Innovating transformative medical devices & growing the local manufacturing sector

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CSIR Conference

5-6 October 2017

PATH

MRC SOUTH AFRICA

SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

Recent initiatives driving medical devices and diagnostics innovation and commercialization

- **2013** MRC with DST support establishes the Strategic Health Innovation Partnerships **(SHIP)** for funding and driving product-focused R&D.
- **2014** MRC partners with PATH (USA) /PATH (SA), a global player in the scaling of appropriate technologies for developing countries, to establish the Global Health Innovation Accelerator (GHIA)
- **2015 (?)** CSIR embarks on a developing a **product innovation platform** to support medical device start-ups and companies with PLM, BI and QMS to help grow the sector through innovation.
- **2016** Formation of the **Medical Devices Stakeholders Forum (MDSF)** made up from numerous stakeholders (ie CSIR, TIA, DTI, IDC, DST, NDoH, MDMSA, WC medical devices cluster, non-profits and university TTOs including biomedical engineering entities).
- **2016** TIA, through the Technology Innovation Programmes (TIPS), and as part of the MDSF, becomes an important player for driving medical device innovation through a value chain approach.

Enter The Fourth Industrial Revolution (4IR)

4IR builds on the current digital revolution (3IR), and is defined by new ways in which technology becomes embedded within societies, business and even the human body. The 4IR is marked by emerging technology breakthroughs in a number of fields, including robotics, genomics, biosensors and wearables, AI, the internet of things, quantum computing, big data predictive analytics, 3D printing/additive manufacturing, advanced materials & nanotechnology.

Prof Klaus Shwab @ WEC 2016

Can the MD innovators and local MD manufacturers collaborate and adapt?

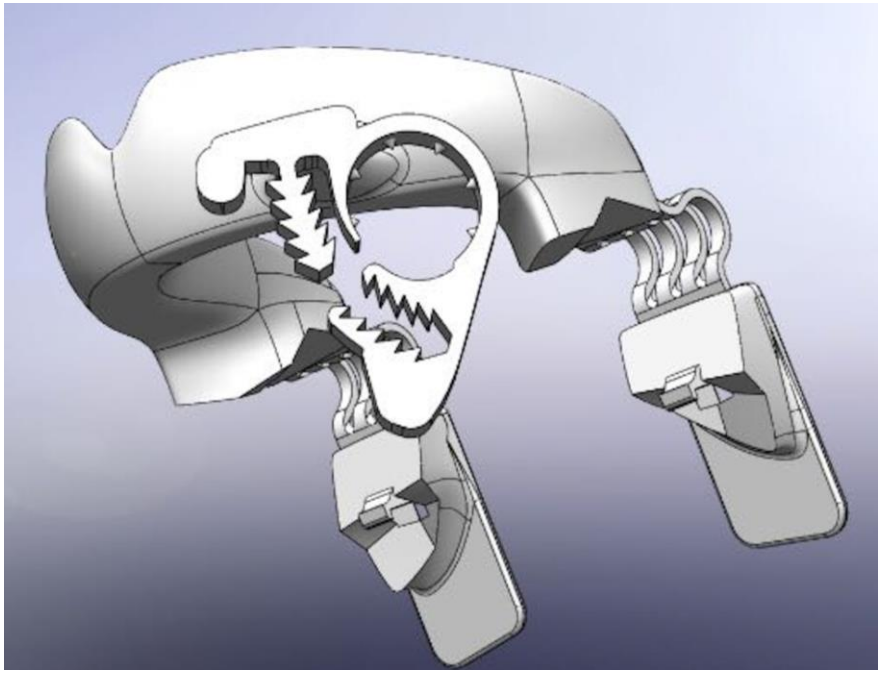
MD Innovators: Universities (especially universities of technology), science councils (mainly CSIR & MRC) and their associated technology transfer offices and other innovators, such as medical doctors at the coal face and in-house R&D by manufacturers.

MD Local Manufacturers: Approximately 200 with about 50 well established companies (landscape mapping needed). Represented by 2 entities- MDMSA and the Western Cape MD cluster.

It cannot be business as usual- the 4IR enables:

- *Point of Care devices* (right place, immediate answers)
- *Right-sizing* versus global obsession with scale and growth
- *Rapid manufacture* of personalized prosthetics and products
- *Personalized devices* and technologies for *precision medicine*

Secure Airway Clamp for safer Anaesthesia



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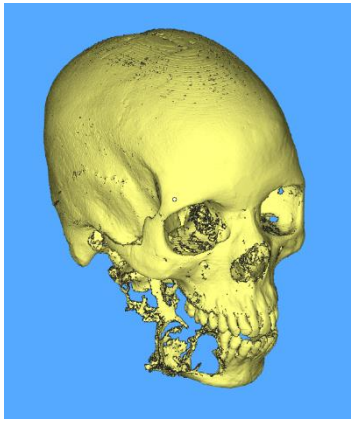
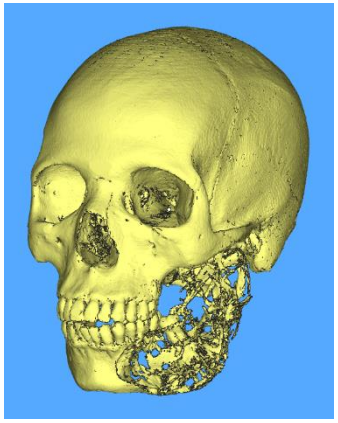
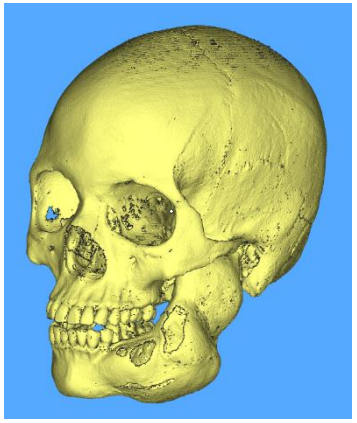
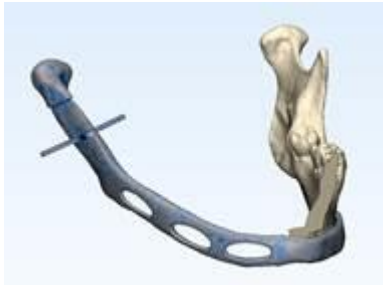
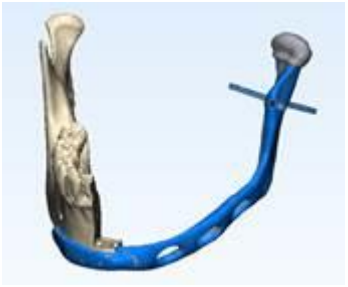
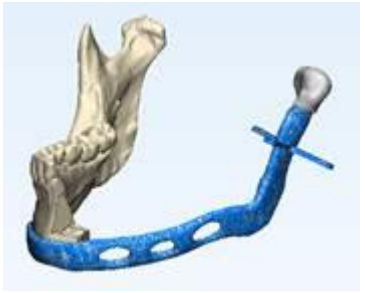
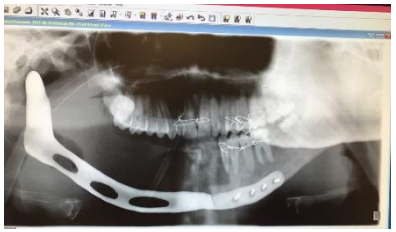
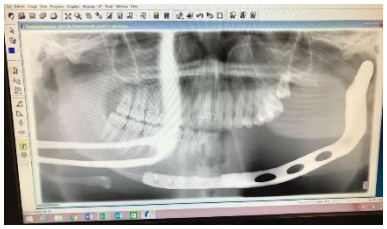
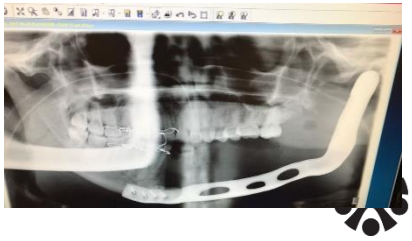
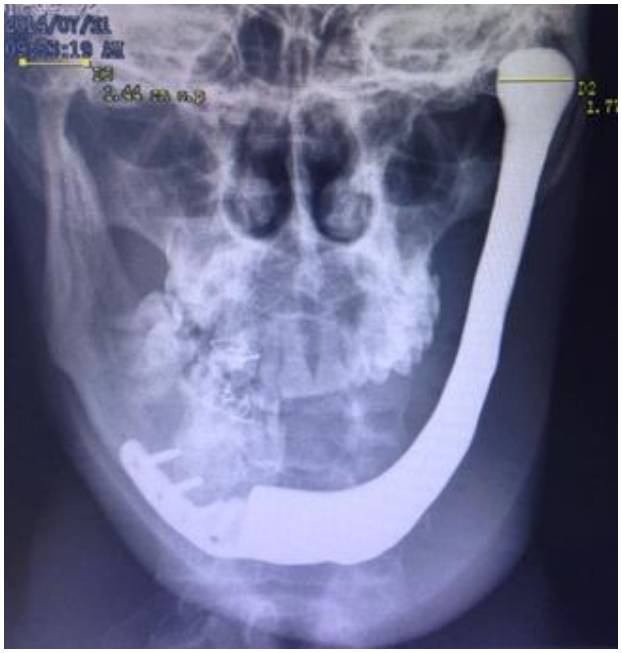
MANDIBULAR IMPLANTS

State patients: Procedures completed during June 2017

	PATIENT 1	PATIENT 2	PATIENT 3
PATIENT CT SCAN			
PROPOSED IMPLANT DESIGN			
3D PRINTED TITANIUM IMPLANT			

THE CARL & EMILY FUCHS FOUNDATION

MANDIBULAR IMPLANTS



Doctors successfully implanted the country's first 3D-printed jaw bone at the Kimberley Hospital Complex during 2013. The patient is a 31-year-old man from Kimberley. Tumour growth had destroyed a large part of his lower jaw bone. The customized jaw was designed and manufactured at the CRPM with titanium powder on an EOS M280 machine to replace the diseased lower jaw

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MID-FACE TUMOUR

Courtesy Dr J Claassen (UFS: ENT)

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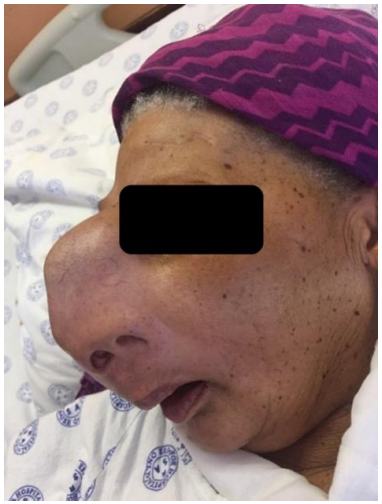

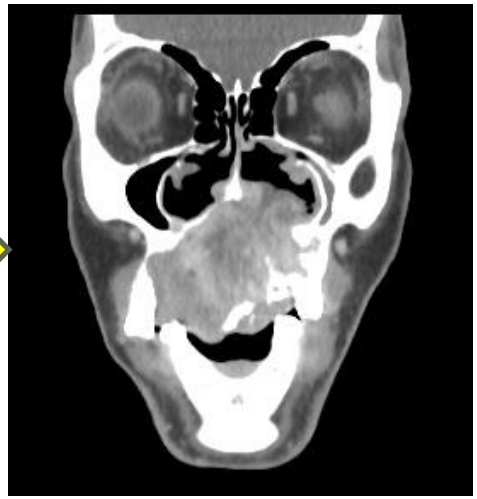

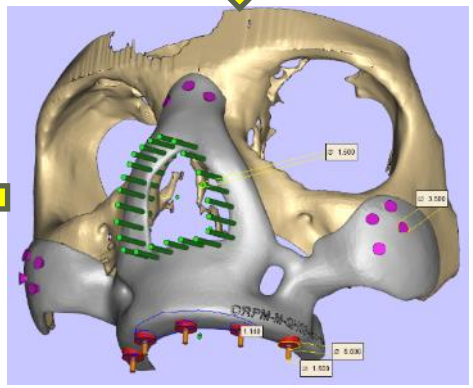

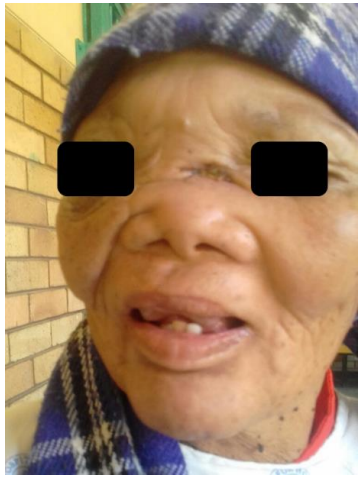

FROM POINT OF APPLICATION ⇨ POINT OF CARE

South Africa-UK Newton Collaborative Research Development Programme in Precision Medicine

Referral

Patient sampling

Rapid ParaDNA test (<1 hour)

ParaDNA Automated Pathway Panel test for detection of cardiovascular disease (CVD) risk factors implicated in most non-communicable diseases (NCDs)

ParaDNA Automated founder mutation test result

ParaDNA Automated Genotype result

Data integration using Gknowmix algorithm

Personalised Patient Report

Single appointment

©para»dna

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MinION portable sequencer

MinION REAL-TIME, PORTABLE, NANOPORE, GENOME SEQUENCING

Future prospects of combining long-read (>150 kb) 3rd and *in situ* 4th generation sequencing with well-established NGS technologies suitable for WES/WGS, has generated much excitement in the genomics community (*Jain et al. 2016; McGinn et al. 2016).*

Magi et al. (2016) reported that the MinION sequencing device can be readily used to detect genomic regions involved in copy number variants with high accuracy, outperforming other state-of-the-art methods in terms of both sensitivity and specificity.

Enter Medical Device Regulations

1965

ACT 101 of 1965

Control of medicines

(MCC)

MRA / Inspectorate

(PIC GMP compliance / Responsible Pharmacist)

Historical

DRUGS CONTROL

1993

EU formed and Directives for free market movement

- Highlight of the MDD medical device directive > MDR 2016

MEDICAL DEVICES emerge

2016

Medical device regulations

Government Gazette No. 40480 (#1515) published on the 9 December 2016 (followed by Act 72 of 2008 with Act 14 of 2015 forming SAHPRA

> MEDICAL DEVICES

to follow MEDICINES regulatory approach

2017

Guidelines

6.21- Licence Application to Manufacture, Import, Distribute or Export Medical Devices

6.22- Licence Application to Import, Distribute or Export Medical Devices (Cells can now expand to allow for wrapping of text)

2.01_General_information_Jul12_v8_showing_changes.docx August 2012

16.03-Guideline for a Licence to Manufacture, Import, Export or Distribute Medical Devices and IVDs

8.02- Medical Devices and IVDs Essential Principles of Safety & Performance

8.05- Classification of Medical Devices and IVDs

9.79- Medical Device Establishments: Licence Requirements

8.04 Recall & Vigilance v2

8.05 Classification of Medical Devices v2

8.06 Access to and Control of Medical devises & IVDs v1

8.07 Medical Device Quality Manual v2

6.24 Licence Application to Wholesale v1

16.04 Wholesale licence guideline

From Simone Rudolph-Shortt ISOhealthSA

Addressing Regulatory & Quality Management issues

Problem:

One of the biggest challenges with respect to the medical device and diagnostic industry are those relating to Regulatory & Quality Management challenges.

Purpose of Regulations

The safety and performance of medical devices depend on two critical elements:

1.Pre-market review contributes to product control

2. Post-market surveillance ensures that medical devices in use continue to be safe and effective.

A third element is the representation of the product to the user - Label, Advertising and Education/ Training

From Simone Rudolph-Shortt ISOhealthSA

BARRIERS- especially for start-ups and small companies

- European standards of safety & performance acceptance as the benchmark requiring European certifications at European costs.
- No notified bodies from South Africa.
- No or little testing infrastructure for medical devices in SA –eg European product safety standards (EN, biocompatability, performance)
- Local manufacturer management, staff and suppliers have limited knowledge of the European and ISO 13485, 14644, 60641 etc standards and practices.
- Local regulator following the historical Act 101 medicines control approach which cannot easily be harmonisation with international medical device regulations
- Maintaining regulatory compliance requires 2-3 people full time!

These are a huge barrier to entry for innovators, start-ups and small companies seeking initial growth in the local market.

From Simone Rudolph-Shortt ISOhealthSA

Suggestions to support local innovators and growth of the MD manufacturing sector

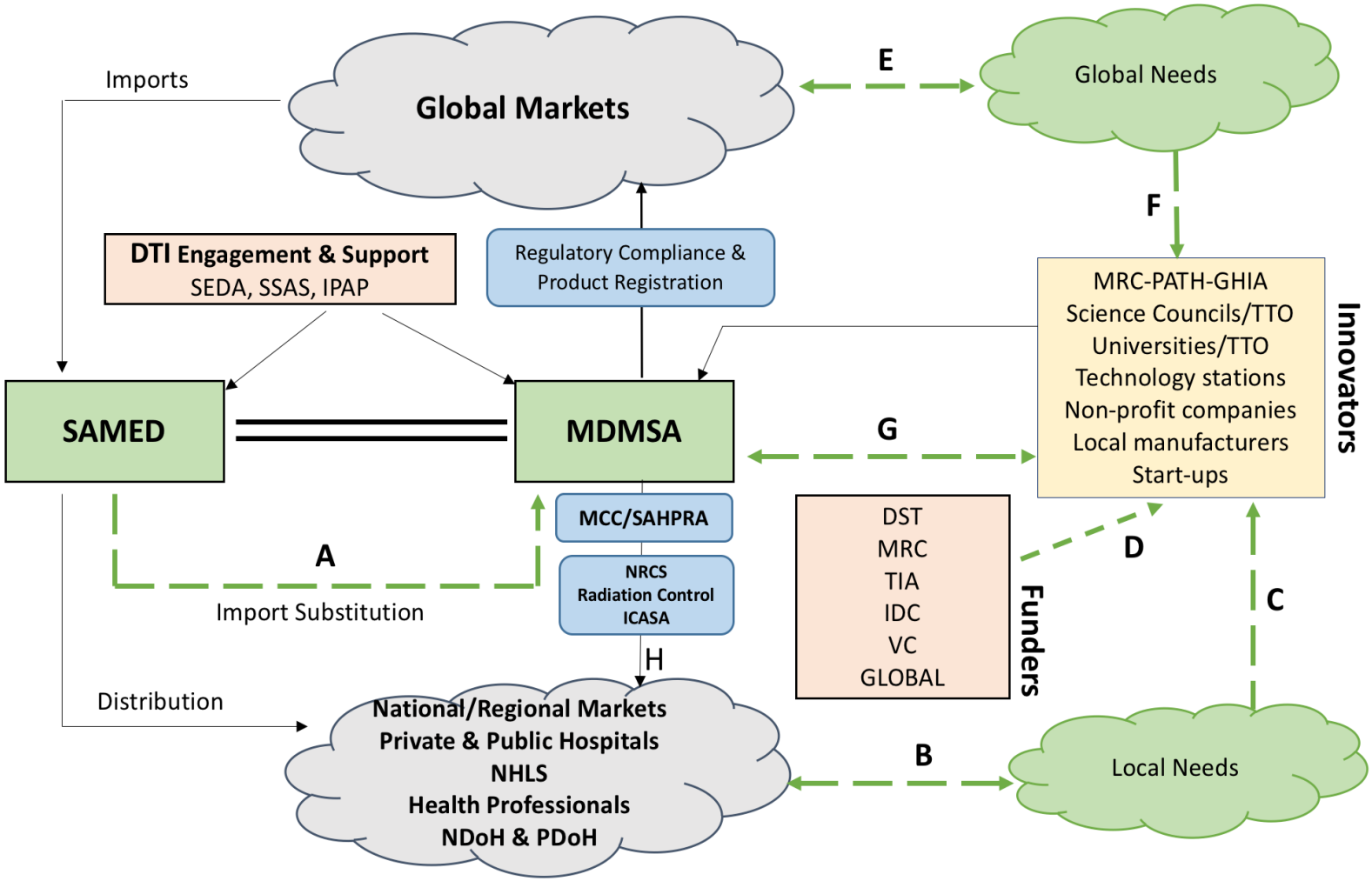
There are currently no advantages for local manufacturers compared to overseas manufacturers- in fact overseas manufacturers appear to be favoured

- Local manufacturers could be exempted from regulatory and MCC/SAHPRA license fees as the large import volumes of MDs (90% of total MDs) can provide sufficient income for the regulator.
- Government- DTI should provide support & funding for;
  - The training of local regulatory auditors
  - Funding support for QMS (ISO 13485 etc), especially to start ups and companies with innovative MDs.
  - Establishing basic SANAS accredited testing facilities??

From Simone Rudolph-Shortt ISOhealthSA

So how do we connect the MD innovators and manufacturers in this complex ecosytem and meet the needs of the other stakeholders (ie DTI, DST, DoH, IDC, TIA)?

THE SA MEDICAL DEVICE INNOVATION ECOSYSTEM



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PROJECT TO HELP GROW THE LOCAL MEDICAL DEVICE INNOVATION AND MANUFACTURING ECOSYSTEM

Build and expand on the previous MD reports and existing data sources- but the following information is needed

- List of companies, what they do (e.g. R&D, manufacture, import, export, distribution), manufacturing capacity, types of products, certification, technical capabilities, competencies, areas of expertise, training requirements, challenges etc.
- HEIs, science councils and associated TTOs involved in medical device innovation and their capabilities, platforms, existing products/spin-outs and pipeline technologies
- Other players in this domain and their capabilities, products and pipeline technologies (e.g. NPCs and entrepreneurs)
- Support agencies and companies (e.g. DTI incentives and SEDA, regulatory support consultancies and auditors etc.) and their current offerings
- Funders and their current MD investments and offerings - DST, TIA, IDC, DTI, MRC, VC
- Consumers in both private and public sector (private hospitals, medical professionals and DoHs)

Objective is to share this information via a web-portal to create the required stakeholder linkages (Meraka is developing a portal that could include this organic MD stakeholder knowledge base)

Thanks

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THE MEDICAL DEVICE INNOVATION PATHWAYS

Crucial pipelines that need to be addressed to optimize innovation leading to growth of the local medical device innovation and manufacturing sector

A: identifying those medical devices currently imported into SA which can profitably be redeveloped and manufactured in SA.

B: working with national and provincial departments of health to set up processes to enable clear articulation of health technology needs that can be addressed by the innovation networks and local manufacturers.

C: translating identified local health needs through the innovation pathways leading to local manufacture and introduction.

D: interacting with **funders** to encourage a focus on medical device R&D, this being "the low hanging fruit" of the health technology spectrum.

E & F: identifying global and developing country health needs that are also pertinent to SA.

G: strengthening linkages between the **innovators** and local manufacturers as represented by MDMSA. This entails bi-directional engagement with universities (specifically universities of technology), science councils (mainly MRC and CSIR) and associated technology transfer offices and other innovators to perform the necessary R&D and subsequent technology transfer for local manufacture.

H: Interacting with NDoH and provincial DoHs to ensure that local manufacturers of medical devices receive preferential procurement incentives to secure government contracts. In addition, private health care groups and medical schemes must be targeted to encourage procurement from local manufacturers.