



# R-2-M

ROUTE-TO-MARKET GUIDE FOR INVENTORS

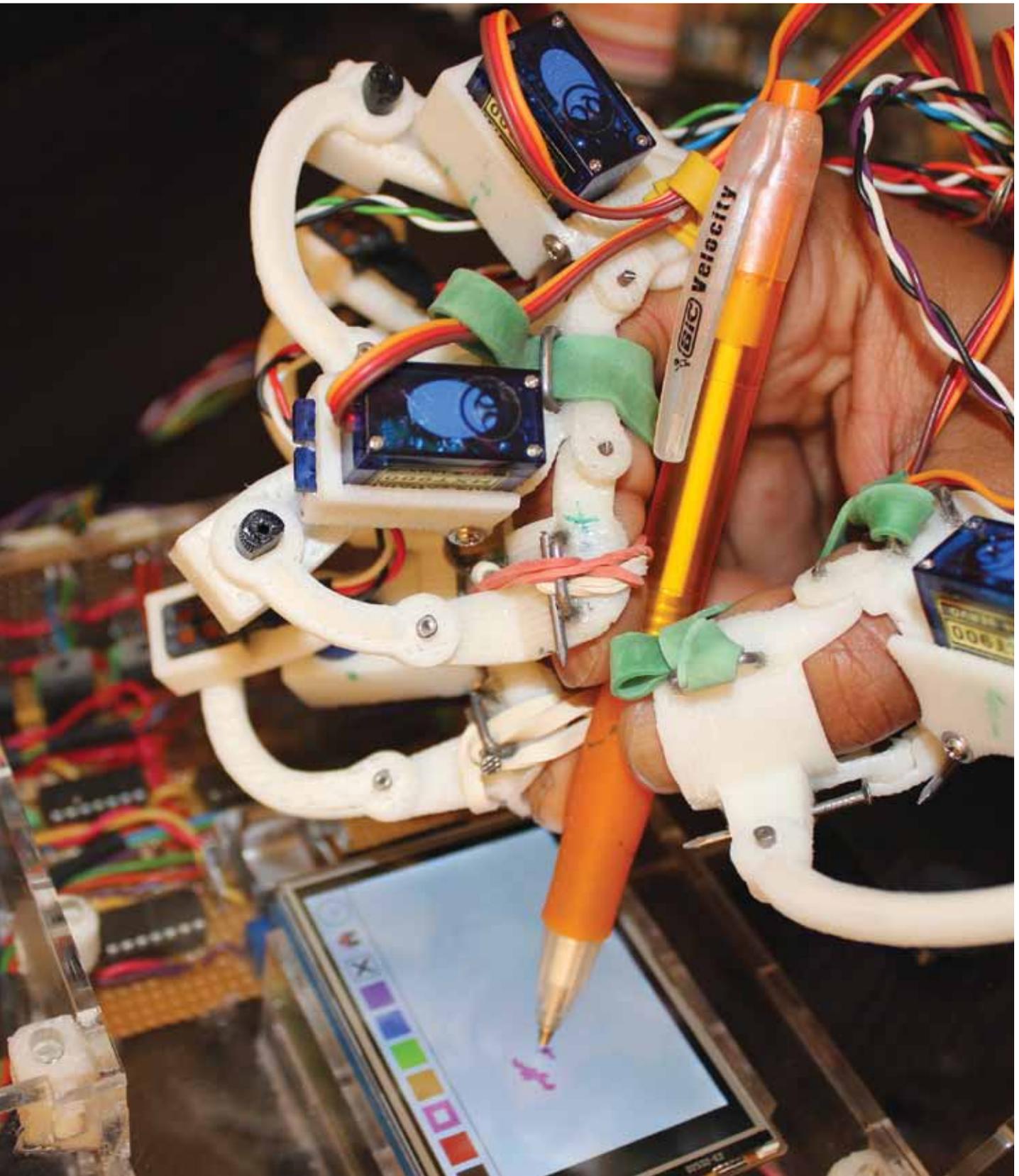


# Medical Devices

A UCT EDITION

AN INNOVATION  
GUIDE FROM LAB TO  
COMMERCIALISATION

2018



## About the Route-to-Market Series

The Route to Market (R2M) series is being developed by the Department of Research Contracts & Innovation (RC&I) at the University of Cape Town using funding from the Department of Science and Technology's National Intellectual Property Office (NIPMO). Each booklet focuses on a specific sector/product type and highlights the key steps and considerations in bringing such a product to market in that sector – with an emphasis on the local South African context. The hope is that this and other booklets will be useful to both Researchers and Innovators, as well as Technology Transfer professionals working at institutional Technology Transfer Offices (TTOs). The books have been released under a Creative Commons license to enable

other institutions to customise them for their own use.

Technology Transfer professionals generally have to deal with a multitude of inventions that span a broad range of categories. This can be challenging for new entrants to the field as well as to those when invention falls into a 'new' sector that the TTO has not previously worked in. Researchers are often unsure of the steps that lie ahead in the areas of development and innovation that follow once their research has been completed. As the support for creating impact from research outputs grows, Researchers are increasingly finding good sources of innovation funding and need to be equipped to work in this space.

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Hardcopies of this and other publications may be obtained at cost by contacting [innovation@uct.ac.za](mailto:innovation@uct.ac.za). A number of sector experts have provided RC&I with material and we are grateful to them for their valuable contribution.

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## INTRODUCTION

Considering the WHO definition of a medical device (please see textbox), it is clear that there is an extremely broad range – everything from a tongue depressant to an artificial heart valve!

They may also be complex in that they can incorporate electrical, mechanical, software and wireless transmission components. Medical devices also have a range of environments in which they are used: invasive, or non-invasive in terms of their interaction with a patient; in a theatre for surgery, intensive care unit for monitoring; in a doctor's rooms for diagnosis; or as part of one's everyday life, like a brace.

Materials of construction vary from metals to polymers to absorbable temporary devices like sutures. They even vary in their method of manufacture, if one now factors in 3-D printing.

We are moving into an age where medical devices are embedded in other everyday items, as part of the "internet of things" e.g. as the multifunctional capabilities of watches and smartphones increases.

The SmartWatch "Embrace"<sup>1</sup> was the first watch to be approved in the USA by the FDA (February 2018) as a medical device that is able to monitor the wearer for the onset of an epileptic fit. It combines a number of sensors, to monitor temperature, the skin's electrodermal activity (conductivity changes with sweating) as well as accelerometers and gyroscopes that indicate that the person has fallen or is having a seizure. The watch is able to send a text alert for help.



## WHO Definition of a Medical Device

'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of conception,
- disinfection of medical devices
- providing information by means of *in vitro* examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.

Note: Products which may be considered to be medical devices in some jurisdictions but not in others include:

- disinfection substances,
- aids for persons with disabilities,
- devices incorporating animal and/or human tissues,
- devices for *in vitro* fertilization or assisted reproduction technologies

<sup>1</sup> <https://www.wired.co.uk/article/empatica-embrace-epilepsy-wearable-medical-device>

The FDA has published guides<sup>2</sup> on 3-D printing in the health space, where it is used for medical devices, biologics and drugs. It lends itself to rapid prototyping but is increasingly finding application as the mode of manufacturing the final product, especially for bespoke or personalised devices. This is bringing in a new approach to design where one needs to consider the stresses that are introduced into a structure depending on the manner in which it is printed.

There is also the issue of ensuring that designs do not encapsulate powder (used for the printing) that could later leach from the device.

As of July 2018, Med Device Online reports<sup>3</sup> that more than 100 medical devices and one prescription drug that are 3-D printed have been approved by the FDA.



3-D printing has ushered in a need for extensive regulatory uniformity – i.e. a device could be designed in one country and printed in another. Added to this, the issue of product liability becomes more complex, if one considers that a device could be printed in a doctor's rooms or at a hospital – design, printer operation, material used equals potentially three different parties involved in the manufacture!

As elements of the “fourth industrial revolution” impact on the nature and capabilities of medical devices being made, it is likely that there will need to be considerable legislative and regulatory development and importantly, harmonisation.

Whilst the regulatory field is complex, devices are classified essentially from low- to high-risk by the different regulatory bodies. Determining which class your device falls into is a key step to determining the path ahead.

This guide starts with a general approach to assessing the market potential of a device that has been invented. Then the “technology readiness levels” that are navigated to mature the product on its route to market and the role of Research Contracts & Innovation (RC&I) in this process are discussed.

Regulatory requirements, trials and the associated ethics approvals are overviewed along with some sources of funding. In the last section we have provided information on UCT's spin-off companies in the sector and timelines regarding their “route to market”.

Two organisations provide a useful network within South Africa: Medical Device Manufacturers South Africa (MDMSA) and South African Medical Technology Industry Association (SAMED). SAMED's website provides useful resources.<sup>4</sup>

<sup>2</sup> <https://www.fda.gov/medicaldevices/productsandmedicalprocedures/3dprintingofmedicaldevices/default.htm>

<sup>3</sup> <https://www.meddeviceonline.com/doc/lessons-for-medical-device-manufacturers-using-d-printing-0001>

<sup>4</sup> [www.samed.org.za](http://www.samed.org.za)

## 1 APPROACHING MEDICAL DEVICE INNOVATION

Whilst the invention may work from a technical perspective, one also needs to consider its commercial potential and what will be required to take the device into the market.

A number of criteria need to be evaluated, such as:

1. What is the unmet clinical need?
2. Is it a medical device?
3. Is it a “me too” product?
4. Would other medical personnel use it?
5. What is the route to market?
6. What are the regulatory requirements and hurdles?
7. Is it patentable?
8. Is there Freedom to Operate?
9. What is the market potential?
10. Who will pay for the device?
11. How will it displace currently used products / processes?

Brief discussions on these points follow.

### 1.1 Unmet clinical need

A key element for success of a new medical device is that it addresses a need that is currently not met. A product that is a variation or improvement on an existing device may have merit, but it could face a significant hurdle to displace existing, known products.

### 1.2 Is it a Medical Device?

“Borderlines with medical devices”, which is published by the Medicines & Healthcare Products Regulatory Agency (MHRA)<sup>1</sup>, provides useful guidance regarding whether a product would actually be considered to be a medical device or not and this importantly

impacts on the regulatory requirement for your product.

Also of note is the fact that different territories may regard the product as a medical device, whilst others may not. Borderline cases also exist as to whether the device is regulated as a medicine or as a medical device, e.g. a drug eluting stent.

Gym equipment that measures a heartbeat is not regarded as a medical device as the equipment is primarily used for exercise. A blood pressure monitor, however - even if intended to be used in a gym - is regarded by the MHRA to be a medical device!

Software associated with medical devices is another complex area and the MHRA have developed a useful Software decision tree.<sup>2</sup>

Different regulators' guides are useful resources to determine how your device is classified and whether it is even indeed a medical device!

### 1.3 “Me too” product

Is this fundamentally a replication of a product that is currently on the market with a few small tweaks?

This can be problematic from two different perspectives: firstly, it may be difficult to achieve patent protection as there would be marginal novelty and most likely no inventiveness. In other words, based on what was in the market already, it would be ‘obvious’. Secondly,

<sup>1</sup> [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/521458/Borderlines\\_with\\_medical\\_devices.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/521458/Borderlines_with_medical_devices.pdf)

<sup>2</sup> [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/717865/Software\\_flow\\_chart\\_Ed\\_1-05.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/717865/Software_flow_chart_Ed_1-05.pdf)

there may be a freedom to operate issue – i.e. you would infringe somebody else's patent.

Fortunately for a lot of entrepreneurs, South Africa has in many cases been overlooked by foreign patentees and if one is looking to supply the local market (and often some African neighbours), there is unlikely to be a patent that is in force in the country(ies) and one will actually not infringe their patent.

#### 1.4 Would other Medical Personnel use it?

It is important to establish whether other medical personnel would use the device or can see the advantage that it offers.

Often there are alternatives that may be well-entrenched in the field that do the job just as well. In such cases, there will be little incentive for people to change to the new product.

If the products are 'peculiar' to, for example, the inventor's approach to a particular surgery, it makes it easier for them, but others would not necessarily derive a similar benefit or be enticed to spend money on acquiring the device.

A focus group, or feedback from independent potential users in the field, is very important in establishing commercial potential.

#### 1.5 Regulatory requirements and hurdles

First, the markets where the product could be sold must be identified and the regulatory requirements of these markets understood (the WHO provides information

on medical device regulations around the world, with contact details for regulatory authorities<sup>1</sup>).

Based on the risk classification in the chosen markets, the regulatory effort could be significant.

Broad areas for understanding the effort are as follows:

1. **Implantable devices** – require safety testing and extensive clinical evidence
2. **General medical devices** – require safety testing and some clinical evidence
3. **Low risk devices** – minimal testing, clinical evidence
4. **In Vitro Diagnostics** – require laboratory data as well as population data

One of the most important early activities is to understand the requirements for regulatory approval. This may include engaging with regulatory authorities to confirm classification of the device, as well as requirements for testing and clinical evidence. A Clinical Research Organisation (CRO) should be involved in such discussions. At UCT, we have the UCT Clinical Research Centre (CRC)<sup>2</sup>, who can provide advice upfront and then aid with the design and execution of clinical trials.

Clinical evidence can either be literature, or a clinical trial, or a combination. This requirement for clinical evidence has become more demanding in recent years – reviewers of technical files expect manufacturers to follow the requirements explicitly.

Many markets around the world have similar systems, with minor differences. The FDA (USA) has an entirely different system where the risk classification is based on

<sup>1</sup> [http://www.who.int/medical\\_devices/safety/en/](http://www.who.int/medical_devices/safety/en/)

<sup>2</sup> <http://www.crc.uct.ac.za/>

identification of a predicate device – or if no predicate device is found, the FDA has to be consulted on the classification.

Other than Class I, all other classes (Class Is, Im, IIa, IIb, and III) require involvement of a Notified Body (NB) in Europe, and a Quality Management System (ISO 13485) at the manufacturer. All products require some testing in an accredited laboratory. Electromedical products require extensive testing.

### 1.6 Patentability

For sustainable development and the ability to attract investment, an invention should be patentable. However, this is not the only strategy to adopt – based on other considerations, it may be possible to achieve commercial success without IP protection. Registered Designs and Copyright also play a role in protecting medical devices. This is discussed in more detail in section 5.

### 1.7 Freedom to operate

Related to the previous item, it may not be advisable to bring a device to market that infringes an existing patent or patents. If your device does infringe a third-party patent, you can approach the patent owner for a license to permit you to use their IP.

### 1.8 Market potential

Arguably, the most important aspect: is there sufficient demand to recover the investment required to bring the product to market and achieve sales? This question includes other aspects such as displacing existing technology, effort to access markets, etc.

Often, even though a device can be produced cheaply and be very effective, there may be little requirement for it – e.g. a single, once-off purchase by a hospital of a product that will last for years.

Being cheap, and assuming the product could not be sold at a significant margin, the amount of income that would be received would not justify the costs incurred during prototyping, trials and in getting regulatory approval.

### 1.9 Who will pay for the device? Reimbursement

When launching the development of a new medical device, consideration of reimbursement is as important as regulatory approval. Reimbursement can also be phrased as “who will pay for the device?”

This is an important question, since in many cases, neither the patient nor the person who selects or requests use of the device pay for it. Therefore, they have little or no incentive to manage the costs of the device or the treatment.

In South African private health care, medical aids choose which devices they will pay for. Authorised devices and procedures have allocated codes against which a fixed amount will be paid to the service provider.

Often, neither the patient nor clinician has knowledge of the cost of the device, nor any incentive to minimise the cost of the device. In the case of an existing procedure or similar device, a reimbursement code will exist, but if the device is new, medical insurance funders may require further data (cost / benefit and efficacy) above that required for regulatory purposes – before

agreeing to create a reimbursement code and pay for the device.

In the public health care sector, introducing a new procedure or device can be difficult depending on the individuals in each province. There is no co-ordinated mechanism to have a new procedure or device approved at national level, for use in provinces.

Reimbursement differs from one country to another. Public health in some countries, such as the UK, have a specific group to consider new technology, but even these are fraught with complications and delays.

Sometimes one also needs to conduct a health economics study, which should ideally be contracted out to an independent service provider, rather than done within the inventor's university to ensure objectivity. The studies look holistically at the particular intervention as the benefit may be seen in other cost components of a particular procedure – e.g. speed of recovery of a patient, improving efficiency during surgery and decreasing the amount of theatre time that is required, duration of anaesthesia, etc.

If the cost of the device cannot be passed on to the patient (or their medical aid), will the clinician pay for the device or the hospital?

If the customer is the public health care system, the decision makers may be far removed from the clinical users who understand the need for the device, and subject to budget constraints, which is especially true in developing countries. Often, too, a tender process would be involved, which can delay market entry significantly.

### 1.10 How will it displace currently used products / processes?

Introducing a new device to the medical device market is challenging. If it is new, much evidence is required to encourage users to adopt it. If it is an improvement on an existing device, effort is required to displace the existing device.

### 1.11 The Route to Market

The figure below shows the various steps involved, from early considerations, through project scoping to the actual project execution for the commercialisation of a new medical device. The process is generic and it may be necessary to adapt it to meet the requirements for specific products.

- **Risk Management** starts with product development and continues until product is withdrawn from market
- **Documentation Management** applies to technical, quality management system (QMS) and company documents
- **Verification** is to test that the product is built right
- **Validation** is to test that the right product is built, i.e. it fulfils its purpose
- **Trials** may occur earlier as needed (animal, human)
- **Tests during Validation** are third party compliance tests
- Electro-medical devices may require **third party compliance tests** before trials
- **Regulatory approval** may require QMS accreditation

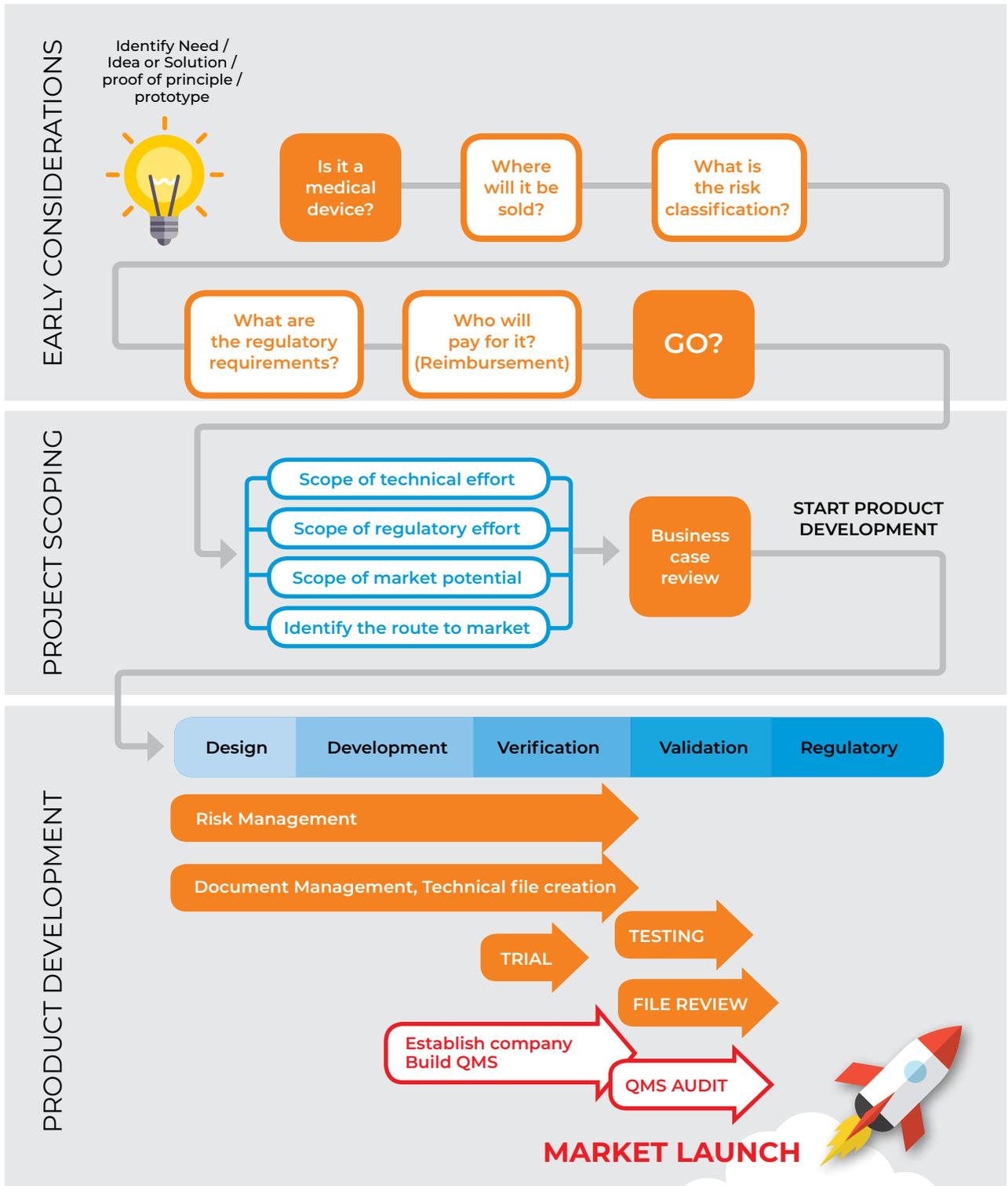
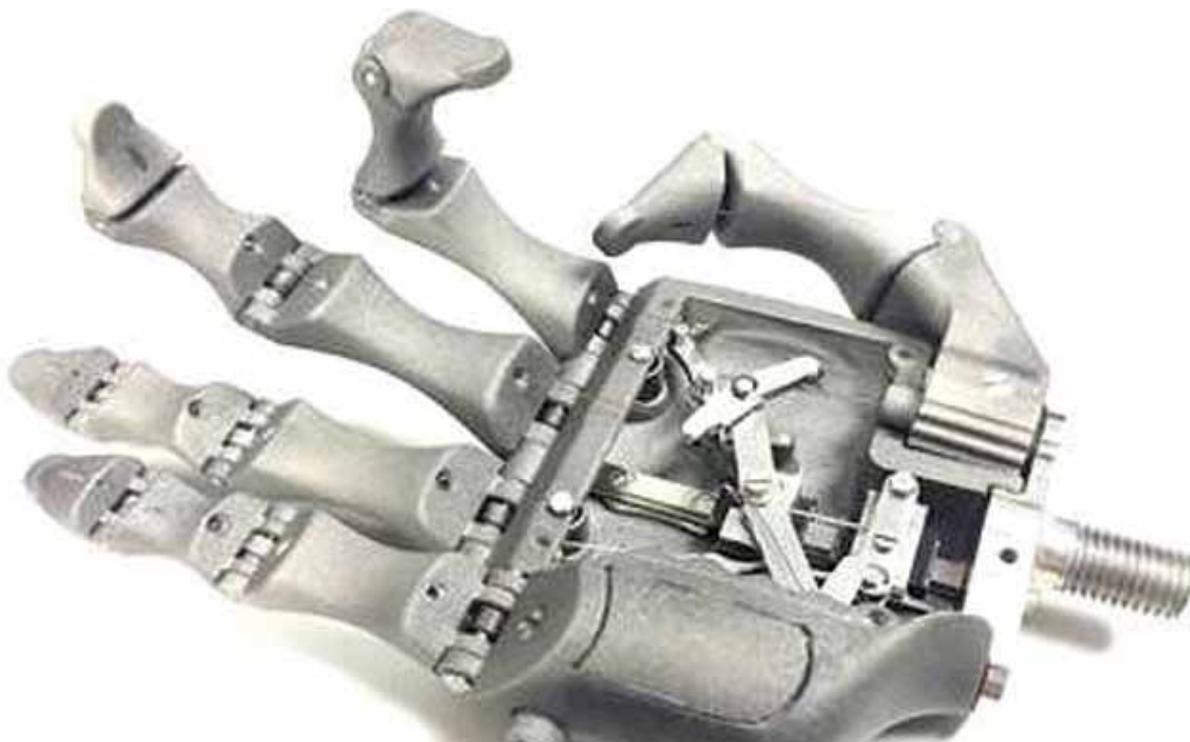


Figure 1: Technology Readiness Levels



The ideal scenario for the development of a device is for the university to partner with an independent company, with the appropriate regulatory infrastructure, that is willing and able to take on products, complete any development necessary, secure regulatory approval, and then place such products on the market.

If the nature of a product is similar to, but not in competition with a product that is already being manufactured and sold by a medical device company, and if the company is amenable, it may be possible to have that medical device company take on the new product as a joint venture, or on a “fee for service basis”.. Unfortunately, the medical device industry in South Africa is small, so opportunities to match new products to existing companies are severely limited.

In the absence of other options, it may be worth considering creation of a company to take the product forward, but this should only be done at a late stage, once most (if not all) technical and product risks have been addressed. The effort and cost to establish a company for one product is substantial, thus the product needs to have significant potential – this is a commercial decision.

An important factor to note is that the company whose name appears on the product (the legal manufacturer) is required to have the regulatory framework and hold the regulatory approvals. The legal manufacturer may outsource any or all aspects of manufacture, but the legal manufacturer remains responsible for the product.

## 2 TECHNOLOGY READINESS LEVELS

Technology readiness levels (TRL) are a method of classifying technology maturity as one moves from TRL 1, where the research had been initiated, to TRL 9 where the technology has been commercialised and in the market for some time.

RC&I has developed the table below, which provides definitions of technology maturity at each TRL in a number of different sectors. Funders are increasingly using TRLs to describe the target of the funding that they provide and also to understand the level of maturity that will be reached once a funded project has been completed.

TRLs are useful as one can classify a project within UCT and understand the steps that will

need to be taken in order to bring a product or service to market.

For medical devices, several of the rows in the table below may be applicable – the “science/engineering”, “software” and then “medical science”. Note that the “medical science” row is geared primarily for pharmaceutical products and with certain medical devices animal or pre-clinical trials may be limited or unfeasible. Cadaver trials sometimes take the place of animal trials. There are also not necessarily the number of phases of clinical trial that one finds with pharmaceutical products.

TRLs were conceived by NASA and their current nine-level scale has gained wide acceptance. You can read more on Wikipedia<sup>1</sup>.

Level	TRL 1	TRL 2	TRL 3	TRL 4	TRL 5	TRL 6	TRL 7	TRL 8	TRL 9
Science & Engineering	Basic Idea	Concept Developed	Experimental Proof of Concept	Lab Demonstration	Lab scale validation (early prototype)	Prototype demonstration	Capability validated on economic runs	Capability validated over range of parts	Capability validated on full range of parts over long periods
				Component and/or system validation in laboratory environment	Laboratory scale, similar system validation in relevant environment	Engineering/pilot-scale, similar (prototypical) system validation in relevant environment	Pilot system demonstrated	System incorporated in commercial design	Proven system ready for full deployment
Software			Software to test and evaluate basic concepts on simple model problems representative of final need.	Escalate model to more realistic representation of industrial system. Confirm basic formulation.	Model contains all major elements of need. Solve industrial strength problems by code developers OR achieve functionality by expert users. Document performance. GUI.	No specialist intervention required from programmers/developers. This includes basic GUI interface. If required, programming to be according to ISO standards.	Install, run and evaluate software in actual goal environment (e.g. prospective client's computers). Demonstrate use by clients	Evaluation done by target representative clients on representative hardware platforms. Complete GUIs, users manuals, training, software support etc. Typical user driven “bug hunting”	Product proven ready through successful operations in operating environment.
Medical Science	Basic Research		Preclinical Research		Late Preclinical Research	Phase I Trials	Phase II Trials	Phase III Trials	Phase IV Trials
Phase	Research			Translation/Development				Commercialisation	

Figure 2: Technology Readiness Levels

<sup>1</sup> [https://en.wikipedia.org/wiki/Technology\\_readiness\\_level](https://en.wikipedia.org/wiki/Technology_readiness_level)

## 3 ROLE OF THE TECHNOLOGY TRANSFER OFFICE / RESEARCH CONTRACTS & INNOVATION (RC&I)

The Research Contracts and Innovation Department (RC&I) acts as the liaison between UCT's research community and the private sector with regards to intellectual property, commercialisation and business development activities.

RC&I has helped to transfer numerous technologies from the university laboratories to industry both locally and internationally. RC&I provides three key areas of support:

1. **IP Protection:** Assistance with the screening of research outputs and the protection of intellectual property (IP) generally through patenting;
2. **Technology Development (Innovation):** Fundraising to support the maturation of the technology, but outsourcing where necessary and moving the project through the various Technology Readiness Levels (TRLs); and
3. **Technology Transfer / Commercialisation:** Understanding the specific market that a medical device will be entering (e.g. competitor devices, etc.), marketing or advertising the IP both generally and to identified targets, e.g. to companies whose product portfolios your device will complement.

### Gate Review

For effective innovation, three parallel processes need to be managed holistically to keep them synchronised. These are: technology development, intellectual property protection and commercialisation (which includes market research).

They need to be matured simultaneously as they impact on one another, e.g. knowledge of potential international markets will inform the patenting strategy, identifying the countries in which patents should be applied for to maximise IP value. Knowledge of a market will also influence technology development, e.g. scale of manufacture, quality or regulatory entry barriers (e.g. clinical trials, certification), etc.

RC&I has established and is refining a stage-gate process, largely driven by the stages of the patenting process (Figure 3), to review these areas and guide prudent spending of UCT's patent budget.

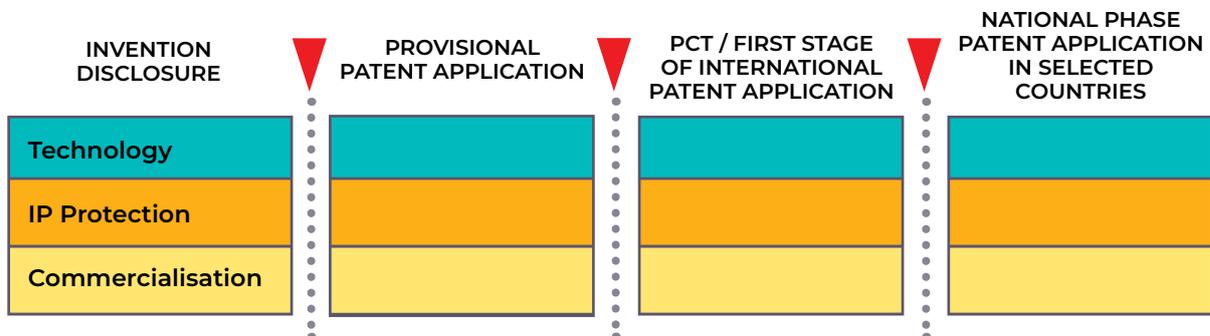


Figure 3: UCT Stage-Gate Process Aligned with Patenting Stages

## 4 INTELLECTUAL PROPERTY (IP) PROTECTION

RC&I assists researchers with the identification, review and protection of IP arising from their research and liaises with patent attorneys who are appointed by RC&I to prepare and file patent applications and manage the patent examination process. UCT has funding to support IP protection (which is supplemented by the National IP Management Office (NIPMO)) that is administered by RC&I.

### 4.1 Patents

To be patentable, the invention needs to meet three criteria:

- **Novel** - this means that the invention is new and has never been disclosed publicly (even by the inventor!), e.g. through journal publications, conference presentations and posters, online web postings or thesis examination. Discussions held with collaborators, contractors or potential commercial partners need to be under the protection of a non-disclosure agreement (contact RC&I and we will ensure that one is put in place if necessary). The invention must also not have been anticipated and publicly disclosed by anyone else or be found in general or patent literature.
- **Inventive** - this is perhaps the most difficult aspect as it is subjective. Essentially it means that the invention is not 'obvious' to a person skilled in the art, i.e. skilled in that particular field. This can generally be regarded as a technician who would typically be carrying out routine tasks.
- **Useful** - this means that there is 'industrial' application and is generally easily met.

RC&I manages patenting on behalf of UCT and more information on patenting is provided in the UCT Inventors Guide<sup>1</sup>.

Following disclosure of an invention to RC&I the patent application process involves the filing of a provisional patent (which runs for 12 months), filing of a Patent Co-operation Treaty (PCT) international patent application (which lasts for 18 months) and finally a once-off selection of regional and national phase applications which, following successful examination where applicable, result ultimately in granted national patents.

A patent's lifespan is 20 years, and this runs from the time of filing the full application (most commonly this is the PCT filing).

### 4.2 Registered Designs

A registered design is cheaper and more easily attained than a patent and it protects the way that a product looks. Often the registration can be restricted to a key 'critical' element of the device.

In some territories, such as South Africa, one has two types of designs that may be registered (and one can register both types for a specific product):

1. **Aesthetic Designs** – which relate to how the product looks, e.g. the shape of a bottle; and

<sup>1</sup> [http://www.rci.uct.ac.za/usr/rcips/ip/inventors\\_handbook.pdf](http://www.rci.uct.ac.za/usr/rcips/ip/inventors_handbook.pdf)

2. **Functional Designs** – protect the appearance again, but here the design features enable the device to function in a particular way, e.g. a tamper-proof tear strip component of a container's lid.

Designs are dimensionless and also do not prescribe its use, or materials of manufacture. In contrast, often all of these parameters can be defined and restricted in a patent.

The drawbacks of designs are that they have a shorter span of protection than patents and also competitors may be able to modify the design sufficiently so that their product does not infringe your registered design – particularly possible in a heavily congested product space.

Patents are stronger than designs in that they protect the broader concept that can be implemented in a number of different ways, whereas designs are specific to one implementation. However, it is useful to protect against direct copying.

### 4.3 Copyright

Software is becoming an increasingly common element of medical devices and, in certain instances, can even be regarded as a medical device in its own right. For example, the UK's Medicines and Healthcare products Regulatory Agency (MHRA)<sup>1</sup> has classified image analysis software used to sharpen x-ray images as a medical device, but a patient management system would not be.

Software is always protected by copyright, which subsists automatically and does not need to be specifically registered. Where programming has been outsourced, it

is important to ensure that the software is properly assigned to the company, or university, so that the software is ultimately owned as part of the product.

One also needs to take care when using opensource software from two perspectives: firstly, licenses generally compel you to release the code if your device is commercialised; and secondly, if code is taken from several sources it can be problematic as not all of the licensing requirements are congruent and one can face the added expense of re-writing code so that it can be released under one license.

Copyright is also limited to the specific expression, so it does not protect the approach or use. If somebody can prove that they have coded independently, they will not infringe the copyright and the same is true if one writes the code in a different language.

To prove whether code has been copied, developers sometimes include some redundant lines of meaningless code, which act as a "fingerprint" to determine whether code has been copied as nobody would have needed to include such code had they not been copying!

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<sup>1</sup> <https://www.gov.uk/government/publications/medical-devices-software-applications-apps>

# 5 REGULATION OF MEDICAL DEVICES

Inventions in a highly regulated industry, such as medical devices, face additional challenges and hurdles to reaching commercial success. As part of the process of evaluating commercial potential, the regulatory requirements must be considered since the regulatory burden may have an impact on the economic viability of a product.

The first step is to identify the target markets where the product may be sold, then consider the regulatory requirements of that market. The EU is a large market, with a well-defined set of regulatory requirements for all products (not only medical).

There are many markets around the world that accept CE marking, or where the work done to comply with CE marking is directly or partially applicable. Thus, consideration of the CE marking requirements is a good start to gauge the regulatory hurdles, effort, cost and timescales.

## 5.1 Overview of CE marking regulations

CE Marking applies to all products that are available on the market in the EU. Visit the EU<sup>1</sup> website to find out more.

In European law, the Medical Devices Directive 93/42/EEC – MDD or the In Vitro Diagnostics Directive 98/79/EEC – IVDD or the Active Implantable Medical Devices Directive 90/385/EEC - AIMD are the starting point and must be adhered to in all respects.

For medical devices, the starting point is the risk classification – as defined in Annex IX of the MDD.

**CLASS I** devices can be CE marked by self-declaration. The device must be registered with the Competent Authority of the country where the manufacturer has their place of business (or Authorised Representative for companies not based in Europe).

**CLASS Is** (sterile) and **CLASS Im** (measurement) devices require review of sterility / measurement aspects by a Notified Body.

**CLASS IIa** and **CLASS IIb** devices require review of the technical file by a Notified Body.

**CLASS III** devices require review of the design file.

For all classes other than Class I, CE marking can be done by Annex IV, V or VI - but these are limited. The most commonly used is Annex II – which requires a Quality Management System accredited to ISO 13485 – audited by a Notified Body.

For **IN VITRO DIAGNOSTICS**, there are 3 classes: General, List A and B. Devices that appear in List A or B (see Annex II of the IVDD), the most commonly used is Annex IV – which requires a Quality Management System accredited to ISO 13485 – audited by a Notified Body. Devices not listed are CE marked by self-declaration as for a class I medical device.

There are three requirements to achieve CE mark:

<sup>1</sup> [http://ec.europa.eu/enterprise/policies/single-market-goods/cemarking/professionals/index\\_en.htm](http://ec.europa.eu/enterprise/policies/single-market-goods/cemarking/professionals/index_en.htm)

- **Technical file** – describes how the product works, is manufactured and tested. Conformance to harmonised standards is required.
- **Quality Management System**
- **Clinical Evaluation** – based on literature or clinical evaluation or both – to prove that the device meets its claims, and that it is safe

Note that the above is a simplification of the process; the MDD/IVDD/AIMD should be consulted for details. Further, the MDD is being revised and will change in the near future. The regulatory environment worldwide is constantly changing, and generally becoming more stringent. A company running an ISO 13485 QMS is required to keep up to date with regulatory changes.

## 5.2 Overview of SA medical device regulations

Prior to 2016 only electro-medical devices required a licence for sale in South Africa and CE marking was a pre-requisite for this license. Medical devices with a medicinal component, even though they are classified as a medical device in Europe and other jurisdictions, are regulated as medicines in South Africa.

As of 24 Aug 2016, the new South African medical device regulations have started being implemented (this also covers In Vitro Diagnostics (IVDs)), and the promulgation of the revised Act 101 of 1965 (as amended) “Medicines and Related Substance Act” and Regulations will bring an end to the current scenario where non-electro-medical devices could be manufactured and used in South Africa without regulatory oversight.

A new regulatory entity is being created, the South Africa health Products Regulatory Authority (SAHPRA), which will absorb the existing MCC. The regulations and guidance documents are available on the MCC website<sup>1</sup>.

In terms of the new regulations, all companies that handle medical devices – manufacturers, importers, distributors, exporters – must be licenced. Devices are classified into four risk classes A to D, with D being the highest risk. The licence requires listing of devices that the company handles, appointment of an Authorised Representative, and a quality management system in place at the company (does not need to be certified). The fee for a licence is R21 000 for a manufacturer, R13 000 for an importer/distributor/exporter.

### Classification of Medical Devices in South Africa

CLASSIFICATION	LEVEL OF RISK
Class A	Low risk
Class B	Low-moderate risk
Class C	Moderate-high risk
Class D	High risk Where risk relates to the patient or to public health

For products in classes B, C and D regulatory approval from another jurisdiction (includes the United States of America, European Union, Australia or Japan) is required for the device to be marketed in South Africa. SAHPRA is establishing capacity to review and approve devices under their regulations, but this will take at least two years, so for the near future, regulatory approval in another market will be the quickest route to bring a product to market in South Africa.

<sup>1</sup> [www.mccza.com](http://www.mccza.com)

Compliance will be phased in. All devices are to be registered (including existing devices that are already being marketed in South Africa), starting with class D in Q3 of 2018, followed by class C in 2019.

The guidelines for the classification of medical devices and in vitro diagnostics that have been compiled by the MCC<sup>1</sup> contains useful decision trees. It is possible that more than one classification rule may apply to a device and the higher classification will be applicable.

A summary table that provides examples

of devices that fall into the different classes has been copied from the Regulations to provide some insight into the classification process.

The duration of use of the medical device is also a key parameter, with less than 60-minutes being considered “transient” (e.g. an injection needle), less than 30 days “short-term” (e.g. a drip) and more than 30 days “long-term” (e.g. a pacemaker). One can understand issues relating to infection, for example, or rejection by the body as the time increases.

Summary of Classification Process (Department of Health, Medicines Control Council)

If the device	then apply Classification Rule/s	Some examples are:	
is invasive - that is, the device penetrates the body through a body orifice or is inserted into the body during surgery	5, 6, 7 & 8 - classifications vary depending on intended purposes	surgical eye probe, ophthalmic knife, eye cannula, ear/nose/throat forceps, interanal tympanostomy tube, tongue depressor, intraoral x-ray sensor, oral gag, oral suction unit, thermometer, vaginal speculum, urethral bougie, anoscope, proctoscope, colonoscope, stomal peg, tracheostomy tube.	
is active - that is, the device depends on a source of energy for its operation and converts energy	9, 10, 11 & 12 - classifications vary depending on intended purposes	diagnostic x-ray sources, MRI, air driven surgical drills and saws, patient monitors, electronic blood pressure measuring devices, diagnostic ultrasound, electronic stethoscopes/thermometers, software, gas regulators, radioactive seeds, mechanical infusion systems.	
contains a medicine	13 - these devices are Class D	antibiotic bone cements, condoms with spermicide, heparin coated catheters, dressings incorporating an antimicrobial agent.	
is for contraception or preventing sexually transmitted diseases	16 - classifications vary depending on intended purposes	condoms, contraceptive diaphragms, contraceptive intra-uterine devices (IUDs), surgically implanted contraceptive devices.	
is for disinfecting, cleaning, rinsing or hydrating	15 - classifications vary depending on intended purposes	contact lens solutions, comfort solutions, disinfectants for haemodialysis devices and endoscopes, sterilisers to sterilise medical devices, washer disinfectors.	
not active and is intended to record x-ray diagnostic images	10(i) - these devices are Class B	x-ray films, photo-stimulable phosphor plates.	

<sup>1</sup> [http://www.sahpra.org.za/documents/91f9ddf48.05\\_Classification\\_Medical\\_Devices\\_IVDs\\_Jul16\\_v1\\_for\\_finalisation.pdf](http://www.sahpra.org.za/documents/91f9ddf48.05_Classification_Medical_Devices_IVDs_Jul16_v1_for_finalisation.pdf)

If the device	then apply Classification Rule/s	Some examples are:
contains viable OR non-viable animal tissues or derivatives	14 - these devices are Class D	biological heart valves, porcine xenograft dressings, catgut sutures, implants and dressings made from collagen, intra-ocular fluids, meniscus joint fluid replacement, anti-adhesion barriers, tissue-fillers based on hyaluronic acid derived from bacterial fermentation processes.
is a blood bag	2 - these devices are Class C	blood bags (including those containing or coated with an anticoagulant).
is an active implantable medical device	8 - these devices are Class D	implantable pacemakers, defibrillators and nerve stimulators.
is a mammary implant	8 - these devices are Class D	mammary/breast implants.
is not covered by any of the previous rules in this table	1, 2, 3 & 4 - classifications vary depending on intended purpose	devices intended to: <ul style="list-style-type: none"> <li>- collect body liquid where a return flow is unlikely</li> <li>- immobilise body parts and/or to apply force or compression</li> <li>- channel or store substances that will eventually be delivered into the body</li> <li>- treat or modify substances that will be delivered into the body</li> <li>- dress wounds.</li> </ul>

### 5.3 Regulation in the USA

The United States of America is the largest medical device market globally (followed by China, Germany, Japan, France and Italy) and accounts for 40% of the spend on medical devices. The Food and Drug Administration (FDA) regulate medical devices and they have a specialised agency within the FDA that deals with devices specifically, the CDRH (Centre for Devices and Radiological Health). They have three classes of devices: I, II and III. An agent needs to be appointed in the USA, with whom the FDA will liaise.

The FDA does not accept ISO 13485 and has the US Quality System Regulation (QSR) which covers Good Manufacturing Process. Emergo, a consulting firm, provides useful resources, videos and information that can be downloaded from their website<sup>1</sup>.

The submission to the FDA includes a technical submission which covers test results relating to the safety and efficacy of the device. Most Class II devices go through the 510(k) process and really innovative new devices as well as class III devices need to go through the Pre-Market Approval process (PMA), which requires clinical data to be submitted. Typically, approval timelines are dependent on the class that is assigned to the device.

The Premarket Notification or 510(k) is a premarket submission that is made to the FDA to provide information as to the device's safety and efficacy and its similarity to a device that is already on a market (substantial equivalence claim)<sup>2</sup>. There are some devices that are exempt from the 510(k) requirements – typically this is where one is selling unfinished devices, the device is not being

<sup>1</sup> This service provider is not endorsed by UCT and content is provided for information purposes only [www.emergo.com](http://www.emergo.com)  
<sup>2</sup> <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm>

marketed or commercially distributed (e.g. during clinical trials of the device) or you are merely repackaging an approved device. If a device is made in South Africa and imported into the USA, the manufacturer in South Africa would require a 510(k), but the distributor in the USA would be exempt. There is no form for the submission, rather a list of requirements and, once approved, the FDA does not issue the company with a certificate, but rather lists the device and company on their website.

Substantial Equivalence (SE) is where the new device is at least as safe and effective as a device that is being legally marketed in the USA (the 'predicate' device).

#### 5.4 Requirements for trials

For CE marking (and FDA 510(k) clearance), clinical evidence is required to prove:

- the benefits of the device outweigh any risks posed
- the efficacy of the device.

Such clinical evidence may either be literature, or a clinical trial, or a combination<sup>1</sup>. The composition and extent of clinical evidence will be unique for each device, but in general, a new device or new procedure will almost certainly require a clinical trial, the extent depending on the novelty of the device or procedure.

As mentioned earlier, it is essential to scope the clinical evidence requirement as early as possible. It is also essential to ensure that the trials are conducted according to the requirements of the regulatory authorities. This approach should be followed from early stages, to maximise the potential to use data collected in early trials.

For medical devices in Europe, ISO 14155<sup>2</sup>, MEDDEV 2.7.1<sup>3</sup> and Annex X of the MDD must be followed.

#### FDA Definition of Substantial Equivalence

A device is substantially equivalent if, in comparison to a predicate it:

- has the same intended use as the predicate; **and**
- has the same technological characteristics as the predicate; **or**
- has the same intended use as the predicate; **and**
- has different technological characteristics and does not raise different questions of safety and effectiveness; **and**
- the information submitted to FDA demonstrates that the device is at least as safe and effective as the legally marketed device.

For *in vitro* medical devices in Europe, the WHO offers useful guidance<sup>4</sup>.

Engagement of a Clinical Research Organisation is not a requirement – most medical device companies conduct their own trials.

#### 5.5 Ethics considerations

All work on humans and cadavers requires ethical approval, usually managed by the hospital or academic institution. The Department of Health has produced Good Clinical Practice Guidelines for trials involving human participants in South Africa<sup>5</sup>. Registered medical professionals are required to take responsibility for tests and studies on humans. This applies in all health care settings. This is dealt with in more detail in Section 7.

<sup>1</sup> Fundamentals of Clinical Trials. Friedman LM, Furberg CD and DeMets DL. 3<sup>rd</sup> Ed. Springer.

<sup>2</sup> <http://www.iso.org/iso/home/store.htm>

<sup>3</sup> [http://ec.europa.eu/growth/sectors/medical-devices/documents/guidelines/index\\_en.htm](http://ec.europa.eu/growth/sectors/medical-devices/documents/guidelines/index_en.htm)

<sup>4</sup> [http://www.who.int/diagnostics\\_laboratory/evaluations/en/](http://www.who.int/diagnostics_laboratory/evaluations/en/)

<sup>5</sup> <http://www.kznhealth.gov.za/research/guideline2.pdf>

## 5.6 First steps to creating a design history file

Regardless of the eventual route to market (through an existing company, or new company), it is well worth the minimal additional effort to start creating a design or technical file for the product. Even without a formal quality management system, it is possible to set up and follow a system to create and manage documentation to support product development.

Such a system would have a framework of the typical documents required for a technical file, a review and approval process, a structured and controlled document storage facility, and some oversight to ensure that the procedures are followed. All of this is sound engineering practice – not specific to medical devices or regulations.

A further very important step is to identify which standards apply to the device and to ensure that the design will meet the standards. Identification of applicable standards requires careful searches through standards databases (ISO<sup>1</sup>, IEC<sup>2</sup>, EN<sup>3</sup> and others for the applicable markets).

## 5.7 Indicative costs for regulatory approvals

The cost of securing medical device approvals is substantial, and likely to increase as the regulatory requirements are generally increasing.

For a company in South Africa, we face the additional hurdle of absence of regulatory approvals in our home market. Many countries around the world will only accept a product from South Africa if the product is successful in South Africa, and we can provide a Free Sales Certificate (FSC) from regulatory authorities in South Africa. Currently, this is not possible – many companies present an FSC from Europe which can be secured for a fee.

An important factor to note is that the company whose name appears on the product (the legal manufacturer) is required to have the regulatory framework and hold the regulatory approvals. The legal manufacturer may outsource any or all aspects of manufacture, but the legal manufacturer remains responsible for the product.

### Indicative costs and timelines of regulatory approval

ITEM	COST	TIME	NOTES
Set up QMS (ISO 13485)	6 – 12 person months	6 to 12 months	Can be shortened by use of consultant, at a cost of R80 000 to R200 000
Create technical file	3-9 person months	1 to 6 months	Over and above development effort
QMS audit	€5,000 to €15,000	1 month	Depends on company size
Safety testing (electro-medical)	€20,000 to €60,000	2 to 4 months	Depends on product type
Biocompatibility testing	€20,000 to €50,000	1 to 2 months	Depends on tests
Technical file audit	€4,000 to €10,000	1 to 2 months	Depends on risk class

<sup>1</sup> <http://www.iso.org/iso/home/store.htm>

<sup>2</sup> <http://webstore.iec.ch/>

<sup>3</sup> [http://ec.europa.eu/growth/single-market/european-standards/index\\_en.htm](http://ec.europa.eu/growth/single-market/european-standards/index_en.htm)

## 6 ETHICS AND OTHER PERMISSIONS

All clinical investigations should be conducted in accordance with the ethical principles embedded in the Declaration of Helsinki<sup>1</sup>. The principles described here are the rights, safety and well-being of human subjects which are most important and should prevail over the interests of science and society.

At UCT there is a Human Ethics Research Committee, as well as an Animal Ethics Research Committee which need to approve the relevant pre-clinical or clinical trials.

The following has been adapted from the UCT Research Ethics Code for Research Involving Human Participants<sup>2</sup>.

UCT adheres to standards and principles under which its investigators must aim to conduct research with scholarly integrity and excellence, with attention to social responsibility, and with respect for the dignity, self-esteem, and human rights of the individuals who may be involved or are affected by research.

The University aspires to articulate standards of conduct and procedures that ensure proper accountability. In the pursuit of its ideals, the University subscribes to the interdependent principles of scholarly responsibility, integrity and honesty, of human dignity and of academic freedom and openness.

UCT affirms the requirement that all research involving human participants be subject to prior ethics review, according to faculty guidelines and the standard operating procedures of the ethics committees charged with the review and oversight of research. This is of specific relevance to investigators in health sciences and who may pursue novel medical agents, drugs, therapies, and devices with implications for intellectual property. For purposes of ethics and responsible conduct, investigators assume broad and full

responsibility for the following:

- The quality and originality of their research questions (avoiding both waste and redundancy, and anticipating needs for reliability, replicability, and verification);
- The design, methodology and execution of their research;
- The development of a research plan that yields a high degree of validity;
- The identification, where appropriate, of alternative hypotheses, methodologies, and interpretations of data;
- The dissemination of findings, and their limitations, to ensure accessibility and opportunities for peer-review.

When planning research, researchers should consider and articulate the appropriateness and foreseeable consequences in their research proposal. In health science research, this often requires consideration of the full range of adverse events and problems that may occur. Furthermore, the researcher will likely be required to distinguish between those that are likely, serious, and relevant to the choice of participation, and merit explanation in study materials.

Researchers should also keep in mind the requirement of prior research ethics review and clearance when planning the timeframes for their research. Ethics approvals may not be obtained retrospectively.

Ethics considerations for research participants are paramount. Research participants should not be harmed in the course of or as a consequence of research, except in those cases in which the research participants have no moral claim not to be harmed in the ways that the research may harm them.

Researchers wishing undertake research that may harm participants must demonstrate that,

<sup>1</sup> World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013 Nov 27;310(20):2191-4.  
<sup>2</sup> [http://uct.ac.za/downloads/uct.ac.za/about/policies/humanresearch\\_ethics\\_policy.pdf](http://uct.ac.za/downloads/uct.ac.za/about/policies/humanresearch_ethics_policy.pdf)

according to faculty guidelines, the participants have no moral claim not to be harmed in the relevant ways.

Risks of harm must be minimised (though not necessarily eliminated as this may not be possible), and balanced against benefits.

Specifically, investigators must minimise or avoid exposure of participants to foreseeable legal, physical, psychological, or social harm or suffering that might be experienced in the course of research. The risk of harm and the likelihood of direct benefit to participants must be discussed as part of the consent process. Researchers should be especially sensitive to the interests and rights of vulnerable populations such as minors, elderly persons, very poor and/or illiterate persons.

As a guiding principle in human subjects research, participants should give informed, voluntary consent, when appropriate, to participation in research. This includes respect of the right of individuals to refuse to participate or, having agreed to participate, to withdraw their consent at any stage without prejudice.

Investigators should provide information that explains the aims and implications of the research project, the nature of participation and any other considerations that might reasonably be expected to influence their willingness to participate. This information must be provided in language that is understandable to the potential participants. While the importance of informed consent does not preclude research that uses observation or deception as part of its methodology, such research must be justified its protocol and comply with best practices and ethics codes of its scientific or scholarly discipline.

Finally, the privacy and confidentiality interests of participants must be taken into account in the research process. Information that may identify individual persons should not be used in research findings unless the person has expressly agreed to its release, having had the opportunity to consider the implications of such release.

Future uses of data and/or biospecimen samples that may be obtained in the course of health science research are especially and increasingly important considerations that bear on innovation. They relate to the responsible conduct of research defined as responsibility and care for the relationships on which the discovery and dissemination of knowledge depends, and the resonance between the conduct of research and the context(s) in which the research takes place and/or has effect.

No research may be conducted on human subjects without the signed permission of a Human Research Ethics Committee (HREC)<sup>1</sup>.

The HREC will consider many aspects of the study including the following principles:

1. Improper influence or inducement
2. Participant informed consent, confidentiality and privacy
3. Compensation and additional health care
4. Responsibilities of the personnel and their designated roles during the investigation.
5. Study design and participant inclusion. It is considered unethical to carry out an inappropriate study design in order to answer the question.
6. If National and Regional HREC requirements are less strict than the International requirements for the project, then the stricter requirements will be upheld.

In addition to ethical approval, if the study is to be carried out on patients at a provincial hospital, it needs to be approved<sup>2</sup>.

This may all seem like a daunting process but there are many people with the expertise to assist you if you are new to clinical trials. There are also flow charts and tools designed to make your journey easier. The steps that are necessary to take a study from conception to implementation at UCT as described in the Clinical Research Centre (CRC)'s toolkit<sup>3</sup> and the CRC can provide further information and assistance. The CRC is also available to assist non-UCT parties with their trials.

<sup>1</sup> <http://www.health.uct.ac.za/fhs/research/humanethics/about>.

<sup>2</sup> <http://www.crc.uct.ac.za/crc/services-facilities/regulatory>

<sup>3</sup> <http://www.crc.uct.ac.za/crc/toolkit>

# 7 SEED AND INNOVATION FUNDING

## 7.1 Seed Funding

Various forms of seed funding are available within UCT and administered by RC&I. These include the PreSeed Fund and the TIA Seed Fund, which is administered within UCT.

Often the PreSeed funding amounts, whilst modest (Explorer: R20k, Concept: R100k), can enable initial prototypes to be built (e.g. 3-D printed) and parts to be obtained. More extensive trials can be supported using the TIA Seed Fund, which currently offers grant funding of up to R650 000 per project and

often supports animal trials in particular.

Regular calls also go out on the Research Funding mailgroup.

Information regarding current seed funding can be found on the RC&I website<sup>1</sup>.

## 7.2 Innovation Funding

Multimillion-Rand-level funding can be sourced from a number of different organisations, both in South Africa and overseas, with funders typically having a particular focus.

### Useful sources of funding or guidance include:

- **The Technology Innovation Agency (TIA):** <http://www.tia.org.za>
- **The South African Medical Research Council (SAMRC)** through its **Strategic Health Innovation Partnerships (SHIP)** unit, which is a partnership between the SAMRC and the Department of Science and Technology.

They also create pools of funding that rely on co-investment by overseas organisations to leverage South African funding.

SHIP funds innovation projects focused on the development of new drugs, treatments, vaccines, medical devices and prevention strategies: <http://www.samrc.ac.za/innovation/strategic-health-innovation-partnerships>

- **Bill & Melinda Gates Foundation:** [www.gatesfoundation.org](http://www.gatesfoundation.org)
- **The Global Health Innovation Accelerator (GHIA)** is a partnership between the SAMRC and PATH, who are an international non-profit organisation. PATH can provide useful market information and advice on how to enter the public health sector in different markets.
- **Jembi Health Systems NPC**, a nonprofit organisation that works in developing countries in Africa and focuses on the development of eHealth and health information systems (HIS) <https://www.jembi.org>.

They recently partnered with the SAMRC to create the Collaborating Centre for Digital Health Innovation – the CC-DHI. The CC-DHI will bring together digital health researchers, innovators and entrepreneurs from universities, private industry as well as public enterprise to assist in aligning and harmonising digital health development for sustainable impact in public health.

- **Wellcome Trust:** offers innovator awards that range between £500k to £750k for multidisciplinary collaborations for up to 36 months (usually 24) that support the development of devices as well as diagnostics:

There is also a “Digital Technologies” programme where technologies include Artificial Intelligence (AI), machine learning, data analytics and informatics, or virtual reality and involve internet of things (IoT) networks and sensors: <https://wellcome.ac.uk/funding/innovator-awards-digital-technologies>

- **Partnerships with large medical device companies**, typically following their licensing of UCT IP.

<sup>1</sup> <http://www.rci.uct.ac.za/RC&I/fundinnov/overview>

## 8 COMMERCIALISATION FROM A UCT PERSPECTIVE

UCT approaches technology licensing and commercialisation on a case-by-case basis and can adopt a variety of strategies to achieve this, such as entering into both exclusive and non-exclusive license agreements, or considering the outright sale of its intellectual property, as well as taking equity (i.e. holding shares) in start-up- and spin-out companies depending on the circumstances.

We also look for potential partners who are able to assist the innovation process through technology development, especially through scale-up, clinical trials and regulatory approval. We often form consortia and partnerships to access funding to support these initiatives, successfully commercialising our technologies in the marketplace.

One of our core objectives is to stimulate the growth of the South African economy by fostering small business development and/or the creation of jobs through the commercialisation of UCT's intellectual property.

In the pharma sector, however, UCT needs to partner with biotechnology- or large pharmaceutical companies to take the new drug to market, due to the level of investment that is required. With medical devices, one is more reasonably able to take a device through to market in South Africa.

RC&I would negotiate an agreement with the commercial partner, which could be in the form of:

- **An exclusive license** to the intellectual property for commercial exploitation – this can be further limited to a particular field (e.g. type of disease) or a region (a particular territory where there is patent

protection). This would mean that the licensee would have the sole right to use the IP for commercial purposes. Note that UCT retains a right to continue to use the IP for research and teaching purposes.

- **A non-exclusive license**, which means one or more parties may have rights to the IP.
- **Assignment of the IP** - Although less frequent, it can sometimes be possible to transfer the ownership of the IP to the other party.

By virtue of the terms of some research contracts, IP may also be automatically assigned to the funder, which is another mode of technology transfer.

In other cases, a funder such as the Bill and Melinda Gates Foundation (BMGF) may have specific requirements in terms of commercialisation of the IP emanating from their funded research (in the case of BMGF it is according to their "Global Access Policy").

Assignment Agreements usually include a single payment for the IP at the time of signing the contract, although instalments can be negotiated that staggered payments are made on completion of certain milestones (e.g. completion of different stages of clinical trials).

Licenses tend to be based on royalties pegged as a certain percentage of invoiced sales. Inventors may also be interested in forming spin-off companies based on the IP that they have developed. RC&I will assist with them with developing Business Plans and conducting market research.

RC&I Pre-Seed funding is available to support these activities, which often require the advice of consultants.

# 9 UCT SPIN-OFF COMPANIES

Three UCT spin-offs are profiled below and their “journey” up until 2014 is shown, which provides some insight into their development.

They have, at the time of writing in 2018, all continued onwards – encountering and passing other hurdles and achieving new successes. The CEO of CapeRay writes an informative blog that is updated every Friday (without fail!) and is a great resource for entrepreneurs as many of the issues that you are likely to encounter have been the topic of an article.

Catch up on the latest developments of CapeRay Medical and Strait Access Technologies on their websites: [www.caperay.com](http://www.caperay.com), [www.straitaccesstechnologies.com](http://www.straitaccesstechnologies.com). Antrum Biotech has just raised a significant amount of THRIP funding but are currently not maintaining an active website.



## ANTRUM BIOTECH (Pty) Ltd

### FOUNDERS



Prof Keertan Dheda



Mrs Khilona Radia

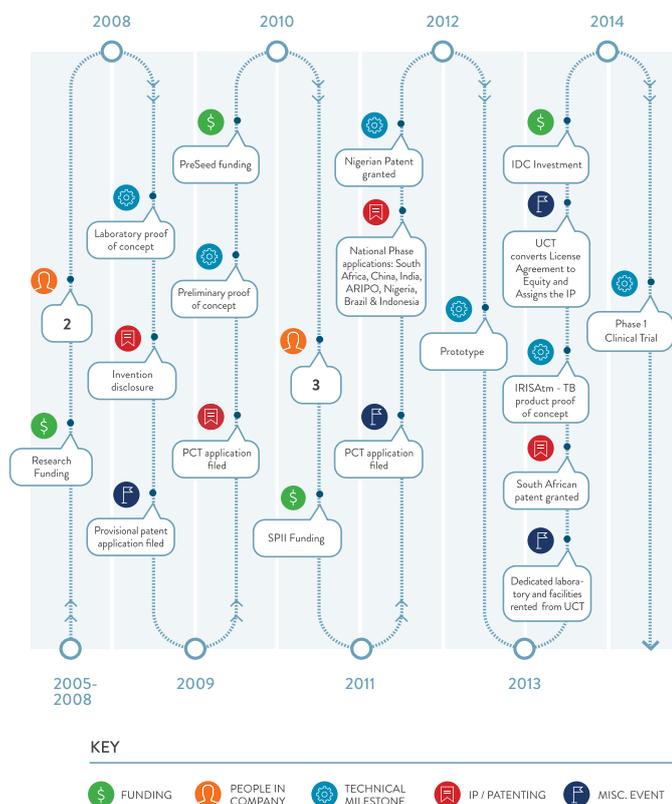
Antrum Biotech (Pty) Ltd was founded in 2008 as a spin-off company from the University of Cape Town to support the need for field-friendly rapid TB diagnostic tools in developing countries.

Antrum Biotech's strategic areas of focus are:

- The identification and exploitation of novel diagnostic biomarkers relating to TB and other poverty-related diseases.
- The incorporation of these biomarkers into appropriate testing platforms.
- The marketing and distribution of these tests throughout Africa and, where relevant, to the rest of the world through international partners.

The founders are Prof Keertan Dheda, a leading pulmonologist and TB physician, and Khilona Radia, a globally experienced business manager, who currently manages the company as CEO.

Antrum's first product, IRISA, a groundbreaking diagnostic tool for the detection of Extra-Pulmonary TB (EPTB), will enter the clinical trial phase during 2014. It is the first point-of-care test for EPTB that can be used at the patient bedside and deliver a rapid accurate result so treatment can begin immediately.



# CAPERAY MEDICAL (Pty) Ltd

## FOUNDER

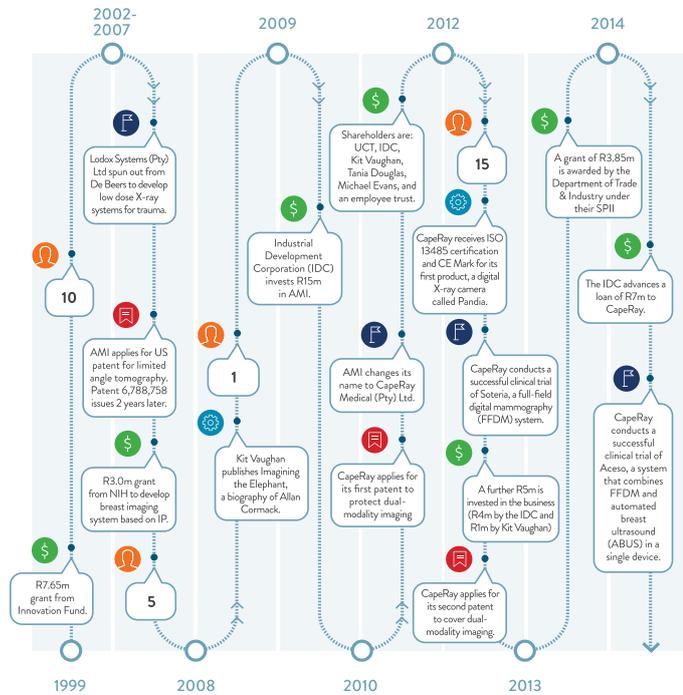


Prof Christopher (Kit) Vaughan

CapeRay designs, develops, manufactures and supplies medical imaging equipment for breast cancer diagnosis. Through expertise in various branches of engineering - including biomedical, computer software, electronic, mechanical and industrial – CapeRay has designed and developed the PantoScanner.

The prefix “panto-” comes from Greek and means “all”. The PantoScanner will be produced and sold in three variations:

1. an entry-level system, known as Soteria (the Greek goddess of deliverance from harm), which is a full-field digital mammography (FFDM) system based on an X-ray scanner;
2. a dual-modality system, known as Aceso (the Greek goddess who personifies the healing process), which combines an FFDM X-ray machine with automated breast ultrasound (ABUS) technology; and
3. a top-of-the-range system, known as Aegle (the Greek goddess who personifies the glowing health of the human body), which combines FFDM, ABUS and digital breast tomosynthesis (DBT), thus enabling the simultaneous capture of 3D images of the breast using an X-ray machine and an ultrasound machine.



KEY

- FUNDING
- PEOPLE IN COMPANY
- TECHNICAL MILESTONE
- IP / PATENTING
- MISC. EVENT



A clinical trial was done with Aceso model during April and May 2014.

The founder of CapeRay is Prof Kit Vaughan, a tenured professorship at the University of Virginia, and 14 years as the Hyman Goldberg Chair in Biomedical Engineering at the UCT.

## STRAIT ACCESS TECHNOLOGIES (Pty) Ltd

Strait Access Technologies (SAT) has designed a delivery device that can implant heart valves without the need for complicated surgery or high-tech operating theatres with advanced imaging systems and surgical teams. This percutaneously-delivered heart valve can be implanted in the simpler operating theatres common in many African countries. The device is the subject of multiple patents and, whilst it is ideal for the developing world, it also has tremendous potential in the developed world where higher prices can be achieved.

In addition to the device discussed above, SAT has also developed a plastic heart valve which is ideally suited for young patients as it will last longer in their bodies. It is also cheaper to manufacture than the currently available valves made from animal tissue.

The key people behind SAT are all acknowledged world leaders in their fields. Prof Peter Zilla is head of the Department of Cardiothoracic Surgery at UCT. Assoc Prof Deon Bezuidenhout is a polymer scientist who specializes in biomaterials. The third founder of the company is Prof David Williams who is one of the world's leading experts in biomaterials and implantable medical devices.

### FOUNDERS



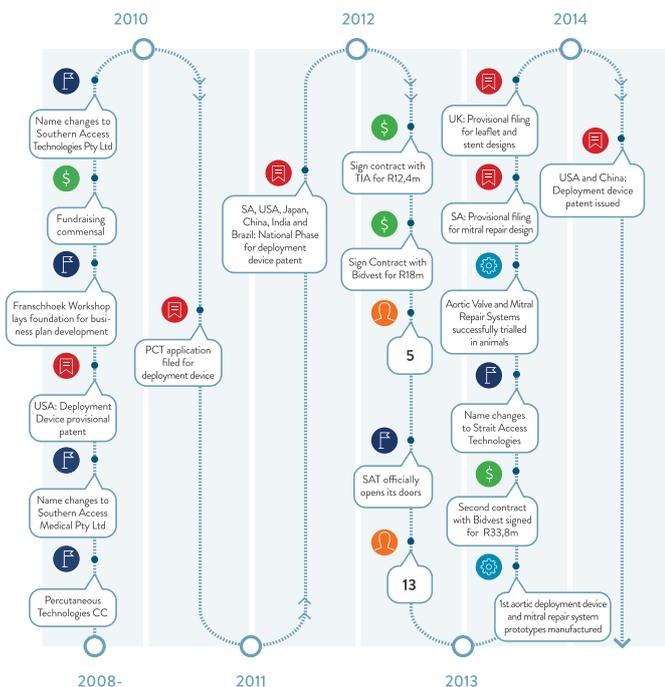
Prof Peter Zilla



Prof David Williams

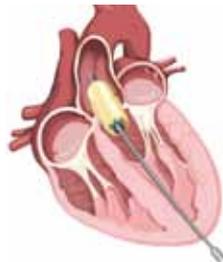
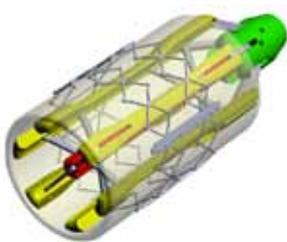


Assoc Prof Deon Bezuidenhout



### KEY

\$ FUNDING   
 Ω PEOPLE IN COMPANY   
 ⚙️ TECHNICAL MILESTONE   
 📄 IP / PATENTING   
 📅 MISC. EVENT







UCT appreciates and acknowledges the support that the National Intellectual Property Office (NIPMO) provides in terms of patenting rebates received from the IP Support Fund, resourcing of Research Contracts & Innovation (RC&I) and for the publication of this book.



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