandemics. Local and international clinical conference activity has accordingly begun to reflect the agendas of donors and industry. There is

little likelihood that continuation of the present situation is compatible with rebuilding and sustaining solid research capacity in the clinical domain, nor can the ideal of well-coordinated state support for a health system, built on the 'intelligence' of good clinical research, ever be realised.

The serious decline in clinical research activity and capacity has prompted this study by ASSAf (<http://www.assaf.org.za>) in order to make recommendations on the overall revitalisation of clinical research in the country within the broad paradigm of essential national health research. An additional stimulus is the emphasis of government in its ten-year science and technology plan on the development of new medicines and other biologically useful agents ('farmer to pharma').

* * *

In **Chapter 1** we engage with the questions as to **what clinical research is, and why it is important**. The following working definition of clinical research has been adopted:

Clinical research is research primarily conducted with human participants (and on material derived from them, such as tissues, specimens and cognitive phenomena) during which investigators examine the mechanisms, causation, detection, progression and reversal of human disease.

Clinical research is important because it can improve health outcomes by establishing the effects of health care interventions, and because it promotes and facilitates best-possible health care practice. It is a crucial element in the education of health care workers and the effective provision of appropriate clinical services. Revitalising clinical research is thus in the national interest and requires efficient and supportive management and encouragement at all levels.

* * *

In **Chapter 2** we engage with the **history of scientific medicine in South Africa**, and briefly assess its achievements and limitations. Specifically, we examine the legacy of colonialism, racism and inequality in medical research, and ask

how this history has shaped the relationship between researchers, government, industry and the South African public.

From the beginning of the 20th century, medical researchers in South Africa began to develop a strong scientific base for clinical research in terms of personnel and infrastructure, conducting important investigations into a wide range of medical problems. The present burden of disease in South Africa is significantly linked to the country's history of racial and gender inequality, violence, oppression and enforced labour migration, and to some of the failures of post-apartheid independence. It is characterised by high levels of both communicable and non-communicable disease, particularly those that are related to poor working conditions and poverty, gender-based violence and injury. Because of the colonial context, clinical investigations (with some notable exceptions) were largely driven by the needs of the mining and agricultural industry, or focused on curative medicine in urban areas, and generally did not aim to improve the health of the population as whole.

Clinical research in the apartheid years was conducted by a cohort of investigators who were mainly white and male, within a system that provided racially unequal access to health care and research training. Institutional capacity to conduct clinical research was concentrated in a few historically white institutions. Some clinical research in the colonial and apartheid eras was racist and unethical, facilitated by an environment of racial inequality, discrimination and high status and wealth differentials under an oppressive state.

After 1994, significant strides were made in reorienting health care and medical research towards the needs of the majority at a policy level, but in practice the tangible benefits of this have been limited by reduced government support for medical research within the health care system, a weak education system, and poor management of existing resources within the health care system, in the face of serious new challenges such as HIV/AIDS and tuberculosis.

Accordingly we recommend that clinical research should be repositioned within a more democratic political and societal context, to build on the advantages of past investment while actively addressing the legacy of

colonialism. Clinical research should contribute to the improvement of the health of the nation by purposefully addressing the largest burdens of disease as empirically determined and consultatively agreed. The training and promotion of clinical researchers should seek to address racial and gender imbalances, and ensure that a strong intellectual leadership is built. The funding of clinical research should seek to develop strengths wherever these can best and most sustainably be built. Finally, clinical research should be based on strong ethical codes of conduct.

* * *

In **Chapter 3** we ask what shape a **national culture** supporting clinical research would have to take for it to be supportive of good clinical research, what its principal components would be, and to what extent present conditions fall short of these requirements. We believe a national culture supporting clinical research will accept the value of clinical research based on the principle that 'the proper study of humankind is humans themselves'; will understand that sustainable health care systems require guidance by a critical mass of clinicians experienced in research and the continuous training of new generations of research-informed clinical care-givers; will recognise the importance of investment in clinical research due to its complex and multi-dimensional nature; will enable an appropriate balance between risks and benefits in clinical research while ensuring ethical practice; will attain an appropriate balance between curiosity-driven and problem-directed research in addressing key health risks in society; will place a clear emphasis on public service and public benefit in the conduct of clinical research, will promote the protection and development of intellectual property; and will enhance public trust in, and understanding of, the role and contribution of research in society.

Accordingly we recommend raising the status of clinical research, both within the broader domain of scientific research and within government programmes funding science; creating a strong public service and benefit ethos based on better programmes promoting public engagement with clinical science and better risk-benefit analyses that inform prioritisation of clinical research

in the country; capacitating local ethics and regulatory bodies for clinical research; developing an interdisciplinary local scientific community through scientific publishing and coordinated promotion activities while encouraging links between laboratory-based and clinical research; enhancing specialist knowledge and competence that is internationally visible without reducing interdisciplinary communication among clinical researchers within South Africa; creating targeted educational programmes, funding, career-pathing and institutional support for the development of new clinical researchers in the country; increasing, and better coordinating, the funding of clinical research; and working towards a concerted and coordinated effort by government, industry and research institutions to promote and develop clinical research capacity at the highest level possible.

* * *

In **Chapter 4** we ask how fostering better **public engagement with science** can promote a national culture supporting clinical research. What do we know about public opinion concerning clinical research in South Africa, and what can we do to improve public understanding of, and trust in, clinical research?

We find that there has been too little research on the public understanding of science or on public perceptions of clinical trials in South Africa, that there is a legacy of distrust and ignorance in the relationship between research participants and clinical researchers because of the history of South Africa, and that mutually beneficial engagement between the public and clinical researchers has not been extensive enough in the past. Although South Africa is still an attractive location for clinical trials, and recruitment of subjects for clinical trials is still relatively easy in the country (due to a large treatment-naïve urban population that is experiencing high unemployment and has difficulty accessing expensive drugs), this may change unless attention is given to public perceptions through careful engagement.

We therefore recommend raising the profile of clinical research on the African continent, for example, in the African Science Communication Network and the Southern African Science Communication Network (SASCON), and

including clinical research as a further flagship research and development cluster for the 2011-15 *African Science and Technology Plan of Action*. We also suggest raising the profile of clinical research within South Africa, for example by broadening National Science Week to incorporate a National Health Research Week, and by establishing an ASSAf award for Promoting Public Engagement with Clinical Science.

We recommend that public engagement with science should be deepened, for example by funding qualitative and quantitative research about the public understanding of science, motivating for a National Research Foundation (NRF) Research Chair in Public Engagement with Science, ensuring that clinical research is included in the agenda, and by including public engagement with science in the NEPAD indicators for African science, technology and innovation.

We suggest reviewing the new curriculum statements in schools, making specific reference to therapeutic/clinical concepts based on an historical (longitudinal) approach in order to make useful connections between chemistry, human physiology (e.g. endocrinology as an internal 'drug-administering system'), mathematics literacy, ethics and economics.

We wish to ensure a more democratic engagement between the public and researchers, so that they share a common understanding of the operation and purpose of clinical research, for example by developing locally appropriate public communication guidelines and ethical protocols for researchers, engaging with public views about clinical research, including geopolitical issues as part of research preparation activities, and promoting rights access and education for trial participants.

Attention must be given to strengthening the capacity of health and science journalists to assist in accurately conveying the essence of clinical research approaches and findings to the public, and permitting the public airing of concerns.

* * *

In **Chapter 5** we examine the current mechanisms of **ethical oversight** of clinical research in South Africa, and ask how well these mechanisms are functioning, how ethical oversight mechanisms for clinical research function elsewhere, and how we can improve ethical oversight of clinical research in South Africa.

We conclude that research should be viewed as a social enterprise, i.e. a contract with society, whereby ethically conducted research will serve to assure society that individuals will not be harmed. The primary function of Research Ethics Committees (RECs) is the protection of research participants, including adequate scientific review for excellence and relevance. The laws governing the conduct of research in South Africa are generally adequate, as are the institutional provisions for ethics governance and regulation; the National Health Act has set the standards for ethics in research but implementation of these standards is far from being realised.

While legislative changes have resulted in increasing numbers of research projects requiring ethics review and approval, there has not been a parallel increase in support of REC functioning, resulting in often unnecessary delays (this is particularly problematic regarding multi-centre studies). Very few RECs are in a position to honour their obligations to monitor and provide oversight of the research they approve, despite the fact that the majority of REC members in South Africa are health scientists and clinicians and that RECs operate largely within university environments. The shift of clinical trial commissioning from academic institutions to the private sector has weakened the access of academic institutions to funding and their ability to develop research capacity, so that only a handful of core researchers are doing trials, and conduct too many trials concurrently.

We recommend that institutions and the Department of Health must both support RECs both from an administrative and review perspective. This must include post-approval responsibilities, including passive and active monitoring of approved research; the monitoring and evaluation of REC functioning; and making information about clinical research widely available.

The National Health Research Ethics Council should register and accredit RECs and expedite their ability to process applications. A system of expedited review for minimal risk research would result in a significant reduction in the overall turn-around time for study proposals. Institutions and RECs should collaborate to reduce duplication in ethics review within South Africa, and thus facilitate multi-centre studies.

Focused, ongoing educational programmes for existing and potential REC members on ethics protocol review, current and past ethics research discourse and debate, and ethics regulation are required to ensure competent, high-quality review, which itself should be subject to quality assurance at pre-determined intervals.

The ethics of publishing needs ongoing attention to avoid the problems of sponsor-driven content, and to ensure complete disclosure of conflicts of interest.

* * *

In **Chapter 6** we investigate what key problems in South African clinical research can be identified by an analysis of **published outputs**, and explore specific interventions that might best promote overall productivity of clinical research in terms of both quality and quantity.

We find that while South African scientific publishing represents a small fraction of world output, it comprises a large proportion of scientific research on the African continent. Clinical research has formed an important part of South Africa's scientific output, in terms of quality and quantity. Although the total number of clinical medicine journal articles has declined since 2003, nearly half of the fields in clinical research have recorded above-average field-normalised and journal-normalised citation rates for the period 2002 to 2006. The trend has been towards increased publication of clinical medicine journal articles in international journals, particularly in a wide variety of specialty journals. Although more female and black authors have been publishing than before, progress has been slow and the proportion of older authors has been rising.

We recommend that more high-quality clinical research should be published in local, especially multidisciplinary, journals, requiring specific steps such as fully recognising and rewarding publications in local journals of high quality. We also recommend increasing opportunities for local publication, for example by establishing vibrant supplements to existing journals and/or establishing a new, open access, multidisciplinary journal for clinical research, possibly as a 'daughter' of the existing flagship publication, the *South African Medical Journal*. A national society for clinical research should be established.

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In **Chapter 7** we seek to address the declining size and increasing age of the **workforce** actively engaged in clinical research, and the paucity of effective training programmes and unattractive career-pathing in the clinical research sector.

We find that the clinical research force is ageing and has been steadily declining in numbers since the early 1990s. The combined burden of clinical teaching and training, health service, and research thus falls on a shrinking and ageing pool of academics in health science faculties. This means that there is limited capacity to increase the production of properly trained health care workers and to train and inspire a new generation of clinical researchers. Simultaneously, the situation has brought about an inability to cope with the increasing demands of clinical service imposed by the colliding epidemics of infectious disease (TB and HIV/AIDS) and non-communicable disease (heart disease and stroke).

There is currently no national plan to provide coordinated support for the training and development of clinical researchers, and grossly insufficient support for research professorships and training fellowships in the clinical research field. There is little incentive for clinicians to train in doctoral programmes, resulting in a very small number of the clinical professoriate having doctoral degrees.

We recognise that the National Human Resources Plan for Health that was launched by the national Department of Health (DoH) in 2006 emphasises

the general shortage of health professionals in South Africa, and consider that clinical research needs to be identified as a priority area for implementation. The Colleges of Medicine of South Africa (CMSA) has a policy forum on tertiary academic medicine and specialist training, which should support these aims. The DST's Ten-Year National Plan for Innovation aims to develop a knowledge-based economy in which the production and dissemination of knowledge leads to economic benefits and enriches all fields of human endeavour: clinical research should clearly be one of the most important focus areas in the Plan.

We recommend the creation of a national plan for research capacity development in the clinical sciences (a 'National Clinical Scholars' Programme') for undergraduate and postgraduate students, and for junior and senior faculty in clinical research, based partly on the idea of the PhD as the key driver for progress in this area, as part of the human capital generation project of the Department of Science and Technology's (DST's) Ten-Year National Plan for Innovation. This should be a publicly funded training programme for the production of the clinician research workforce from undergraduates with the necessary talent and aptitude (through student research fellowships), and from 20% of postgraduates (through clinical research fellowships). A target should be set for 500 PhDs to be produced in the clinical research field over the next 10 years, while 30 national research chairs should be earmarked for the clinical sciences.

The objectives of the proposed 'National Clinical Scholars' Programme' may be achieved through expansion of the intercalated research year model of selective training of motivated undergraduates in carefully planned curricula designed to establish a life-long interest in research, re-design of the MMed research component to enhance its effectiveness in research training and competence, and to serve as the basis for MD/PhD study, and stimulating PhD degrees for professional graduates by widening the necessary opportunities and support mechanisms, including use of modules and learning methodologies from BSc Med honours programmes. Provision should also be made for the purposeful training and career-pathing of non-clinical graduates who can become important partners in clinical research programmes.

We also propose the creation of a flexibly managed and supported clinical academic career track in all disciplines in the Academic Health Complexes under the Health Sciences Academic Development Programme of the DoH. A new cadre of clinical lectureships and clinical professorships needs to be established in all clinical disciplines to rejuvenate and expand the pool of clinical research trainers and academic clinicians in general. We suggest the promotion of training for biostatisticians and other supporting professions for clinical research at universities. We propose the incorporation of ethics into clinical research training and education. We ask for the establishment and funding of learnerships for graduates in the research facilities of large multinational and national companies, and suggest the development and support of a network of skilled mentors who can lead the development of young clinical researchers.

The establishment of large-scale research institutes dedicated to collaborative clinical research and innovation is a cost-effective and efficient way of developing high-level capacity at the cohort level, recognising as it does the integration of multiple skills and disciplines in order to address complex health problems and create new approaches to health promotion and treatment of prevalent and burdensome diseases.

We also ask for the creation of a 'National Clinical Research Coordinating Centre' at the MRC to link and coordinate clinical research centres and clinical trials programmes at universities, research councils, government and industry. Such a network (which would operate best if accorded a large measure of operational independence while retaining overall accountability) would foster collaborative research efforts, training programmes and research projects aimed at strengthening patient-orientated research. The Centre should seek to increase the participation of foundations, pharmaceutical companies, health insurance firms and the managed care industry in the clinical training enterprise.

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In **Chapter 8** we ask how much developing countries should be **spending** on medical and particularly clinical research. Specifically, we look at how

much the South African Government spends on research and development (R&D), and of this, how much is spent on medical, and specifically clinical, research. How are funding priorities determined? Through which institutions is government funding allocated? What are the other sources of funding?

We believe that 2% of the gross domestic product (GDP) of developing countries is a necessary minimum investment in indigenous science and technology development, with health research receiving at least 20% of that amount.

South Africa is spending more on R&D than before, but this is still less than 1% of GDP. The largest part is spent on engineering and technological sciences, and on the natural sciences (40% of total R&D expenditure; about 20% each), while expenditure on the health sciences is 15% of the total (about 0.15% of GDP). The government spends a large amount on services in the public health sector (about 10% of all state expenditure), but much too little of this money is spent on health research, which is also poorly coordinated and inadequately documented. Clinical trial expenditure by industry is not included in this figure. Most of the current funding for health research comes from donors outside the country and the pharmaceutical industry. More than half of the total expenditure on clinical research is done by the private (business) sector.

We encourage the DoH to enable the National Health Research Committee, or a similar body, to perform the key functions of creating an enabling environment to conduct research in South Africa; building better relationships between scientists and clinicians and between clinician-researchers and policy-makers; promoting clinical research in South Africa; communicating between the research community, National Treasury and the various national departments; ensuring that institutions provide technical and managerial support services to all their researchers; and improving regulatory procedures. A non-politicised *modus operandi* would provide the best results.

We believe there has to be more effective tracking and monitoring of funding streams for clinical research and substantially increased public funding of clinical research, applied in such a way that national health priorities are more

effectively addressed than is currently the case. The DoH should apportion 2% of its allocation to health research.

Regional clinical research centres/hubs should be established, each with clinical and preclinical expertise and facilities.

We believe that the policies and operational plans of various participants such as the DoH, and the Departments of Higher Education and Training, Science and Technology and Trade and Industry, the NHLS, the MRC and the provincial health departments should be more effectively coordinated, facilitated by the new Ministry of Coordination and Planning.

A 'National Joint Agreement' should be formed between universities and departments of health and education, which should systematically provide a 'research platform' alongside the clinical and teaching platforms of the Academic Health Complexes, as envisaged in the National Health Act of 2003.

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In **Chapter 9** we look at the existing **institutional arrangements** for specific investments in clinical research in South Africa, and ask what kinds of interaction are needed between government, parastatal institutions, academia and industry to revitalise clinical research.

We believe South Africa could and should be recognised internationally as a centre of excellence for clinical trials that could attract more investment in trials. This would ensure retention of skilled scientists, sustain the ability of medical research facilities at universities or research institutions to continue to conduct basic research and novel medicinal research, and attract foreign direct investment to the benefit of the South African economy.

The present Medicines Control Council's (MCC's) Clinical Trials Committee performs a review function on all clinical trials. This process, which has improved recently after its legislated change into a Regulatory Authority (RA), is still experiencing serious problems, including approval delays, variation in reviewer quality and inadequate supervision of trials.

We recommend that the new RA should rigorously meet its newly set statutory requirements to ensure that any medicines used in the country are safe and effective. The authority should rely on sound ethics review.

An increase in the number of clinical trials conducted in South Africa (with recognition of South Africa as a 'centre of excellence' for conducting such studies) would require agreement on a reasonable time-to-approval for clinical trial applications (e.g. a reduction of approval time to less than eight weeks), efficient processing of all applications with clearly understood requirements, and regular dialogue between the new South African Health (products) Regulatory Authority and all role-players. The regulatory process for approval of clinical trials could be expedited in a number of ways. For example, after auditing, standardisation and accreditation of RECs by the National Health Research Ethics Council (the NHREC), a system could be envisaged in which RECs approve or reject clinical trials and simply notify the RA of the clinical trials concerned. In addition, once an application to conduct a clinical trial had been submitted to the RA, the company or institution could proceed with the trial if a no objection letter is received from the RA within a specified time frame. Where application has been made for the registration of an identical product under another trade name for strategic marketing reasons, only one 'Master Dossier' could be submitted and reviewed. There could be recognition of prior approvals in selected countries. To make these measures work, the RA could require local RECs to conduct ongoing audits of studies they have approved.

The implementation of the Intellectual Property Rights for Publicly Financed R&D Act, *Act 51 of 2008*, needs to be carefully aligned with the ethical-regulatory framework to maximise benefits in both sectors and to prevent them from impeding the proper functioning of the other.

* * *

In **Chapter 10** we ask what kinds of interventions have been used successfully **elsewhere in the world** to address the kinds of challenges South African clinical research is facing.

We find that although health research, and especially clinical research, is acknowledged as indispensable for improving health, promoting equity and stimulating development, it tends inexplicably to be neglected in sub-Saharan Africa in terms of planning, status and funding. Much attention has been paid to promoting clinical research in the North, in the face of challenges similar to those afflicting the South, so it is possible that solutions already found elsewhere could also be applied here. These include maintaining the supply of skilled clinical researchers, improving facilities for clinical research, increasing funding and strengthening translational research.

We believe that government commitment and partnership is needed to revitalise clinical research. The government of Singapore, for example, invests in clinical research to translate the biomedical research emanating from its highly competitive research institutes into clinical applications; to inculcate a knowledge- and evidence-based approach to health care; and to retain the highest level of medical talent in the public hospitals.

There must be a closely cooperative and mutually trusting relationship between researchers and health policy-makers and implementers. The National Health Service (NHS) in the UK, the Department of Health and Social Services in the US (through the National Institutes of Health [NIH]), and the Ministry of Health in Singapore all engage in partnership with the research community through numerous channels and at numerous levels to support clinical research.

Efforts should be targeted at building indigenous research capacity. Singapore has a definite career path for clinician-researchers, and promotes and rewards performance in clinical research through special awards for research excellence.

High-profile advocates are required to promote clinical research. One example of an advocacy body is the Initiative to Strengthen Health Research Capacity in Africa (ISHReCA), bringing together health researchers in Africa to promote the creation of self-sustaining pools of excellence capable of initiating and carrying out high-quality health research in Africa.

Better strategic planning and coordination for health research is required. An example of such an initiative is the Health Research Capacity Strengthening Initiative partnerships in Kenya and Malawi.

* * *

In **Chapter 11**, the final chapter, we list what we consider to be the **barriers to revitalising clinical research in South Africa**:

1. Inadequate public engagement with clinical research

- Government does not promote clinical research sufficiently in the public domain;
- Researchers do not engage sufficiently with issues of importance to research participants and policy-makers.

2. Lack of research planning, regulation and coordination

- Lack of a coordinated national plan to balance excellence on the world stage (i.e. quality and impact) with relevance to local problems;
- An inefficient regulatory framework for clinical trials and registration of new medicines is hindering the conduct of innovative clinical trials.

3. Inadequate capacity for clinical research (human resources and infrastructure)

- Poor teaching of and matriculation rates in mathematics and science in schools;
- Lack of appropriately trained clinical scientists and career structure to support them (i.e. 'frozen demographics' of ageing white male clinical scientists with too few young, black and woman researchers);
- Lack of appropriate facilities and infrastructure (i.e. virtual absence of dedicated clinical research centres).

4. Lack of adequate and appropriate funding

- Inadequate funding for clinical trials and other types of clinical research (e.g. the MRC project grant has an upper limit of R130 000 p.a.);
- The cost-recovery regimen of the provincial departments of health and the National Health Laboratory Service (NHLS) prohibits investigator-driven, non-industry clinical research in academic health complexes.

5. Absence of monitoring and evaluation

- No monitoring of adherence to standards and performance of individual researchers, academic institutions, research councils, government departments, the health industry and other funders of research.

We now list the proposed synergistic solutions:

1. National Strategic Planning, Regulation and Coordination of Clinical Research:

- We propose the formation of a 'South African Clinical Research Coordinating Centre' at the MRC, with maximum possible operational independence, to serve as an advocacy group and a partnership of organisations working to establish South Africa as a world leader in clinical research by harnessing the power of all stakeholders, including universities, government departments, the NHLS, the health industry and research councils;
- The proposed Coordinating Centre should engage with a re-energised National Health Research Committee on how optimal planning, regulation and coordination of clinical research may be achieved, in consultation with the Departments of Health, Higher Education, Science and Technology, and Trade and Industry;
- The proposed Coordinating Centre should interact with the newly established National Planning Unit in the Presidency on the planning needs of clinical and health research;

- The proposed Coordinating Centre should seek to play an advisory role to the proposed Medicines Regulatory Authority (MRA; successor to the Medicines Control Council) and the National Ethics Committee in order to deal with the regulatory environment and ethical oversight for clinical trials and health research in general;
- The proposed Coordinating Centre should ensure the alignment of the clinical and health research effort with the principles of Essential National Health Research and other policies of the government;
- The proposed Coordination Centre should oversee the implementation of the Intellectual Property Rights Act and ensure that it results in a proper alignment between the ethical-regulatory regimens and the protection of new intellectual property in the clinical domain.

2. Human and Infrastructural Capacity:

- A 'National Clinical Scholars' Programme as part of the Ten-Year Plan for Innovation of the DST;
- A target of 500 PhDs to be produced in clinical health sciences over the next ten years as part of the plan by the DST to increase the graduation rate of PhDs in general to 6 000 per year between 2008 and 2018, plus a target of 150 postdoctoral fellows per annum working in South African clinical research environments;
- A target of 30 research chairs in clinical research areas to help tackle the 'Farmer to Pharma' Grand Challenge and other strategic areas.

3. The creation of clinical research centres and research institutes as national hubs in the academic health complexes and other sites:

- Develop a National Joint Agreement between universities and the Departments of Health, Education and Science and Technology in order to provide a 'research platform' alongside the clinical and teaching platforms in the academic health complexes and other sites;
- Create a 'National Clinical Research Training Coordinating Initiative' to link and coordinate clinical research training at universities,

research councils, government and industry. This initiative will serve as a warehouse of education and training opportunities (i.e. projects, funding, courses, degrees), and a meeting place for supervisors and potential students at a national level;

- Establish large-scale research institutes where opportunities for high-level collaborative clinical studies exist, and a critical mass of principal investigators, postdoctoral fellows, graduate students and research assistants can be assembled.
- Establish attractive, high-capacity training programmes for undergraduate and postgraduate students in the clinical health sciences, as well as for junior faculty in clinical research, as part of the human capital generation project of the DST's Ten-Year Plan for Innovation;
- Fund learnerships for graduates in the research facilities of large multinational companies;
- Foster a clinical-plus-research academic career track (lectureships and professorships) in all clinical disciplines in South African institutions;
- Develop and support a network of skilled mentors who can lead the development of young clinical researchers.

4. National Funding Scheme for Clinical and Health Research:

- Raise the national R&D budget to 2% of the GDP, of which 20% should be allocated to health research (DST);
- Implement the Mexico declaration commitment by the national DoH to spend 2% of the national health budget on research and development, and amend the Research and Development Tax Incentives Policy to encourage innovative R&D in South Africa by removing the specific exclusion of clinical trials (DTI);
- Incentivise the health care industry (pharmaceuticals and private hospitals) to spend 2% of its turnover on R&D (pharmaceutical manufacturers and others);

- Follow up on the recently implemented Clinical Training Enhancement Initiative with a well-aligned approach to clinical research training.

5. Monitoring and Evaluation of the Clinical and Health Research Enterprise:

- Evaluation of the performance of the clinical research enterprise in South Africa, possibly under the aegis of the Academy of Science of South Africa, by reviewing the implementation of the recommendations of this report at five-yearly intervals;
- Monitoring by the National Health Research Committee of the efficiency of the research spend of the MRC and other statutory bodies entrusted with publicly funded health research;
- Monitoring by the new Monitoring and Evaluation Unit in the Presidency of government's ability to meet the target of spending 2% of GDP on R&D, and 2% of the health budget on health research.

MEMBERS OF THE STUDY PANEL

Professor BONGANI M MAYOSI, BMedSci, MB ChB, FCP SA, DPhil, FESC, FACC, FRCP, MASSAf (CHAIRPERSON)

Professor AMABOO (AMES) DHAI, MB ChB, FCOG, LL.M., PGDipIntResEthics

Professor DANIEL NCAYIYANA, MD, FACOG, FCM, MASSAf

Professor GREGORY HUSSEY, MB ChB, MMed, MSc, DTM&H, FFCH, MASSAf

Professor JAGIDESA (JACK) MOODLEY, MB ChB, FCOG, FRCOG, MD

Professor JIMMY VOLMINK, BSc, MB ChB, DCH, MPH, DPhil, MASSAf

Professor LETTICIA MOJA, MB ChB, MMed (O&G), MBA

Ms MAUREEN KIRKMAN, BSc (Pharm)

Dr NANDI SIEGFRIED, MB ChB, MPH (Hons), FCPHM, DPhil

Dr NONHLANHLA MADELA-MNTLA, BCur, MCur, DCur, Cert. in Advanced Health Management, Diploma in Health Outcomes Research

Professor PETER FOLB, MB ChB, MD, FCP SA, FRCP Lond, FRSSAf, MASSAf

Professor WIELAND GEVERS, MB ChB, MA, DPhil, DSc *honoris causa*, FCP SA *ad eundem*, MASSAf, FTWAS

Professor WILLIAM PICK, MB ChB, MMed, FFCH (CM), MFGP, DPH, DTM&H, MASSAf

ABOUT THE ACADEMY OF SCIENCE OF SOUTH AFRICA

The Academy of Science of South Africa (ASSAf) was inaugurated in May 1996 in the presence of **then President Nelson Mandela, the patron of the launch of the Academy**. It was formed in response to the need for an academy of science consonant with the dawn of democracy in South Africa: activist in its mission of using science for the benefit of society, with a mandate encompassing all fields of scientific enquiry in a seamless way, and including in its ranks the full diversity of South Africa's distinguished scientists. The South African Parliament subsequently passed the **Academy of Science of South Africa Act, Act 67 of 2001**, which came into effect on 15 May 2002. ASSAf is thus the official national Academy of Science of South Africa, recognised by Government and representing South Africa in the international community of science academies.

Internationally recognised science academies are similar in that they are:

- **self-perpetuating**, with a merit-based membership that creates an upward aspiration for quality and excellence in scientific endeavours;
- **multidisciplinary**, striving to represent science as a continuum of knowledge, insight and practical solutions;
- **independent of government**, but can be funded by government for performing certain tasks;
- a **credible voice of science** to be heard on topics of national concern, independent of institutional or commercial linkages, obligations and agendas;
- linked together in an **independent global community** that can mobilise scientific thinking, skills and knowledge across the world.

ASSAf places particular emphasis on **excellence in the application of scientific thinking to the problems and challenges facing South African society**. It draws its membership from all population groups and from all scientific disciplines.

OBJECTIVES

Scientific thinking for the good of society

According to the Act, the **objectives of the Academy** are to:

- promote common ground in scientific thinking across all disciplines, for example the physical, mathematical, life, human, social and economic sciences;
- encourage and promote innovative and independent scientific thinking;
- promote the optimum development of the intellectual capacity of all people;
- provide effective advice and facilitate appropriate action in relation to the collective needs, opportunities and challenges of all South Africans;
- link South Africa with scientific communities at the highest levels, in particular within Africa, and further afield.

VISION

An engine of excellence in scholarship and intellectual cooperation

ASSAf aspires to be the apex organisation for science and scholarship in South Africa, internationally respected and connected, its membership simultaneously the aspiration of the country's most active scholars in all fields of scientific enquiry, and the collective resource making possible the professionally managed generation of evidence-based solutions to national problems.

MISSION STATEMENT

Clarifying the niche of the Academy

Like democratic South Africa in general, ASSAf aspires to play both a national and an international role, particularly with respect to the African continent. We see the Academy as being usefully at arm's length from government and other organised sections of the state, comprising an assembly of excellent scholars from many disciplines who are well networked both nationally and internationally, and have shown their interest in and capacity for promoting the development of a prosperous and fully enabled society. Membership of the Academy (by election) is both an honour and an obligation to work individually and collectively (as the Academy) to ensure that decision-making requiring scholarly scrutiny and analysis is based on the best and most integrated understanding and insights available to the country. The academicians thus represent an organised, independent but responsive scholarly voice to help guide the development of the country and its people.

The mission of ASSAf is thus to:

- become increasingly associated in the mind of the nation with the highest levels of scholarly achievement and excellence in the application of scientific thinking for the benefit of society;
- consolidate its infrastructure and capacity, and to expand and mobilise the membership to ensure that scholars from a full disciplinary spectrum are available for its work, and that these are indeed both thinkers and doers, willing to put significant effort into the Academy's activities;
- embark on a programme of systematic studies of evidence-based issues of national importance, some proposed by government or other sectors, and some identified by the Academy itself;
- develop a sound and robust methodology for constituting consensus study panels, organising their work, including conferences and workshops, and producing authoritative reports that are well-disseminated and have significant impact;

- alternatively, constitute committees to oversee the Academy's work in broad areas of focus, usually expressed by the holding of national forums on particular key issues, leading to forum reports that have a significant impact on policy and practise;
- publish science-focused periodicals, especially a multidisciplinary journal of high quality (the *South African Journal of Science*) and a science magazine that will showcase the best of South African research to a wide national (and international) audience (*Quest – Science for South Africa*); and to promote the development in South Africa of an indigenous system of research journals of internationally recognised quality and usefulness;
- develop productive partnerships with other organisations, especially (but not only) the National Departments of Science and Technology, Education, Health and Agriculture; the National Advisory Council on Innovation; science councils; higher education institutions, etc., with a view to the building of capacity in science and its applications within the National System of Innovation (NSI);
- create new and diversified sources of funding for the sustainable functioning of an independent Academy;
- communicate effectively with the general and specific public, as well as with partners and sponsors;
- develop a plan for the expansion of the activities of ASSAf in partnership with the national science academies of other countries, including contracted partnership with the US National Academies;
- play a significant role in the international science system, particularly in Africa, through organisations such as the InterAcademy Panel (IAP) and the InterAcademy Council (IAC), the Academy of Sciences of the Developing World (TWAS), the International Council on Science (ICSU), as well as the Network of African Science Academies (NASAC), all in the context of the New Partnership for Africa's Development (NEPAD).

MEMBERS

Core asset of the Academy (each styled 'MASSAf')

After nomination by four existing Members (at least two of whom do so from personal knowledge of the candidate), new Members of the Academy are elected in a secret ballot. The normal criterion for election is significant achievement in the advancement or application of science, and, in addition, Members should be persons who can be expected significantly to assist the Academy in achieving its objectives. By October 2006, ASSAf had over 250 Members drawn by self-categorisation from the earth, economic, life, mathematical, physical, social, technological, education and agricultural sciences as well as the humanities.

COUNCIL

Steering Academy activities and taking responsibility

The affairs of the Academy are governed by a Council comprising 12 members, each of whom holds office for four years. This Council is elected by the Members every two years. For the sake of continuity, six Members continue to serve a further term, while six new Members are elected once they have been nominated according to the constitutional mechanism. To provide a better balance of race, gender or disciplinary area, the Council can co-opt additional Members from persons who were nominated for election to the Council.

The office-bearers are the President, two Vice-Presidents, a General Secretary and a Treasurer. Committees can be formed in order to carry out specific functions, but each must be chaired by a Member of the Academy or, preferably, of its Council. Reports drawn up by its committees or ad hoc task groups are approved by the Council before entering the public domain.

INTERNATIONAL CONNECTIONS

Crucial catalyst for Academy-type activities

ASSAf is an active member of the IAP (InterAcademy Panel on International Issues), a growing organisation that embraces the national science academies of over 90 countries. The Academy of Sciences for the Developing World now has an office in Africa based in Nairobi, and the Network of African Science Academies, of which the President of ASSAf is a Vice-President, is also located in that city. ASSAf became an 'intense partner' of the US National Academies (together with the Nigerian and Ugandan Academies of Science) as part of the African Science Academy Development Initiative (ASADI), receiving a substantial five-year grant to build its capacity for generating evidence-based advice for the government and the nation in general.

STRATEGIC PLAN AND POLICY DEVELOPMENT

The way to go

ASSAf has developed a comprehensive strategic plan following a thorough process for identification of its strengths, weaknesses, opportunities and threats. Through its governing Council, the Academy has developed policies and guidelines for its activities. The initiation of the ASADI partnership with the US National Academies prompted the generation, proposal and adoption of the following items:

- Guidelines for proposals of science-based topics in terms of the ASSAf Act;
- Guidelines for proposals of science-based topics (project proposals);
- Guidelines for the appointment of consensus study panels and forum steering committees;
- Policy on conferences;
- Formation of a forum steering Committee on Science for Poverty Alleviation (first example of an ASSAf 'Board');

- Panel for the Consensus Study on Nutritional Influences on Human Immunity, with special reference to clinical tuberculosis and HIV infection (first ASSAf consensus study).

ASSAf's strategic plan and the Academy's policies and guidelines are publicly featured on the ASSAf website at <http://www.assaf.org.za>

RESEARCH PUBLISHING

The core of the quality assurance system for the dissemination of research findings

The Academy of Science of South Africa signed a contract in 2001 with the DST for various activities in connection with the strategic management of research journals published in South Africa. The first component was a comprehensive study of the present and best-possible future role of research journals published in South Africa, now completed through the release of a full report in March 2006, with evidence-based recommendations, and a range of follow-up project integration and implementation strategies.

SAJS

Publishing the *South African Journal of Science*

The *South African Journal of Science* is the leading multidisciplinary research journal in Africa, and features a great diversity of original work by researchers throughout the country and abroad, concentrating on articles that have an appeal that is wider than that of single disciplines. Among the highlights of the volume published in 2005 were articles featuring the research at historically black universities supported by the Royal Society-NRF bilateral programme. The journal appears six times a year, and is accessible online as one of the e-publications managed by Sabinet.

QUEST

Publishing *Quest*: A quarterly magazine of high quality, presenting science for South Africa

The Academy publishes the national science magazine *Quest: Science for South Africa* which was launched in 2004. *Quest* serves as a platform for communication about scientific research done in South Africa. It strives to showcase South African science in action, and is aimed at the broad scientific community, decision makers, the public, students, and especially the senior grades at secondary schools.



Academy of Science of South Africa
1st Floor Block A, The Woods, 41 De Havilland Crescent, Perseus Park

PO Box 72135, Lynnwood Ridge 0040, Pretoria, South Africa
Tel: +27 (0)12 349 6600, Fax: +27 (0)12 349 5461
www.assaf.org.za
