

## **Product Development Lessons from the Eyeborn Experience**

by

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### **Abstract**

Eyeborn<sup>®</sup> is an innovative hydroxyapatite orbital implant used to replace the eyeball of a patient who has lost an eye. A prosthetic eye cap is fitted on the front of the Eyeborn<sup>®</sup> implant, restoring the patient's appearance and improving his quality of life. The product was developed with funding from the South African Innovation Fund.

This paper shares some of the lessons learnt during the development of the Eyeborn<sup>®</sup> implant and the technology transfer to a South African SME, Cerdak (Pty) Ltd. Aspects, such as the concurrent engineering approach, which required early involvement of all players, resulted in continuous inputs of medical experts. Other activities such as clinical trials, patenting, development of the commercialisation model, identification of a marketing company and a manufacturer, accessing funding and contracting were planned well in advance. The technology transfer process included compliance with international quality system standards and the acquisition of the CE Mark for the product. Timing of the market launch and subsequent complications regarding provision in market demand during the technology transfer phase posed special challenges. In this regard the role of the marketing company, VisiCare (Pty) Ltd, is discussed.

### **Introduction**

If an eye is severely damaged due to trauma or disease and is irreparable, it is removed to prevent the devastating development of a sympathetic deterioration in the remaining good eye. This would result in bilateral blindness. The patient is then left with a disfiguring empty socket, which is both unsightly and draws attention to the disfigurement. Until recently, a glass or silicone sphere was implanted into the socket. This is a cheap but primitive method to diminish the disfigurement. Orbital trauma with ruptured globes leads to the loss of sight and the eye in 200 patients annually at St John Eye Unit at Chris Hani Baragwanath Hospital in Johannesburg.

The problems mentioned above have largely been solved with the use of either coralline hydroxyapatite (HA) or synthetic hydroxyapatite sheres. These spheres are implanted into the orbit. Because they are porous they allow blood vessels to grow into the orbital implant, which prevents migration.

Furthermore, as they become fully vascularised they can fend off infection. They are also biocompatible and excite no immune response.

Until recently only imported coralline hydroxyapatite spheres were available. However, the imported implants cost more than R4000 each. A large percentage of people who lose an eye are disadvantaged patients at state hospitals. The state cannot afford to procure this imported implant. Given this predicament, a research and development team at the CSIR in Pretoria has successfully developed an orbital eye replacement implant that costs less than half of similar products from abroad, while providing increased comfort to patients. The synthetic hydroxyapatite spheres have the advantage of not only being cheaper than coral, which is a limited natural resource, but also of not needing a mesh or scleral cover to prevent extrusion.

Funding was made available from the Innovation Fund in 2000 for the development of this orbital implant. The formal launch of Eyeborn® (the trade name of the product) as a commercial product at the annual congress of the Ophthalmological Society of Southern Africa in February 2004 marked the completion of the full process from concept to successful product clinical evaluation. This was followed by a phase of technology transfer from the CSIR to the manufacturer, Cerdak (Pty) Ltd, which culminated in the awarding of the CE mark to Cerdak for production of the product in October 2006.

### **Product Development**

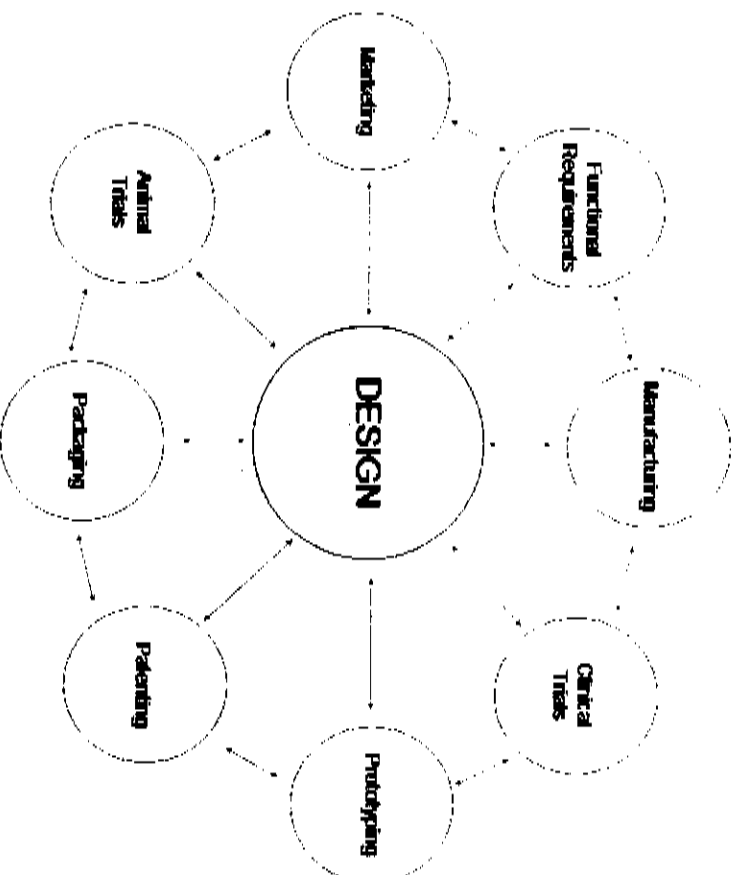
#### ***Concurrent Engineering***

The multidisciplinary nature of the orbital implant development demanded a concurrent engineering approach, especially regarding early involvement of all players. This design approach is illustrated in Figure 1. A consortium consisting of the CSIR, Meyer, König & Partners (MKP, members of the Pretoria Eye Institute) and the WITS Health Consortium (WHC) lead the product development. Expertise in the fields of animal trials, statistics required during clinical trials, tooling production and commercialisation was contracted in. Wherever possible, the consortium interacted with these experts at an early stage of the project. During the technology transfer and commercialisation phases the CSIR team interacted extensively with the manufacturer, Cerdak and the distributor, VisiCare.

#### ***Hydroxyapatite engineering***

The “magic” ingredient is hydroxyapatite (HA), a calcium phosphate material, which is the main component of bone and teeth in the body. HA makes up around 5% of the body weight and can therefore be described as a “body-friendly” material. Ceramics that are synthesised from HA are bioactive bioceramics, since they naturally form an interfacial bond with body tissue. The HA ceramic is therefore readily accepted by the body. This is in contrast with so-called biologically nearly inert material, such as alumina and zirconia, where tissue forms a non-adherent fibrous capsule around the implant.

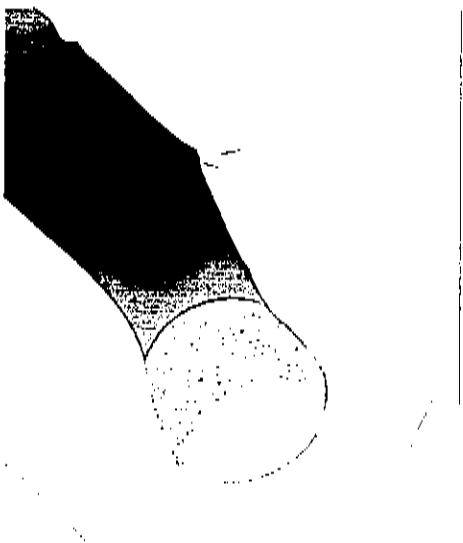
Orbital implant products from natural coral, the commonly used material, have fixed pore size and porosity. The Eyeborn<sup>®</sup> HA product, on the other hand, differs in that the materials are synthesised and the porosity and pore size distribution optimally designed and engineered.



**Fig. 1:-Diagram illustrating the Concurrent Engineering Design process applied in this project (see ref 1)**

### ***Product design***

The surface of an orbital implant produced from natural coral tends to have sharp protrusions that could damage the epithelial layer that grows over the implant, leading to infection. An improvement with the present orbital implant design, which was conceptualized jointly between the CSIR materials scientists and ophthalmic surgeons from both the Pretoria Eye Institute and the University of the Witwatersrand (WITS), is that it has a smooth front surface that does not damage the epithelial layer (see Figure 2).



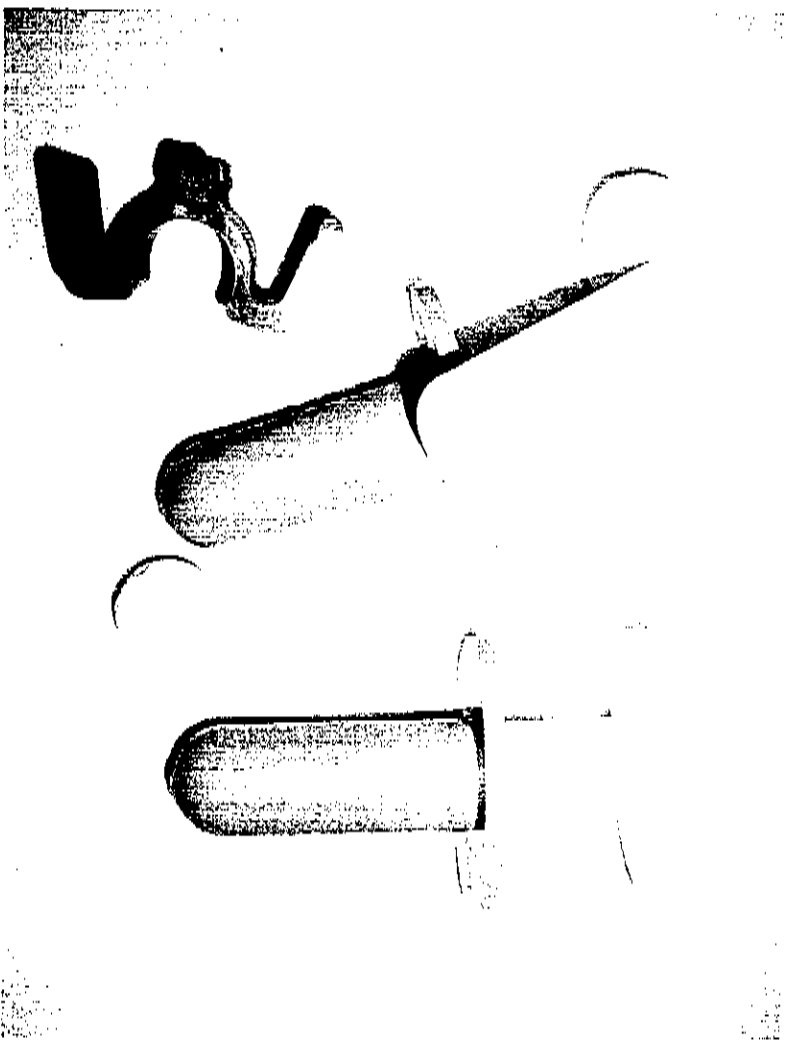
**Fig. 2: The Eyeborn<sup>®</sup> hydroxyapatite orbital implant**

The integrated prosthesis also has improved mobility because of extraocular muscle attachment to the implant [2]. This means that the Eyeborn<sup>®</sup> implant allows synchronous movement of the artificial eye with the normal one, which obviously has a very positive impact on the self esteem and quality of life of the patient (see Figure 3).



**Fig. 3: Synchronous movement of the Eyeborn<sup>®</sup> artificial eye with the normal eye experienced by a patient**

When the first prototype orbital implants were produced by the CSIR materials scientists, the ophthalmic surgeons in the consortium raised the need for a delivery device to insert the implant in the eye socket of a patient during surgery. The CSIR designers took up the challenge and subsequently generated the inserter shown in Figure 4.



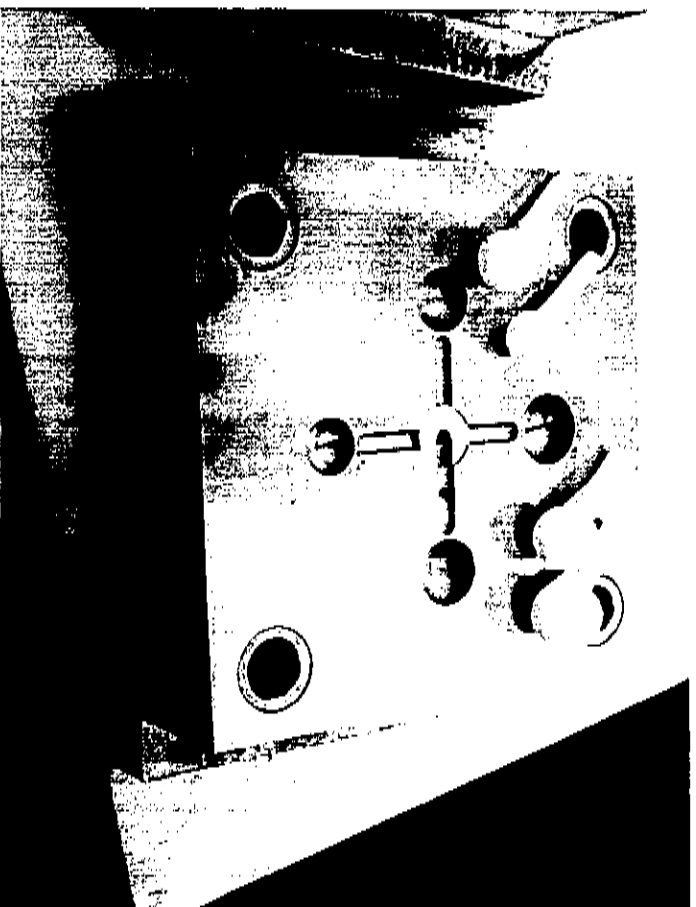
**Fig. 4: The Delivery Device for inserting the Eyeborn® orbital implant during surgery**

#### ***Tooling Design***

Moulds for forming the orbital implant and for injection moulding of the different parts of the delivery device were designed by the CSIR tool designer and manufactured by a local toolmaking company with which the CSIR had an existing working relationship. This facilitated interaction between the CSIR designer and the toolmaker during the manufacturing process.

#### ***Manufacture of Sizer Die***

As part of the procedure of inserting an Eyeborn® orbital implant during surgery, the surgeon uses a sizer to determine the size of orbital required for implant. The sizers generally used are surgical stainless steel and due to the price are supplied by Visicare on consignment and then returned to Visicare following the surgery. Following discussions with Visicare it was decided that the manufacture of sets of disposable sizers would add to ease this procedure and also add to the marketability of Eyeborn®. A die has since been manufactured to produce 16, 18, 20 and 22 mm sizers and is shown in Figure 5.



**Fig. 5: The Sizer Die with examples of the different sizers**

### ***Prototyping***

Production of prototype orbitals during the design optimisation and for the clinical trials was done by the CSIR in their R&D laboratories. The different processes, i.e. powder acceptance and preparation, powder pressing, machining of the green part and sintering of the product, were developed and optimised to ensure reproducible results.

### ***Product Qualification***

#### ***Laboratory evaluation***

The chemical reagents that were used in the study were of a grade compatible with the human body. The chemical and phase purity of the final material were verified by state of the art analytical techniques such as inductively coupled plasma mass spectrometry (ICPMS), direct laser ablation analysis and x-ray powder diffraction according to internationally accepted standards. The product samples were also evaluated for pore interconnectivity, mechanical strength, mass, density, physical dimensions, sphericity, cracks, chips, integrity, blemishes and physical appearance.

#### ***Animal trials***

The hydroxyapatite material is fully FDA approved and the chemical has undergone extensive international biocompatibility animal and human trials over many years. The locally produced bioceramic material has also been

used in ethics committee supervised primate trials during bone substitution applications over an extended period to verify its bioactive and biocompatible characteristics.

### ***Clinical trials***

After obtaining a full informed consent, the orbital implants made by the CSIR were implanted into 64 patients at various hospitals in Johannesburg and Pretoria over a period of two years. A very strict monitoring program was enforced during the progressive implant schedule. After more than two year's follow-up on these patients a success rate of over 99% could still be reported.

### **The commercialisation process**

The locally developed product makes expensive procedures such as eye implants more accessible to the poorer section of our nation and leads to significant cost savings in the healthcare environment. Besides enhancing quality of life and affordable healthcare delivery, the bioceramic product also has good export potential.

Members of the product development consortium formulated a commercialisation strategy to maximise the product's potential. Several options were considered, among them licensing of the technology to an existing international company, forming an alliance with an outside company or in-house manufacture.

### ***Commercialisation model***

As explained in the introduction, the intention with the Eyeborn® development was to provide an affordable alternative to the broader South African population. This, together with another driver, i.e. to stimulate local small enterprise development, meant that regular commercialisation principles could not be applied without some customisation. After careful assessment of local SMEs that could potentially play a role in the Eyeborn® commercialisation, a marketing and distribution partner, VisiCare (Pty) Ltd, as well as a manufacturer of the product, Cerdak (Pty) Ltd, were selected. Figure 6 shows the contracting model for the commercialisation process.

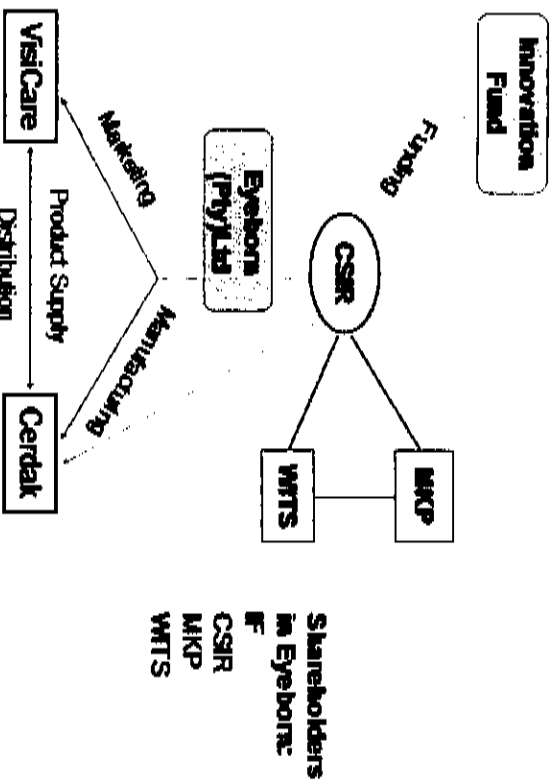


Fig. 6: The Eyeborn® commercialisation model

The consortium that developed and commercialised the orbital implant consisted of the CSIR, Meyer, König & Partners (MKP, members of the Pretoria Eye Institute) and the University of the Witwatersrand through WITS Enterprise (WITS). In agreement with the Innovation Fund, this consortium established Eyeborn (Pty) Ltd to manage the contract relationship with VisiCare and Cerdak.

### Accessing Funding

Initially, various funding options for the commercialisation process were considered by the consortium. However, venture capitalists were not willing to take the risk associated with transferring the technology to an SME with a limited track record in the field.

Eventually, the consortium approached the Innovation Fund (IF) again to provide financial support for the commercialisation of Eyeborn®. The IF took up the challenge and worked with the consortium to plan and execute the technology transfer and commercialisation process. The Innovation Fund decided to involve the CSIR's Intellectual Property and Commercialisation office to manage the technology transfer process and the contracting and flow of funds. This model increased the number of parties involved in the investment and related agreements, slowing down the negotiation process and at times also the progress approval and payments. With this number of parties involved, there is also the challenge of resolving differences of interpretation of the project plans and agreement obligations. On the positive



side, the multi-disciplinary approach required for this type of project was at least well covered.

### **Product Launch**

Based on the commitment from the IF, the consortium went ahead with the market launch of the Eyeborn® implant soon after the completion of the clinical trials. Eyeborn® was formally launched as a commercial product at the Annual Congress of the Ophthalmological Society of Southern Africa (OSSA) held at Sun City from 28 February to 3 March 2004.

A scientific paper was presented at the OSSA congress by Dr Mark Minnaar, an ophthalmic surgeon who was part of the consortium, outlining the clinical trials that had been done with the implants involving 64 patients. He reported a success rate of over 99% [3].

A workshop was also held for ophthalmologists by one of the other surgeons in the consortium, Dr Lewis Levitz, outlining the operation protocols to implant this prosthetic device. This workshop was attended by about 60 surgeons who responded very positively to the potential of the new product.

### **First sale into Africa**

The first sale of two Eyeborn® implants, to an ophthalmic surgeon from Zambia, was made at the launch by the local company, VisiCare, the distributor of the product (see Figure 7).



**Fig. 7: Laurinda Sumares, CEO of VisiCare, with the Zambian eye surgeon**

### **Technology Transfer**

The transfer of the production technology for the orbital implant from the CSIR to the manufacturer, Cerdak, formed a major part of the commercialisation of

the product. Various complications and stumbling blocks were encountered on the way, from which many valuable lessons were learnt.

### ***Industrialisation - Scaling up from laboratory prototype to commercial production***

The CSIR team produced orbitals in their R&D laboratories for the clinical trials, as well as for supplying the market while the technology transfer was in progress. Clearly, the manufacturing processes used in such an environment are not optimised for large volume commercial production and it was important that an appropriate industrial partner be found to take over this role. An additional complexity of planning and managing the commercialisation of Eyeborn® was to estimate the production costs of the product before the technology transfer to Cerdak had been completed. Although a fairly detailed costing of the prototype production could be done, this could not be related directly to the eventual manufacturing cost of the commercial product.

### ***Product quality***

With a product of this nature and the intent to also market it internationally, it was clear from the start that the CE Mark had to be obtained for the product. Since Cerdak had already received this accreditation for their existing product range, they were familiar with the required process to get a product accredited. This had a significantly positive impact on the effort required to comply with this aspect of the commercialisation of Eyeborn®. Due to an excellent effort from the Cerdak and CSIR staff, the CE Mark was awarded to the company in October 2006.

### ***Procedures***

The conversion of the laboratory production procedures to production manuals for commercial production formed a substantial part of the technology transfer process. This required close collaboration between the development team and the manufacturing team of Cerdak. The importance of finding the suitable technology partner who speaks the appropriate 'technology language' and who understands all aspects of the relevant technologies and is able to accept the technology cannot be overemphasized. Without the above qualities, frequent interaction in both localities and a free flowing two-way communication process, the success of the transfer process would be at risk.

### ***Procurement of manufacturing equipment***

Attempts were made, where appropriate and meaningful, to duplicate equipment or to acquire equipment similar to that which had been used in the development and pilot production stages in order to reduce the risk of introducing variations in the production process.

### ***Production trials and qualification***

After the technology to produce the implants had been embedded with Cerdak the latter had to produce a trial batch of implant samples for critical evaluation by CSIR for acceptance. These samples were subjected to a stringent investigation on a number of important quality checks. Only once these samples passed the various tests it was accepted that the technology transfer had been successfully completed and that Cerdak could routinely produce the implants to a high standard for the international market.

#### ***Scheduling the technology transfer process***

Although the technology transfer process was planned to a significant level of detail, based on the experience of the CSIR, the execution of the process was delayed extensively due to the very lengthy contracting process. It took more than two years from the product launch to commissioning of the production line at Cerdak. This delay can be mainly attributed to the fact that the orbital implant was developed by a multi party consortium and that the establishment of the manufacturing facility took much longer than originally planned. The consortium consisted of academic and governmental institutions, partnerships, individuals and private companies (see Figure 5). Significant time delays were caused by the process of defining licensing and contracting entities and establishing the contracts with all parties.

One of the results of this was that the CSIR had to continue with their pilot production for more than a year longer than the original plan, as an interim measure to provide in the market demand. While this emergency effort by the CSIR helped to continue growing the market, without creating disillusionment that would have followed from an inability to supply in the market demand, the non optimised production costs had a negative effect on the eventual return on investment.

#### ***Cash flow management***

A further result of the extended contracting process was that Cerdak experienced serious cash flow problems, which influenced their ability to purchase and commission equipment within the planned time schedule. This in turn delayed their establishment as commercial manufacturer of the product.

#### ***Impact***

The penetration of the market in the private clinic sector was almost immediate with a steady growth over the first two years. Almost without exception, the patients were delighted with the results they experienced and testified to the improved quality of life they experienced (see Figure 8).



**Fig. 8: A patient before (a) and after (b) having received an Eyeborn® implant**

However, the greatest challenge, which still remains, is to penetrate the public health system with this product and to fully realise the ultimate goal of the project, i.e. a more affordable, higher quality solution for the wider South African population. Marketing efforts to achieve this are on-going.

At this time in November 2006, more than 300 patients, most of them South Africans, have received the Eyeborn® implant with exceptionally satisfying results. The product holds strong potential for utilisation in African countries, as well as for the rest of the international world.

### **Conclusions**

A number of important lessons were learnt during the development and commercialisation of the Eyeborn® orbital implant, which could be of use for others that are engaged in similar product development challenges.

- The importance of establishing a multidisciplinary network of carefully selected collaborating experts, including specialists in the medical field, for the development of a product such as Eyeborn®, can hardly be over-emphasised.
- In the modern paradigm time to market is always important and the business plan should ensure that the window of opportunity is not missed.
- Careful planning should be done and great care taken to develop the market in synergy with the technology transfer and establishment of production facilities.
- A project like Eyeborn is a huge opportunity for a small technical medical device company like Cerdak. The technical data was well defined, and project funding was pre-approved. Realities, however, are that in a growing small enterprise resources are limited and contractual and financial delays can have a hugely negative impact on the growth of the business.
- Where possible it would be beneficial to the progress of the technology transfer if a single person was dedicated to the transfer and made responsible for monitoring progress, performance and payment of all parties.

- As with all worthwhile causes in life, dedication, patience and a significant measure of perseverance are required to achieve eventual success!

### **Acknowledgements**

*The vision of the then Minister of Arts, Culture, Science and Technology, Dr Ben Ngubane, who personally approved the funding, administered by the Innovation Fund, for the development of Eyeborn<sup>®</sup>, is gratefully acknowledged.*

*The technology transfer and commercialisation of Eyeborn<sup>®</sup> was made possible by the commitment and sustained funding of the Innovation Fund.*

*The authors pay tribute to one of the inventors of Eyeborn<sup>®</sup>, the late Dr Michael Thomas, who passed away in 2003 before completion of the clinical trials.*

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