Eyeborn – Restored Quality of Life for the Visually Impaired

by

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Abstract

Eyeborn® 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 in front of the Eyeborn® 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 commercialisation of the product and the technology transfer to a South African small enterprise, Cerdak (Pty) Ltd. Aspects, such as the inputs of medical experts, clinical trials, development of the commercialisation model, identification of a marketing company and a manufacturer, accessing funding and contracting, are discussed. 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 cancer 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 spheres or orbital implants. These spheres are implanted into the orbit. As they are porous they allow blood vessels to grow into the sphere which prevents migration. 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 loose 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 will cost 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.

The Technology and the Product

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 to 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 HA product, on the other hand, differs in that the materials can be synthesised and the porosity and pore size distribution optimally engineered and designed.

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 the ophthalmic surgeons of 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 1).

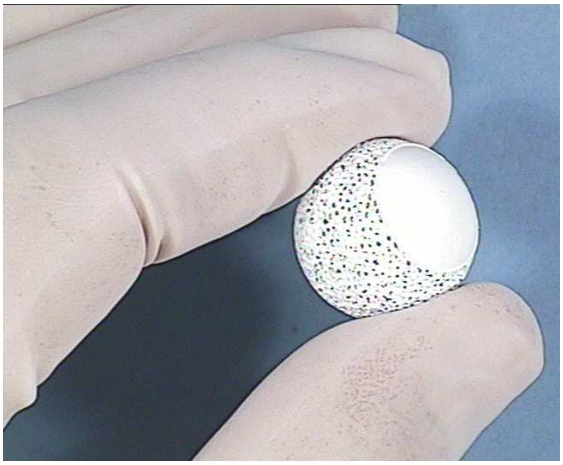

Fig. 1: The hydroxyapatite Eyeborn® orbital implant

Restoration of quality of life

The main advantage of the present product is that it makes affordable orbital implants locally available. At present orbital implants are imported at a high price that makes them unaffordable for use in government hospitals. The integrated prosthesis also has improved motility because of extraocular muscle attachment to the implant [1]. This means that the Eyeborn® 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 2).

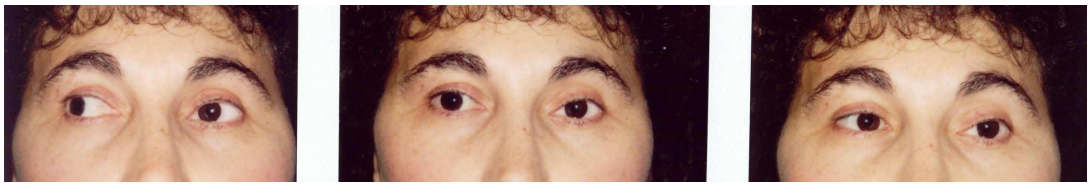

Fig. 2: Synchronous movement of the Eyeborn® artificial eye with the normal eye experienced by a patient

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 orbitals 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% can 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 lead 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.

Basic 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 SMMEs 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 3 shows the basic contracting model for the commercialisation process.

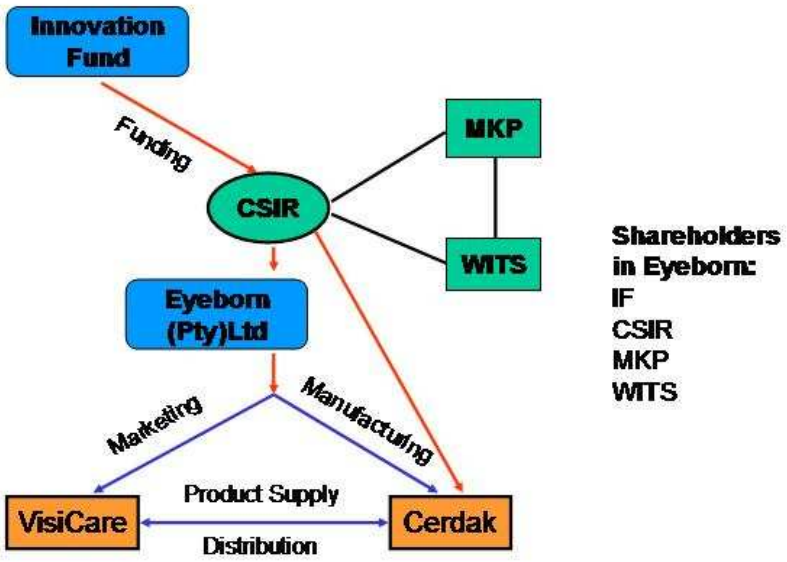

Fig. 3: The basic commercialisation model

The consortium that developed and commercialised the orbital implant consisted of the CSIR, Meyer, König & Partners (MKP, members of the Pretoria Eye Institute) and WITS 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, the reality of the very limited sources of venture capital in South Africa was emphasised, as with other similar developments which do not promise a short term financial return. Generally, the venture capitalists were not willing to take the risk associated with transferring the technology to an SMME with a limited track record in the field.

Eventually, since the product development was funded by the South African Innovation Fund (IF), the IF was approached again to provide financial support for the commercialisation of Eyeborn®. They took on the challenge and worked with the consortium to plan and execute the technology transfer and commercialisation process. However, working with public funding introduces rigours and constraints of that entity. The Innovation Fund elected to involve the CSIR's technology transfer office to manage the technology transfer process and manage contracting and flow of funds, to streamline that process through an entity that has capacity to undertake such work. This increased the number of parties involved in the investment and related

agreements, slowing down the negotiation process and at times had an impact on progressing 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. At the same time, the multi-disciplinary approach required for this type of project was at least well represented.

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) that was 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% [2].

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 4).

Fig. 4: Laurinda Sumares, CEO of VisiCare, with the Zambian eye surgeon

Technology Transfer

The transfer of the production technology for the orbital implant 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 that could apply in similar exercises with other products in the African context.

Industrialisation - Scaling up from laboratory prototype to commercial production

The initial production of orbitals for the clinical trials, as well as for supplying the market while the technology transfer was completed, was done by the CSIR in their R&D laboratories. The manufacturing processes used in such an environment are obviously not optimised for large volume commercial production and it was important that an appropriate industrial partner be found to take over this role.

Costing issues

One of the complexities of planning and managing the commercialisation of Eyeborn® was to estimate the production costs of the product. 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 obviously had a significant positive impact on the effort required to comply with this aspect of the commercialisation of Eyeborn®. The CE Mark is now pending, with all essential elements of the process to obtain it complete, thanks to an excellent effort from Cerdak staff.

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 in the technology transfer process, 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 likelihood of introducing variations in the production process.

Production trials and qualification

When 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 passed the various tests was it accepted that the technology transfer had been successfully completed and that Cerdak would routinely produce the implants to a high standard for the international market.

Scheduling of 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 3). 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 prototype production for longer than a year more 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 what the market demanded, 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 5).

(a) **(b)**

Fig. 5: 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 population. Marketing efforts to achieve this are on-going.

At the time of this conference, in June 2006, some 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. For entry into the European market the CE Mark is a prerequisite, which is expected to be in place in the next month.

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 may want to engage in similar exercises.

- 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 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 ventures in life, dedication, patience and a significant measure of perseverance are required to ensure eventual success.

Acknowledgements

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The technology transfer and commercialisation of Eyeborn® was made possible by the commitment and sustained funding of the Innovation Fund.

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

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