

## Nanotechnology Institutions contribution

Admire Dube\* and Naushaad Ebrahim

# The nanomedicine landscape of South Africa

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**Abstract:** Nanomedicine is one of the most exciting applications of nanotechnology and promises to address several of mankind's healthcare needs. South Africa is one of the countries engaged in nanomedicine research and product development on the African continent. In this article, we provide a top-level description of the policy, infrastructure, and human capital development programs supported by the South African government. We also highlight the nanomedicine outputs (publications, patents, and products) that have emanated from South Africa. This description of a “newly industrialized” country engagement in nanomedicine is important within the global context of nanomedicine development.

**Keywords:** nanomedicine; nanoparticle drug delivery; nanotechnology in South Africa; nanotechnology policy.

## 1 Introduction

Nanotechnology is recognized as one of the most important scientific fields of the 21st century. Nanotechnology is the application of engineered structures in the nanometer-scale size range (often 100 nm or smaller, but also 1–1000 nm), which possess desirable properties, e.g. magnetic, optical, biochemical, or electronic properties, and are generally applied to the benefit of mankind. Nanomedicine is the application of nanotechnology in the field of health and has demonstrated capability to improve the diagnosis and treatment of diseases by providing novel disease biosensors and improved drug delivery [1, 2]. Nanomedicine is a multi-disciplinary field, encompassing pharmaceutical and biomedical sciences, medicine, and physical sciences, and is a field of intense global research and product development [3]. To illustrate the extensive ongoing product

development, a study by Bobo et al. reported that there are currently 51 US Food and Drug Administration (FDA)-approved nanomedicines, 77 products undergoing clinical trials, and approximately 40% of clinical trials were listed in the clinicaltrials.gov database in 2014 or 2015 [4].

On the African continent, South Africa is one of the countries engaged in nanomedicine research and product development. South Africa is part of the five major emerging economies or newly industrialized countries, together with Brazil, Russia, India, and China. The South African government has made extensive investment toward creating a critical mass of infrastructure, equipment, and human capital for nanotechnology research [5, 6]. In this article, we provide a top-level overview of the nanotechnology policy, funding, equipment, and human capital development programs supported by the South African government. We also highlight the nanomedicine outputs (publications, patents, and products) that have emanated from South Africa. This description of a “newly industrialized” country engagement in nanomedicine is important within the global context of nanomedicine development [7–9]. Finally, we provide our opinion of future strategies to leverage existing framework and investment to support translation of nanomedicine research findings for commercial and public benefit.

## 2 The South African disease landscape

To contextualize nanomedicine research in South Africa, it is important to describe the disease landscape. Africa, in particular Sub-Saharan Africa, is disproportionately challenged by a burden of infectious diseases (IDs) including tuberculosis (TB) and HIV/AIDS, which negatively impact its economy and the quality of life of African people [10, 11]. The burden of TB in South Africa is among the highest in the world. Total TB incidence (TB alone plus TB-HIV co-infection) in South Africa is estimated to be 834 per 100,000 population; and the mortality rate is unacceptably high at 133 per 100,000 population [12]. TB that is resistant to existing drug therapies, i.e. multi-drug resistant TB, is on the rise globally, more so in South Africa, which is ranked among the high burden countries [12]. A large number of people are living with HIV in South

\*Corresponding author: Admire Dube, Nanomedicine Research Group, School of Pharmacy, University of the Western Cape, Bellville, South Africa, e-mail: adube@uwc.ac.za.  
<http://orcid.org/0000-0002-5684-6094>

Naushaad Ebrahim: Nanomedicine Research Group, School of Pharmacy, University of the Western Cape, Bellville, South Africa

Africa, and the country has the largest number of people on treatment in the world (approximately 3.4 million people on treatment) [13].

In recent times, a new threat has emerged in the form of non-communicable diseases (NCDs), i.e. cardiovascular disease, cancer, chronic respiratory disease, and diabetes. In Africa, the probability of a person dying from one of the four main NCDs (in persons aged between 30 and 70 years) is over 20%, among the highest in the world [14]. Mortality due to NCDs is also high in South Africa [14].

Despite technological advances in medical diagnosis and treatment, deaths due to IDs and NCDs are still common. Among the current requirements to mitigate deaths is the need for more simple, inexpensive, rapid, and sensitive point-of-care diagnostic tools, and drug therapies providing uncomplicated treatment regimens (e.g. short-duration oral treatments, once daily to weekly dosing intervals) reduced toxicity and side effects [15, 16]. Nanomedicine has the potential to provide solutions to these needs, enabling improved disease detection and delivery of drugs. The reader is directed to some reviews on the application of nanoparticles in diagnostics and drug delivery [17, 18]. It is against the backdrop of disease burden and the promise of nanomedicine that researchers in South Africa, with the support of the government, have embarked in research and product development in this field.

### 3 South African nanotechnology policy and funding framework

National strategic leadership in nanotechnology is provided by the Department of Science and Technology (DST) ([www.dst.gov.za](http://www.dst.gov.za)) and is described in National Nanotechnology Strategy (NNS) (<http://www.gov.za/documents/national-nanotechnology-strategy>) published in 2005. The publication of this strategy essentially heralded the start of public funding in nanotechnology, with an investment of ZAR170 million (approximately USD 12.2 million at an exchange rate of 1 USD = 14 ZAR) over the first 3 years. The NNS is aligned to the broad development goals of South Africa and compliments other national strategies, in particular, the Advanced Manufacturing Technology Strategy, as well as the Biotechnology Strategy and the Skills Development Strategy. The strategy emphasizes nanotechnology research and development, i.e. material synthesis, characterization, and fabrication. Health (nanomedicine) is among the focus areas of the strategy. The key initiatives of the NNS include establishment and

support of nanoscience characterization centers, funding for research, and human resource development. Complementary to the NNS is the Nanoscience and Nanotechnology 10-year Research Plan (<http://www.gov.za/documents/nanoscience-and-nanotechnology-10-year-research-plan>), which was released by the DST in 2010, whose main purpose is to focus national research efforts to deliver on the goals of the NNS. Key research questions within the nanomedicine scope of the research plan include development of nanotechnology-based rapid, simple, and user-friendly point-of-care diagnostic kits for HIV and TB, nano-biosensors for *in situ* detection of glucose levels, and the development of nanoparticle-based drug delivery systems for TB treatment.

### 4 National nanotechnology infrastructure

Public funding has facilitated the acquisition of nanotechnology-specific equipment for various research councils and universities, through the National Nanotechnology Equipment Programme (NNEP) (<http://hicd.nrf.ac.za/?q=node/19>). The NNEP was a specific funding instrument as part of the implementation of the NNS, intended to acquire, upgrade, or develop research equipment for the analysis and characterization of nanomaterials in South Africa. The NNEP ended in 2015, after a 10-year investment and over ZAR400 million (over USD 28.6 million using an exchange rate of 1 USD = 14 ZAR) invested. This amount excludes funding provided by other equipment programs, e.g. the National Equipment Program, which also provide for purchase of equipment used for nanotechnology research. Table 1 summarizes the key national facilities for nanotechnology research in South Africa and some of the equipment and instruments available at the facilities.

### 5 Human capital development

By and large, nanotechnology education (including nanomedicine) is provided at postgraduate level [6, 19]. The flagship program in nanoscience and nanotechnology education is the DST-funded 2-year Master's degree program leading to an MSc Nanoscience qualification. This program is offered through collaboration between the University of the Western Cape (the program-managing institution), University of Johannesburg, University

**Table 1:** List of the key national nanotechnology facilities in South Africa.

Facility name and location	Equipment
Centre for Nanotechnology Innovation Rhodes University, Grahamstown <a href="https://www.ru.ac.za/nanotechnology/equipment/">https://www.ru.ac.za/nanotechnology/equipment/</a>	TOF-SIMS
Microscopy Centre for High Resolution Transmission Electron Nelson Mandela Metropolitan University, Port Elizabeth <a href="http://chrtem.nmmu.ac.za/">http://chrtem.nmmu.ac.za/</a>	ARM-TEM, STEM, FIB-SEM, AFM and nanoindenter
National Centre for Nano-Structured Materials Nelson Mandela Metropolitan University, Port Elizabeth <a href="http://chrtem.nmmu.ac.za/">http://chrtem.nmmu.ac.za/</a>	FIB-SEM, small- and wide-angle X-ray scattering, AFM, TEM, SEM
National Cleanroom Facility DST-Mintek Nanotechnology Innovation Centre (NIC) <sup>a</sup> , Pretoria <a href="http://www.nic.ac.za/">http://www.nic.ac.za/</a>	Clean room, TEM, SEM, AFM

Selected key pieces of equipment available at a facility are listed.

ARM, atomic resolution microscope; SEM, scanning electron microscope; TEM, transmission electronic microscope; STEM, scanning transmission electron microscopy; FIB, focused ion beam; AFM, atomic force microscope; TOF-SIMS, time of flight-secondary-ion mass-spectrometer.

<sup>a</sup>NIC composed of research nodes located at three universities, i.e. Rhodes University (focused on the development of sensor technologies), the University of the Western Cape on bio-labeling and drug delivery and the University of Johannesburg (focused on water treatment).

of the Free State, and Nelson Mandela Metropolitan University. Students undergo 9 months of didactic learning, followed with a research project completed at any one of the participating universities, under the stream of either nanochemistry, nanophysics, or nanomedicine. In 2006, the DST and the National Research Foundation (NRF) established the South African Research Chairs Initiative (SARChi) (<http://www.nrf.ac.za/division/rcce/instruments/research-chairs>). The major expectation of SARChi grant recipients is the production of high-quality post-graduate students and research and innovation outputs. To date, there are seven research chairs in nanotechnology (with at least one chair focusing on nanomedicine).

## 6 Nanomedicine research in South Africa

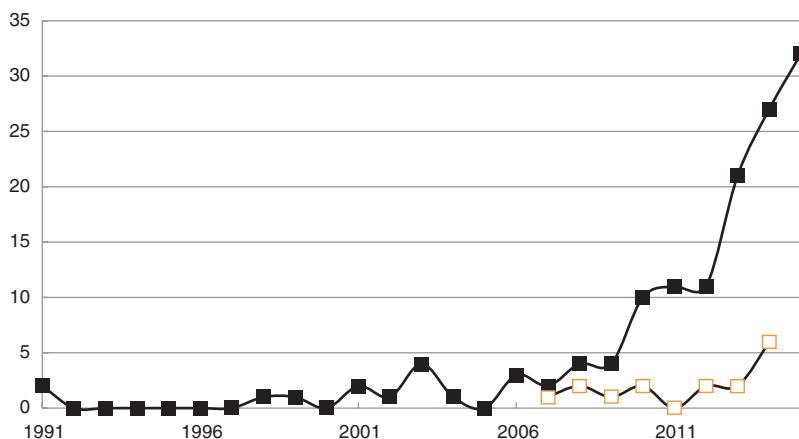
### 6.1 Drug delivery

We performed a review of publications emanating from South Africa in the field of nanomedicine. We conducted a search on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed>) using a Boolean search string, which included the keywords nanoparticle or liposome, drug, protein and gene delivery, and included an author/co-author based at a South African institution. PubMed was selected as it is one of the largest archives of biomedical literature and

also conducts a review of scientific quality of journals prior to indexing. Therefore, we have some indication of the level of quality of the publications captured by our search.

We retrieved 137 eligible articles (published up to December 2015), with the earliest article published in 1991. Analysis of the number of articles per year is shown in Figure 1. In the past decade, a surge in nanoparticle drug delivery publications has been observed. This trend could be related to the availability of nanotechnology funding through the NNS and the NNEP. Of the articles published during this period, 46% was in the ID space, with the rest being related to NCDs, or not focused to a particular disease, e.g. general nanomedicine reviews. This statistic reflects the balance of the disease landscape in Africa. All articles retrieved were preclinical studies, except for two clinical studies, although it should be noted that these clinical studies involved evaluation of the efficacy and safety of commercially available nanomedicine products and were not a clinical evaluation of nanomedicines developed by the researchers [20, 21].

Publications emanated primarily from 14 higher education institutions and science councils, i.e. the University of KwaZulu-Natal, University of the Witwatersrand, Stellenbosch University, CSIR, University of Pretoria, University of Cape Town, Rhodes University, University of the Western Cape, Tshwane University of Technology, North-West University, University of Zululand, Nelson Mandela Metropolitan University, South African Nuclear Energy Corporation, and MINTEK. Higher education institutions



**Figure 1:** Nanomedicine publications emanating or including a South African institution up to December 2015. The source of the publications is PubMed, and publications were retrieved based on key words outlined in the text. (■) indicates drug delivery articles, and (□) indicates articles in the nanoparticle diagnostics space. No eligible research articles in nanoparticle-based diagnostics, on PubMed, meeting the inclusion criteria were identified for 2015 and, therefore, are not shown.

and science councils are also the focus of the NNS. We retrieved three patents that relate to nanoparticle drug delivery systems [22–24] by applying similar search criteria (as used in PubMed) using the search site Google patents.

It is notable that MINTEK has commercialized its research outputs and markets gold, nanospheres, and nanorods, including polyethylene glycol (PEG)-gold nanoparticles and PEG-Biotin-gold nanoparticles to the research community and industry (<http://www.nic.ac.za/products.html>).

## 6.2 Diagnostics

We performed a search on PubMed of articles reporting research into diagnostics for diseases, which incorporate nanoparticles. Fogel and Limson performed an excellent review of general biosensor research in South Africa [25], and the reader is also directed to this review. Our search string included the words surface plasmon resonance, lateral flow, sensors, biosensors and cantilever/nanocantilever, disease, as applied by Wagner et al. [1]. The search resulted in 15 articles meeting the criteria. Most articles were published in 2014 (6) (Figure 1) with the first PubMed-identified article published in 2007. An equal distribution of publications was found when comparing research for IDs versus NCDs (7), with one article including both. These publications emanated mainly from six academic institutions and science councils, namely, University of Johannesburg, University of Pretoria, University of the Western Cape, University of the Free State, University of the Witwatersrand and Nanotechnology Innovation

Centre, Advanced Materials Division, MINTEK. At this time, no research outputs have been commercialized.

## 7 Concluding remarks

Over the past 10 years, the South African government has laid a strong foundation for research and product development in nanotechnology, establishing policy framework and making significant investments in equipment and infrastructure, research funding, and human capital development at universities and science councils throughout the country. The reader is directed to further reviews of the education and nanotechnology (in general) research activities in South Africa [6, 19, 26].

Moving forward, we believe the foundation laid is sufficient to enable increased research outputs, and their translation to the clinic, to benefit South Africans and the global community. However, to accelerate progress, the government and other stakeholders may need to consider nanomedicine-specific program initiatives. Such initiatives could include nanomedicine-specific funding opportunities and development of nanomedicine centers of excellence having a critical mass of experienced researchers, postgraduate students, and requisite in-house equipment. An example of such an approach can be drawn from the current eight Nanomedicine Development Centers in the US, funded by the National Institutes of Health (<https://commonfund.nih.gov/nanomedicine/index>). Postgraduate teaching and research programs under such an initiative could focus more toward developmental/translational aspects of the technology.



Technical difficulties experienced in the nanomedicine space in South Africa include limited intra-country collaboration and the absence of structured network channels between various institutions. One way to facilitate collaboration and greater investment in the field is to create an online interactive geographic map of nanotechnology activities in South Africa, such as the one produced in Germany (<http://www.nano-map.de/>). Such a map can provide current information including research and commercialization projects at the various universities and science councils, nanotechnology infrastructure and equipment available, and details of funding bodies and industry partners. Enhanced coordination has obvious benefits. A pitfall to avoid is the funding of a broad portfolio of nanomedicine projects, as this may miss the requisite concentration on important topics and research questions needed to advance the national agenda [27]. Borrowing from global best practices, South Africa could establish a technology platform to advance nanomedicine, similar to European Technology Platform for Nanomedicine (ETPN) (<http://www.etp-nanomedicine.eu/public>). Such a platform could also be established at continental level. With respect to the industry's involvement, it is not only an issue of resource support and collaborative research, but it would be critical to also ensure employment opportunities for the nanomedicine graduates.

In summary, the future of nanomedicine in South Africa looks bright given the foundation established by the government, and with greater coordination, more products are likely to be produced to the benefit of the public.

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## Bionotes



### Admire Dube

Nanomedicine Research Group, School of Pharmacy, University of the Western Cape, Bellville, South Africa.

<http://orcid.org/0000-0002-5684-6094>

[adube@uwc.ac.za](mailto:adube@uwc.ac.za)

Admire Dube is a pharmaceutical scientist and Senior Lecturer in Pharmaceutics at the School of Pharmacy, University of the Western Cape (UWC) in Cape Town South Africa. He previously held a position as Senior Researcher at the Council for Scientific and Industrial Research in Pretoria South Africa where he was involved in commercializing nanomedicines for malaria and tuberculosis treatment. At UWC, his research group focuses on developing immune-modulatory nanomedicines for treatment of infectious diseases. He holds a PhD in Pharmaceutical Sciences from Monash University, Australia, and Post-doctoral training in nanomedicine from the University at Buffalo, USA. He has an interest in seeing Africa commercialize its first nanomedicine, as well as enhancing pharmaceutical production in Africa.



### Naushaad Ebrahim

Nanomedicine Research Group, School of Pharmacy, University of the Western Cape, Bellville, South Africa

Naushaad Ebrahim obtained his Bachelor of Pharmacy degree at the University of the Western Cape (UWC), South Africa, and a PhD at the same institution. He is a Pharmacist by training. Dr. Ebrahim is currently a Senior lecturer in the Discipline of Pharmaceutics and a Deputy Director at the School of Pharmacy at UWC, where he has served as an academic for the last 15 years. His research field is in nanomedicine focusing on liposomal and phytosomal carrier systems, which include the development of percutaneous absorption models for medicinal plants. Current projects he is involved with include polymer coating of liposomes and phytosomal structures for increased drug delivery and stability.