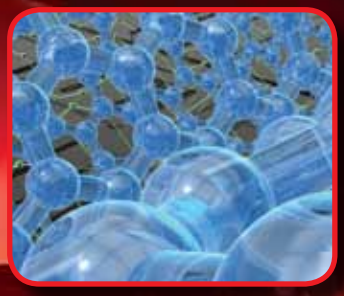

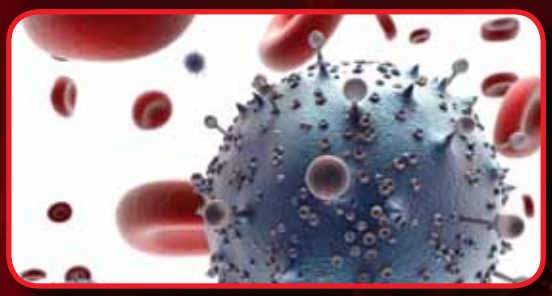

NANOTECHNOLOGY
PUBLIC ENGAGEMENT

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Nanotechnology and Health

'I sit before you today with very little hair on my head. It fell out a few weeks ago as a result of the chemo-therapy I've been undergoing. Twenty years ago, without even this crude chemotherapy, I would already be dead. But 20 years from now, nanoscale missiles will target cancer cells in the human body and leave everything else blissfully alone. I may not live to see it. But I am confident it will happen.'

Spoken by Richard Smalley, Nobel Prize-winning chemist and nanotech pioneer on 22 June 1999. He died of non-Hodgkin's lymphoma on 28 October 2005. (Jennifer Kahn, 2006, National Geographic).

The Healthcare Challenge

With over 33 million people living with HIV, including an estimated 24.5 million in sub-Saharan Africa, healthcare is a challenge for all countries across the globe. Opportunistic infections such as tuberculosis (TB) often accompany this high rate of HIV infection, and as a result, in Africa, HIV is the single most important factor contributing to the increase in the incidence of TB since 1990. This heavy disease burden is placing a huge strain on national health infrastructure in South Africa and is draining resources that ought to be used in addressing other diseases that are also important and growing in urgency e.g. diabetes, cancer, heart disease, sexually translated diseases, malaria, arthritis and asthma. New solutions are needed to manage these diseases.

Rapid diagnosis and more effective treatments are needed, especially for infectious agents, to improve the lives of infected patients and to prevent further spread. One of the approaches being explored in many countries, including South Africa, to tackle this healthcare challenge is nanotechnology.

Nanotechnology is often called an 'enabling' or 'refining' technology as it allows the specificity of existing technologies to be improved. A large part of nanotechnology focuses on manufacturing materials, capitalising on the novel properties seen at the nanoscale, using 'nano-architecture'. Changing the shape, structure and formation of materials at this scale greatly impacts the characteristics of the final product, and thus the use.

How can Nanotechnology Help Healthcare?

Nanoparticles can be engineered in different shapes, sizes and forms to perform different tasks and 'transport' specific substances to specific points in the body. The increased surface area of nano-sized drug carriers enhances solubility, dissolution and bioavailability, leading to more rapid onset of action. The small size of the engineered nanoparticle allows them to easily enter living cells, and potentially deliver the drugs directly to the diseased cell or pathogen specifically, thus destroying it without damaging nearby healthy cells.

What is Nanotechnology?

Nanotechnology is the act of manipulating materials at very tiny scales (generally regarded as nanoscale) – essentially at the atomic and molecular size levels. When materials have one or more of their dimensions under 100 nanometres, the normal rules of physics and chemistry often no longer apply. As a result, many materials start to display unique and sometimes, surprising properties. Their strength, ability to conduct electricity and rate of reactivity increase dramatically. For example, solids such as gold turn into liquids at room temperature, silver shows increased anti–microbial properties, inert materials like platinum and gold become catalysts, and stable materials like aluminium become combustible. These newly discovered properties of nanoscale materials have opened up exciting fields of study and applications in areas that can improve the quality of human life in the fields of water and health.

NANOSCIENCE is the study and discovery of these properties.

NANOTECHNOLOGY is the use of these properties in special products and applications.

(Source: Manfred Scriba, CSIR)

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NRF National Research Foundation
SAASTA South African Agency for Science and Technology Advancement

Tailoring this 'nano-architecture' to perform specific tasks could provide radical improvements to existing medical practices, making them more affordable and accessible in remote, isolated areas. The types of nanomaterials being investigated include dendrimers, nanocrystals, nanocapsules, nanotubes, nanofibres, nanowires, nano-micelles, quantum dots, nanoshells, etc.

> *'In a nutshell, nanomedicine aims at delivering drugs where you want it, when you want it, without wasting it.'*
>
> Jennifer Kahn, 2006, National Geographic

Introducing... Nanomedicine

Nanotechnology is being used to develop nanodevices and nanostructures to prevent, treat and monitor disease. The goals of nanomedicine are to:

- Diagnose as accurately and early as possible.
- Treat as effectively as possible without side effects.
- Evaluate the efficacy of treatment non-invasively.

The principle applications of nanomedicine include:

- ***Diagnostics and monitoring*** – Highly sensitive, portable point-of-care (POC) test kits which offer all the functions usually provided by a laboratory are being developed to enable quick, early and accurate detection of disease. Nanotechnology can also be used to deliver *in vivo* imaging agents to enable early detection, diagnosis, monitoring and treatment of disease. For example, nano-biosensors are being developed for the *in situ* detection of glucose levels in diabetes therapy. Nanotechnology could eventually enable potential screening tests for several pathogens simultaneously and could be used for wide-ranging screening in remote clinics.
- ***Drug discovery, development and delivery*** – The use of nanoparticles to deliver specific therapeutic substances/drugs to the source of the disease as early as possible increases efficiency and minimizes side effects. Additional possibilities include controlled release of drugs/therapeutic substances and using nanoparticles to stimulate the body's innate repair mechanisms, such as through stem cells.
- ***Tissue engineering*** – This includes developing new materials that are bio-compatible for use as implants in tissue replacement, repairing damaged tissues and manufacturing tissue and organs e.g. liver, pancreas, bone, cartilage, etc. Nanomaterial based scaffolds are being investigated to artificially stimulate cell proliferation to trigger cell regeneration.
- ***Medical instruments and devices*** – Research areas include the further miniaturisation of medical devices, the use of carbon nanotubes in place of glass pipettes, the incorporation of nano-devices into catheters and silver nanoparticles for their antibacterial properties.
- ***Surgical treatments*** – Nanotechnology can be used to reduce the invasiveness, complexity and associated risk of surgery and surgical procedures.

Benefits of Nano-based Healthcare

Some of the potential benefits of nanomedicine include:

- ***Earlier and less invasive diagnosis*** – Due to improved and more sensitive analysis, diseases could be detected much earlier using less invasive methods such as a finger prick or saliva sample. Nanotechnology based imaging technologies could pinpoint the precise localisation of diseases before severe complications occur.
- ***Reduced side effects*** – The use of more effective, targeted drugs could reduce the negative impacts of the drugs upon healthy cells and tissue. It could also enable different therapies to be combined.
- ***More cost effective*** – With nanomedicine research focusing on using existing materials on a smaller scale rather than discovering or developing new molecules or substances, lower costs could be incurred.
- ***Greater efficacy*** – Improved/enhanced drug delivery leads to superior performance characteristics of the medicine.
- ***Increased patient compliance*** – With reduced side effects, increased effectiveness and simpler regimes, patients are more likely to comply and complete treatments.

South Africa and Nanotechnology

Nanotechnology has been embedded in South African strategy and policy since the publication of the White Paper on Science and Technology in 1996, culminating in the National Nanotechnology Strategy (NNS) launched in 2007. This was followed by a Ten–Year Research Plan on Nanoscience and Nanotechnology published in 2010 as a road map to support successful implementation of the NNS. In addition to the commitment to long term nanoscience research, the strategy focuses significantly on developing the human capacity and infrastructure required to develop the sector and stimulate links between research and industry.

Health, specifically improved primary healthcare, is one of six focus areas highlighted in the NNS where nanotechnology can offer the most significant benefits for South Africa. To date, through the Department of Science and Technology (DST), the government has invested over R170 million in different aspects of nanotechnology research and development (R&D). Two Nanotechnology Innovation Centres, at the Council for Scientific and Industrial Research (CSIR) and at Mintek, have been commissioned and have formed collaborative partnerships with industry, universities and other bodies to conduct cutting-edge research.

Using Gold at Mintek

At Mintek, one of the Nanotechnology Centres of Innovation, portable test kits for various infectious diseases are in the final stages of development. Much of this work and related drug delivery research is focused around the use of gold nanoparticles.

The therapeutic uses of gold colloids date back to the 4th Century AD. In the past 20 years, research has focused on developing and optimising methods for the preparation of gold nanoparticles. In nanoscience and nanotechnology today, gold nanomaterials appear to be the most widely used by both academic and industrial researchers. The extraordinary optical, catalytic, and magnetic properties of these precious metal nanoparticles have put them at the forefront of South African research, especially for healthcare applications.

Mintek is producing gold nanoparticles for use in the health sector as drug delivery systems, but also as tools for advanced rapid diagnostic tests. Both optical and electrochemical rapid diagnostic methods are being developed for the detection of human and animal health diseases. In particular, low-cost, fast, stable and accurate POC diagnostic test kits for TB and malaria have reached advanced stages. These gold nanoparticle-based POC prototypes were tested using serum and blood samples. They are simple and robust devices that can be used by individuals at home without the need for trained professionals to diagnose diseases of interest. It is envisaged that after clinical evaluation the prototypes will be available to the majority of South Africans to diagnose relevant diseases and hence improve their quality of life.

Risks of Nanomedicine

Although nanotechnology, and specifically nanomedicine offers a multitude of potential uses and rapid advances, this technology may also have unintended effects on human health and the environment. There are concerns that the same properties (size, shape, reactivity, etc.) that make nanoparticles so useful could also make them harmful to the environment and toxic to humans. Materials that are harmless in bulk forms can become highly toxic at the nanoscale, for example, if they enter and build up in drinking water supplies and the food chain, and do not biodegrade. These concerns are exacerbated by the current poor understanding of the fate and behaviour of nanoparticles in humans and the environment. As yet, little data are available on the unintended and adverse effects and how nanoparticles might affect or interfere with the biochemical pathways and processes of the human body.

The understanding of toxicity and potential health risks associated with nanomaterials is extremely limited. The inhalation of airborne nanoparticles and the impact upon lung disease is a specific concern, with recent studies showing a similar response by the human body to some forms of carbon nanotubes as to asbestos particles, if inhaled in sufficient quantities. Other concerns include oral ingestion/skin penetration which may adversely affect patient immune responses; the effect of different shapes of nanoparticles on toxicity; the entry of nanoparticles to non-desired sites and the various mechanisms of toxicity, e.g. particles that enter the blood-

stream may affect the blood vessel lining/function or promote blood clot formation. The length of time nanoparticles remain in the human body, the effects on cellular and tissue functions, access to systemic circulation through dermal exposure, and unanticipated reactions *in vivo* are other areas of interest.

Nanotechnology risk assessment research for establishing the potential impacts of nanoparticles on human health and the environment is crucial to aid in balancing the technology's benefits and potential unintended consequences. Scientific authorities acknowledge this as a massive challenge, since monitoring the huge volume of diverse nanoparticles being produced and used and their consequent impact is very difficult to track.

In South Africa, a research platform is currently being established by DST to investigate the environmental, safety and health related aspects of nanotechnology. Other initiatives include the establishment of the Ethics Committee constituted by the government, made up of representative stakeholders to ensure that the technology adheres to the ethical issues.

Regulation of Nanotechnology

Although nanotechnology must adhere to general standards such as those set out by the South African Bureau of Standards for materials and the Medicines Control Council for medicines, nanotechnology regulations in South Africa are currently still being developed. This delay is mainly due to the relative infancy of this emerging technology, and the lack of evidence and scientific data to demonstrate the impact of products already in use. This also accounts for the relatively 'loose' regulations that have been developed around the world (Canada, the USA, Japan and the European Union). It is likely that these regulations will be modified and 'tightened' accordingly as new data becomes available.

It is important that nanotechnology is developed in a safe, responsible, acceptable, and sustainable manner. For this to happen, the entire life cycle of nanoparticles needs to be carefully considered from production to disposal, to allow an informed assessment of the potential human heath and environmental impacts. Risk assessment of nanotechnology is currently starting at several universities and science councils in South Africa – and is expected to become an integral part of the nanotechnology research in this country.

Key Issues

Other issues to be considered include:

- ***'Promise versus reality'*** – Translating the research from the laboratory to the commercial sector is challenging. How much of what is being promised by nanotechnology and nanomedicine will be delivered?
- ***Access and availability*** – Once developed, how accessible will this type of technology be to the average South African? Will it be limited to specific socio-economic groups that can afford it or will it be available to all?
- ***Scaling up and bulk manufacturing issues*** – Quality control issues?

Slow Release TB Drug Alternative

Researchers from the CSIR's drug delivery group measure the size of nanoparticles that are used in the Nano-TB drug delivery programme. Photo: CSIR

A new method of delivering TB drugs to patients could overcome the current problems faced on TB control programmes, at a significantly lower cost. The daily routine of taking a pill of each of four antibiotics every day for months on end is a struggle for many patients, who have to travel long distances for a nurse to ensure that they take the drugs. Combined with the side effects of the medication, this often means many give up before completing the course (known as non-compliance), which causes multidrug-resistant strains to emerge, and ample opportunity for the disease to spread, requiring a second line of defence.

Researchers at the CSIR are heading up the development of a new way to deliver this drug cocktail using nanotechnology. The drugs are incorporated into nanoparticles which are then slowly released into the patients' bloodstream and transported around the body. This dosage is only required every 7-10 days, which should increase patient compliance and contribute to the complete elimination of the disease.

The safety and uptake of the nanoparticles is being tested in TB-infected mice and the effectiveness of the nanodrug is being compared to conventional therapy to see whether a weekly nano dose is as effective as the standard daily treatment regime. Human trials for the antibiotic are scheduled for the near future.

- ***Patents and profits*** – How will this new technology impact patents and profit margins – will it further increase the divide between rich and poor? If this new technology displaces existing classes of pharmaceuticals, massive shifts in economic value could result among pharmaceutical companies.
- ***Regulatory issues*** – Ensuring compliance of a new technology with complex regulatory specifications for medicine/device registration could be very challenging - how will this be adequately monitored and enforced?
- ***Key success factors*** – The science itself will not be enough and there are various other key factors that are needed for it to succeed, including a relevant regulatory framework, funding and infrastructure, public participation and engagement, including with medical professionals, health workers and the general public, to help in the sustainable uptake of the technology.
- ***Occupational health*** - What about the occupational health of the researchers undertaking nanotech research? Are nanoparticles hazardous? Can exposure to nanoparticles pose a toxic risk to the scientists? What measures are being taken?

The Nanotechnology Public Engagement Programme (NPEP) is an initiative funded by the Department of Science and Technology (DST) and implemented by the South African Agency for Science and Technology Advancement (SAASTA), a business unit of the National Research Foundation (NRF). Launched in early 2008, the NPEP aims to promote credible, fact-based understanding of nanotechnology through awareness, dialogue and education to enable informed decision making on nanotechnology innovations to improve the quality of life.