Appendices

Appendix 1: Cochlear Limited

Professor Graeme Clark began his physiological research on electric stimulation of the cochlear nerve in animals in 1967. Eleven years later, in 1978, he was able to implant his first human patient with a 10-channel prototype cochlear device. Subsequent implants led Professor Clark, head of the Department of Otolaryngology at the University of Melbourne, Australia, to believe the prototype could be improved and made available to a larger group of people through commercial development. The Australian Government, seeking to encourage high-tech development in 1979, called for tenders from companies able to perform a market study and write a development cost plan for the commercialisation of the implant system (Vandermerwe, 1991). Nucleus Limited, an Australian holding company for a group of medical device companies including cardiac pacemakers and diagnostic ultrasound imaging equipment, won the tender.

In 1981, with the University of Melbourne and the Australian Government, Nucleus Limited set out to develop a commercially viable cochlear implant and to carry out a worldwide clinical trial. Cochlear Pty Limited was established in 1983 as a corporate entity in order to continue the commercial operations. Nucleus Limited, including Cochlear Pty Limited, became a wholly owned subsidiary of Pacific Dunlop by 1988. In 1995, Cochlear Pty Limited was sold by Pacific Dunlop and successfully floated on the Australian Stock Exchange as a publicly listed company. Since the float, Cochlear Limited has continued to grow at a very impressive rate, with market penetration in 120 countries employing more than 700 people worldwide (company website). In March 2001, the company celebrated the 30,000th Nucleus Cochlear implant recipient (2001 annual report); by July 2003 that number had grown to 50,000 implant recipients (press release 16.07.03) and a further growth in sales of 20% was projected for the coming year (2002 annual report).
Although Cochlear is a case study that began over 20 years ago, it illustrates an issue that is currently of interest to Australian biotechnology ventures. The difficulties of commercialising biotechnology innovations encountered by Australian biotechnology companies are not always recognised. Although there are now a number of surveys available listing features of biotechnology firms this information is supplied out of context. Detailed qualitative study, such as this case study, is required to explore the processes of resource acquisition undertaken by such firms in their efforts to emerge from scientific institutions and evolve into major companies.

The technology

In a normally functioning ear, sound waves travel from the environment to the outer ear. The sound waves then move on to the middle ear where they cause the eardrum and three tiny bones to vibrate. These vibrations move through the fluid in the snail-shaped inner ear (cochlea) where a multitude of sensory, or hair cells, are each connected to a hearing nerve. Thousands of these tiny hair cells in the cochlea change the vibrations into electrical energy. This electrical energy stimulates the hearing nerve and sends sound signals to the brain. In the profoundly deaf, the hair cells are so damaged that hearing is prevented.

Profound deafness can be present at birth. Injury or an illness such as bacterial meningitis or mumps can also cause profound deafness. Profound deafness is different from the hearing impaired. The latter group can be assisted to hear through the amplification of sound by various means such as hearing aids. For the profoundly deaf amplification of sound will not help them to hear.

The cochlear implant system places a device into the cochlea to directly stimulate the hearing nerve. Micro-electronic engineering has been adapted to the latest research on hearing physiology to produce a high-tech system that consists of four parts, all of which are necessary to enable the profoundly deaf person to hear:

1. Microphone: Speech and environmental sounds are picked up at the ear level microphone and sent into the speech processor.
2 Speech Processor: The speech processor filters, analyses and digitises the sound into coded signals. These signals are sent from the speech processor to the transmitting coil. The coil sends these signals as a form of pulse code modulation to the cochlear implant under the skin.

3 Internal Components: The cochlear implant delivers the appropriate electrical energy to the electrode array inside the cochlea. The electrodes along the array stimulate the remaining nerve fibres in the cochlea. The electrical sound information is sent through the auditory system to the brain for interpretation.

4 Speech Coding Strategies: Speech coding strategies control the digital processing of environmental and speech sounds. Different strategies emphasise different pitch, loudness and timing cues. Cochlear implant recipients may prefer their quality of sound, and demonstrate improved speech perception when using a specific speech coding strategy designed to meet their needs.

The bionic ear therefore has been defined by Professor Clark as “a device that restores useful hearing in severely-to-profoundly deaf people when the organ of hearing situated in the inner ear has not developed, or is destroyed by disease or injury. It bypasses the inner ear and provides information to the hearing centres through direct stimulation of the hearing nerve” (Clark 2000:191).

Technology – historical context

Auditory sensation as a result of direct electrical stimulation dates back as far as 1800 with experiments by Volta (House & Berliner, 1991). However the modern history of electrical stimulation of the auditory nerve has been acknowledged as beginning with reports published by Djourno and Eyries (1957) in France (Clark et al., 1987; House & Berliner, 1991). Due to technological difficulties and negative perceptions of long-term benefits, progress in the research of the device was hindered for several years. In addition it has been noted that the scientific community was not ready to accept this new challenge. For instance Blair Simmons, working at Stanford, attempted to discuss
his 1964–1965 implant experiments with prominent researchers in speech coding and auditory psychophysics during that time. He wrote; "I got a distinct impression...that most everyone was either incapable of thinking about the many problems involved or would rather not risk tainting their scientific careers" (House & Berliner, 1991:11).

As pacemakers continued to be implanted and improved materials were developed, progress in auditory electrical stimulation began to take shape, especially on the West Coast of the USA. The first breakthrough from the merely experimental period into the clinical application period of cochlear implants came in the late 1960s in Los Angeles. William House had teamed up with an engineer called Jack Urban. They were able to guide further engineering development that resulted in the first stimulator package which could be worn by the patient without impeding his professional or social activities. By 1973 the House/Urban team had also developed a pre-operative diagnostic test battery for selection of patients and a post-operative rehabilitation program (Clark et al., 1987).

From this time on, all over the world research groups began to form, representing multi-disciplinary teams including audiologists, bio-engineers, speech and hearing therapists, psychologists, social workers and otologists who took responsibility for selecting, operating and guiding the implanted patients. Technical progress was now very rapid. Intra- and extra-cochlear implants were developed; single-channel electrodes were replaced by multi-channel devices, speech processors became smaller and more efficient. This technical evolution was only feasible by means of progress in electronic engineering on the one side and an intensive neurosensory research on the other (Clark et al., 1987).

It is within this evolutionary environment that Professor Clark, together with his research group in Melbourne University, developed the multi-channel cochlear implant. Later the Nucleus device provided spectral information in addition to temporal and intensity cues, thus allowing profoundly deaf post-lingual adults not only to perceive the complex noise of their acoustic environment and function as a supplement to lip-reading but also to recognise words in sentences often without visual cues. C.R. Pfaltz considered the development of this multi-channel cochlear implant "a second breakthrough, closing the period of clinical studies and opening a new area of practical application and clinical testing of cochlear implants" (Clark et al., 1987).
The first Cochlear device was approved by the FDA in October 1985 and many subsequent improvements continued to be made over ensuing years. More recently improvements in technology have enabled the Nucleus system to be modified and improved so that by November 2000 the USA FDA gave approval for the Nucleus 24 Contour device to be implanted in children as young as 12 months.

**Technology market – size and growth**

A market study conducted in 1979 by Telelectronics/Nucleus concluded that there was a significant world market for the product, particularly in the United States and Europe. While the study concluded that the total number of potential customers who were profoundly deaf was approximately 500,000 worldwide, the survey team estimated that only about 10% of this market, or about 50,000 patients worldwide, were possible implant candidates (Smith, 1999). The data in 1979 also suggested that another 3,000 new cases occurred each year worldwide.

Professor Mark Haggard, then Director of the MRC Institute of Hearing Research at the University of Nottingham in the United Kingdom, estimated in 1991 that it would take 5–10 years for clearance of the adult prevalence backlog. He estimated that by then children would probably provide the majority of candidates on an incidence basis. He had little doubt that steady improvements in the computing power of microcircuity would eventually lead to such algorithms giving materially greater average benefit scores for current candidates and a greater range of circumstances in which implants could be used effectively (Haggard, 1991).

Haggard’s predictions have proven to be accurate and the 50,000th patient, a Japanese child, is today able to hear with an implant system that has seen some major technological improvements to the original device. Markets in China and India also continue to attract attention and now that cochlear implants have become an accepted clinical tool with patients who are severely and not profoundly deaf also prepared to have the device implanted. The original study found that although “people whose hearing problems were not being satisfactorily improved by hearing aids could have become a market for implants...many potential users were wary of having an electronic device inside the body” (Vandermerwe, 1991:4). Thus since 1991, positive changes in
the perception of the device, have further extended the market. It is not surprising therefore that the company continues to experience average sales growth rates of 20%.

The growth of the market is further enhanced with the acceptance of the device by the clinical sectors in the industry. In the early 1980s Clark had already “realised that the opinion makers (in the industry) were the surgeons and the audiologists” (Clark, 2000:160). The acceptance and promotion of the device by the various groups of the medical sector to the public and thereby the governments that support public health systems can only lead to a very positive future for the company and the industry as a whole.

**Overview of Cochlear’s competitive position**

There have been some major changes in Cochlear’s competitive position during its 20-year history. In August 1978, as Clark made his first human implant, 33 adult patients had already received the House single-electrode cochlear implant in the US. By 1982 the House/Urban team had teamed with the 3M company to develop a smaller, lighter-weight system. “The US FDA recognised the 3M Cochlear Implant System/House Design as a safe and effective treatment for profoundly deaf adults by granting marketing approval to the manufacturer” (House & Berliner, 1991:20) and thus giving the US team the lead in the implant market for that year.

The initial market lead reflected the historical development of the device. “The first worldwide developments were directed towards designing an implant and processor that would successfully provide speech understanding...Single electrodes were considered safer in the earlier years of cochlear implant research which were easier to manufacture and often could be used with already existing speech processors” (Mecklenburg & Lehnhardt, 1991:51). Mecklenburg and Lehnhardt (1991) have estimated that more than 40% of implants designed outside North America up to 1985 were single-channel. However, comparative studies in France designed to evaluate speech perception abilities between single and multi-channel systems (French National Commission (1985–1988)), confirmed “the superiority of the multi-channel device for speech discrimination without lip-reading” (Rouleau & Matha, 1989:419).
As well as having FDA approval, the House/3M cochlear implant was one-third the price of the Nucleus system and initially was able to dominate 95% of market share. From 1985, following FDA approval for the sale of the Nucleus implant, Cochlear experienced real momentum. With US regulatory approval, US health insurers provided coverage for the product and the surgical procedure necessary to implant it and Nucleus “unit sales increased from 409 in 1987 to 596 the following year” (Vandermerwe, 1991). Cochlear’s competitive advantage was its ability to demonstrate that its multi-electrode device was better in providing speech understanding. The superior reliability of the Nucleus system was reflected in its price and made a material contribution to the widespread acceptance of implantation of the device (Haggard, 1991). It took Cochlear about 18 months to clearly demonstrate that its performance rate was much better. In that time the 3M market share fell from 95% to 5%. “The US firm continued to lose market share and faded from the scene late in 1989” (Vandermerwe, 1991:9).

The partnership of 3M and the House/Urban research group was an important development in the marketing of the device. Throughout the 1980s devices were designed with faster processing, significant miniaturisation and less power consumption requirements that enabled increasing reliability and greater access to useful speech information. “Better understanding of anatomical considerations had also evolved, along with improvements in surgical approaches, intra-operative testing, reduction of medical complications and enhanced rehabilitation techniques” (Mecklenburg & Lehnhardt, 1991:53). Such groundbreaking developments made it viable for commercial medical manufacturing companies to play a larger role in the field of cochlear implants. This association was very necessary as a means of accessing additional resources, desperately needed to advance the large-scale clinical application of these prostheses. In addition to the 3M company and Nucleus Limited, Symbion (later Ineraid) became associated with the University of Utah implant to implement the research of Dr Don Eddington. Richards Medical Company eventually took on this project. A variety of companies including 3M, Storz and MiniMed collaborated with the University of California at San Francisco to develop the research of Michelson, Merzenich and Schindler. In West Germany, the Banfai/Hortmann research group teamed with EMG manufacturing and later Implex to develop an extra-cochlear system. In Vienna the research team of Burian, Hochmair and Hochmair-Desoyer originally licensed their IP to 3M. With the demise of 3M, Hochmair established the company Med-El. In Antwerp,
Antwerp Bionic systems developed the LAURA device through the research of Marquet, Peeters and Offeciers. In addition to providing printed literature and training courses to a 'professional' level, these companies also provided much-needed support for repair and maintenance of patient equipment. They also obtained the regulatory approvals that became necessary with the introduction of the FDA medical device regulations in the USA (House & Berliner, 1991).

"The presence of commercial companies took the cochlear implant out of the realm of academia and private non-profit institutions and placed it in the commercial marketplace where the objective of scientific excellence is complicated with additional objectives that focus on rapid development of profitable products" (House & Berliner, 1991:26). In 1990 the House/Berliner team lamented that "projected numbers of consumers by marketing studies have failed to materialise" (House & Berliner, 1991:31). They were seriously concerned that if the market was not large enough to induce manufacturers to go through the considerable expense of performing clinical trials, the cochlear implant would remain an 'orphan product' without sufficient commercial resources expended towards future improvements. It is perhaps one of the most telling of the Nucleus team's marketing strategies that as companies such as 3M withdrew from the cochlear implant market, it negotiated with them to acquire their cochlear implant assets and liabilities. The strategy was implemented in an effort to maintain the viability of the industry as a whole. Cochlear Pty Limited therefore made the decision to acquire the 3M implant business in 1989. Symbion and Antwerp Bionic Systems were soon also purchased, as well as the responsibility of looking after their patients. This action meant buying out competitors' patents, taking over all spare parts for repairs and simultaneously taking over all responsibilities for servicing.

By 2003 Cochlear Limited had become the leader in the worldwide cochlear implant market. It won the international medical design excellence awards and with its strong philosophy of support for recipients and clinics throughout the lifetime of every Nucleus cochlear implant system, the company continues to maintain its leading market position.
The founders

The Scientist, Professor Graeme Clark

Professor Graeme Clark has acknowledged that as a young boy his reading of the scientific challenges, careful scientific experiments and the determination to succeed of Louis Pasteur had a strong influence on his “curiosity about biology and his desire to make discoveries” (Clark, 2000:24). His reading of Dale Carnegie’s book on How to Win Friends and Influence People developed an understanding at a very early age of the enormous benefits in listening carefully to people and how impressed they would be if you understood what they were really saying. He acknowledges that his Christian faith taught him the benefits of contemplation that assisted in developing his ideas for research (Clark, 2000:25). Therefore from very early in his life, Clark developed a world-view of the work he would undertake and its possible impact on issues outside the laboratory.

In 1967 Clark began researching the possibilities of an electronic implantable hearing device. Inspired by his close relationship with his father, who had been hearing impaired throughout his life, Professor Clark’s goal was to find a way to improve hearing, and the quality of life for people who are deaf.

At the beginning of 1969, Clark had completed most of his experimental work on the normal functioning of the brain centre, and was set to study the comparison of the responses of auditory brain cells to electrical stimulation with those to sound of the same frequency (Clark, 2000). During his three years at the University of Sydney he had become committed to continuing the research on electrical stimulation of the hearing nerve, but there was little future for research of this nature in the university’s Department of Physiology. “Physiologists both locally and internationally thought it was outrageous to suggest that electrical stimulation of the inner ear could adequately reproduce frequency information to help profoundly deaf people understand speech” (Clark, 2000:52).

Later that year Clark successfully applied for the position of the inaugural Chair in Otolaryngology at the University of Melbourne and put his energies into developing further research “into the surgical treatment of perceptive deafness” (Clark, 2000:52).
He remained the research leader at the Department of Otolaryngology at the University of Melbourne from 1970 till his retirement in December 2003. The traits he developed early in life assisted in transmitting that commitment to the many interdisciplinary teams of audiologists, bio-engineers, speech and hearing therapists, psychologists, social workers and otologists on which the development of his concept would ultimately depend. Without the close cooperation of the various disciplines and skill sets, the development of the Cochlear implant would not have occurred. The ability to attract and manage such a diverse group of professionals was essential for the acquisition of the initial intellectual resources of the project. Maintaining the momentum and interest of the group appears to have been made possible by a passionate commitment to the vision, which Clark maintains to this day.

At this early phase of development, the research team’s major resource was its unique intellectual property. However, progress in the research required access to additional financial resources which was always a major problem. Access to financial resources was hindered by the conservative nature of the scientific community of the 1960s and early 1970s. "The prevailing view was that successful electrical stimulation of the hearing nerve to help people understand speech would not be possible in the foreseeable future" (Clark, 2000:195). Such objections made it difficult to convince commercial interests to invest in the device.

By 1973, the research team was desperate for additional funding. If Professor Clark was to advance the team’s research from bench top to start-up phase, the continued ability to access resources of a commercial nature was essential. Through studies in experimental animals, he and his team had now established that it was imperative to develop a multiple-electrode implant for speech understanding to be achieved. The ability to extend that research to the development of a human prototype meant expensive engineering and access to an estimated $75,000 (in 1973 terms) over the next 3 years.

"The breakthrough in the funding problem came when Sir Reginald Ansett, the owner of the Channel 0 (now Channel 10) television station, contacted Clark to say he wanted to run a telethon to help raise funds" (Clark, 2000:68) for the project. The telethon produced a lead-up documentary produced by Mr Hector Crawford and contributions of $30,000. Although short of the $75,000, "the channel set out at the end of 1973 to plan for a major telethon late in 1974" (Clark, 2000:71). Subsequent telethons promoted and
gave exposure to the “bionic ear”, a term coined at Channel 0, to a public well beyond
the scientific community. The promotion led to a network of alliances with fund-raising
bodies and connections with influential industry and political leaders. The exposure also
promoted the concept to a number of profoundly deaf people who were keen to be the
first to receive the implant.

Clark recognised the opportunities that the promotion made available to him and was
able to make the key connections to extend the team’s resources in an effort to develop
the concept further. In order to ensure access to government assistance, he wrote to the
then Prime Minister, Malcolm Fraser. In order to build commercialisation capabilities,
he wrote to Paul Trainor, owner of the Australian heart pacemaker firm, Telelectronics
and the 3M company, encouraging a meeting. He followed up with fund raising bodies
and interviewed prospective patients. Furthermore he extended the network of surgeons
in Ear Nose and Throat (ENT) clinics. At this point Clark clearly demonstrates two
essential characteristics for successful commercialisation of a biotechnology start up.
Long before the firm is registered, the scientist is able to perceive the project as
operating in the real world, that is, he has acquired critical market awareness. In
addition the eventual acceptance of the technology will depend on the credibility that is
acquired within the professional group.

The Entrepreneur, Paul Trainor

Paul Trainor studied commerce at Sydney University, but gave up studying to join his
father’s firm. He had always been interested in the business and as a 15-year-old he
often joined his father at work. Trainor senior was originally an optician and later
skilled in the field of X-rays and microscopic analysis, providing the young Paul with
erly experience in the field of medical engineering. The son would visit his father’s
workshop after school and often spent Saturday mornings there. Quite frequently this
led to accompanying his father’s engineers on calls to a hospital or private rooms and he
developed a keen interest in medical engineering. He eventually became a director of
Watson Victor but left his father’s firm to set up his own business in 1964. Later in
1966 he took an interest in a fledgling medical electronics business in Lane Cove called
Teletronsics. The group made cardiac monitors during business hours and worked on research and development projects after business hours and in their spare time.

Trainor's ambition was reflected in his philosophy of management which he articulated in a summary in November 1988. "Sell house - select 'A' graders - do business plan - give mission 'aims and goals' policy of share earnings - do cash flows, and go wrong - develop people - be honest with staff and clients alike - 12 hours days policy - think - think - ten plus years ahead - have fun - have guts - develop new people - have problems (challenges) - develop more true grit - be lateral - keep modesty - mow down tall poppies and any potential bureaucrats - avoid centralisation - develop internationalism - create an innovational environment - pick the non-conformist - create a motivational environment. Go on and on - make decisions - do not procrastinate - think positive - six months equals one year".

As outlined in his summary, he always tried to select people who, irrespective of their qualifications, were top grade. He hoped they would work thirteen to fourteen hours a day and sometimes at weekends. He favoured employees with a strong ethical sense and strong character. An individualist, he was tolerant of other individualists, preferring people who, like him, responded to challenge and he set up a scheme of profit-sharing for them. He was delighted when the business grew in great leaps and some of his staff received more in an annual bonus than in annual salary. In 1970 his firm, though barely in its fifth year, had three hundred employees.

As a sideline his firm entered the emerging business of pacemakers. Nucleus pacemakers were electronic devices operated by a battery, generating an electric pulse which made the heart beat regularly. The technical standards of Nucleus were very high because their product made the difference between life and death both for the patient and the business. As the main market for pacemakers was overseas, Trainor sold his products first in New Zealand and then in India and England. The first European implant was in England and sales quickly grew right across that continent. When in the early 1970s Nucleus decided to open a French factory, at Chatellerault just south of Tours, it already possessed about 20% of the European market for the device. Additional factories were bought in the USA and Brazil throughout the early 1980s and by the mid 1980s the main market for the company was in the USA.

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Teletronics became the world leader in the kind of pacemaker that controlled heart spasms and so reduced the risk of heart attack. Constant research was essential because the best product in the market was quickly superseded and $25 million a year was spent on some 100 different investigations to improve the device. The latest research in physiology or a new way of cutting the weight of the tiny pacemakers quickly gave one product an advantage over another. At the same time a new product was often easily copied and world patents were not always a complete protection. Moreover the products could be the subject of frequent litigation. One faulty product ran the risk of losing through lawsuits, the profits of the previous couple of years.

Hirshorn agrees that Trainor’s “real strength was his genius as an entrepreneur”. “He knew where to go to raise money, he was very good with government relations and he was extremely good with people”. These attributes meant that he was good at persuading the Australian Government to recognise important issues. In addition he had an extraordinary talent in choosing good people and working with them. David Money, the first Chief Executive of Cochlear Pty Limited, has said that the timing for the project was also exactly right. The company was ready to diversify and had the connections in the regulatory field to facilitate commercial success. Paul the entrepreneur and business strategist, had the necessary resources to champion the project, and he did.

Clark also thought highly of Trainor. The Professor found that “Paul strove hard to ensure that the commercial effort dove-tailed with our (Melbourne University) research, and as time went on, together we developed such a rapport in explaining our work at symposia that it seemed to me we performed like a ‘Punch and Judy Show’. Above all, I was impressed by Paul’s high ethical standards – he would not make exaggerated claims, regardless of the effect on the share market, and he did not trade innuendo for innuendo when dealing with competitors” (Clark, 2000:147). The insistence on not making exaggerated claims was a strong ethical issue within the company and contributed significantly to their credibility and acceptance in the global market.

Money is of the view that “there would have been very few companies that could have made a commercial success of the cochlear implant. No other Australian company could and there would have been relatively few international companies that could have managed it at the time. This was partly because pacemakers were the only implantable
electronic devices that were commercially successful at that time. The good work in Melbourne would have gone nowhere if it had not been picked up by a pacemaker company”. Money contributes several key factors to the commercial success of Cochlear, but emphasises that among these was “a balanced team, which was an absolutely vital element in taking the company forward. Balancing the efforts of talented people with a variety of skills to ensure a reliable, fast to market product, honest claims and a realistic price” has ensured continued success.

The founding process

Three stages can be identified in the founding process of the project and its early growth. The first stage covers the early history of the project within the university where the concept was developed. The second stage includes the feasibility study and assessment of its commercial viability. The third and ongoing stage includes the evolution of the original business plan and the expansion of the company into global markets.

Early history at Melbourne University

Through 1971–1972 Professor Clark brought together an able group of research students who were actively engaged in research, to establish whether the rate of stimulation on a single electrode would be adequate for speech understanding. By 1973, the small student research team had clearly demonstrated that electrical stimulation on a single electrode would not reproduce speech frequencies. This finding was vital in taking the direction that eventually gave Cochlear Limited the competitive edge in the multi-channel cochlear implant industry. The eventual Nucleus device, unlike the single-channel competitor, allowed profoundly deaf post-lingual adults to perceive the complex noise of their acoustic environment and also to recognise words with and without visual cues. The development of this new multi-channel cochlear implant has been described as a second breakthrough in the rehabilitation of the profoundly deaf (Clark, 1987).
The project progressed in four sections that now make up the implant product. The first step involved understanding the physiology of how sound was processed by the brain. The second section focused on the more expensive task of developing an electronic package and an electrode array that could be implanted within the inner ear. The third section focused on connecting external electrical stimulation to the hearing nerves. The fourth section focused on speech processing strategies and their ability to analyse sound.

Throughout the project funding was always an issue. At each stage of the development new resources in the form of skills and equipment needed to be accessed and these were not available without the appropriate funding. Funds for essential equipment were obtained from various sources including the Apex Club of Melbourne. The award of a cheque by the Apex Club for the amount of $2,000 for the development of an implant to electronically stimulate the hearing nerves in the hope of curing sensori-neural deafness was seen on the evening news by Reg Ansett, founder of Ansett Airways in 1973. Reg Ansett eventually provided access to telethons, through which the team was able to collect close to $500,000, thus enabling it to extend the research to the development of a prototype.

In addition, positive publicity enhanced the ability of the project to access valuable relational assets. “The publicity surrounding the telethons since 1973 heightened public awareness, and profoundly deaf people were learning that a bionic ear might one day be able to help them” (Clark, 2000:97) hear. The Australian Association for Better Hearing, an organisation of people who mainly had hearing before going deaf, referred other potential research subjects and initial potential customers to Clark. Development of such networks resulted in the researchers identifying four people to become the first research subjects to test the prototype at the proof of concept stage of the innovation.

Suppliers were always very difficult to locate for an innovative product. For instance a suitable bundle of wires for the implant couldn’t be purchased though Clark tried all around the world, even using his links with the Australian airline industry through Ansett Transport Industries to contact high-tech specialised firms in the United States. He did, however, find interest with the Weapons Research Laboratories in Salisbury, South Australia that had the facilities and interest in helping with the research for developing the wires. The government body did not charge for their work, considering it to be in the public interest and good for public relations if their assistance was provided
free of charge (Clark, 2000). Furthermore, contact with Mr Malcolm Fraser, Prime Minister in 1978 and Bob Hawke then the leader of the ACTU and later Prime Minister from 1983, became valuable contacts for funding.

At this stage of its historical progress, the project had become dependent on external sources for funding to continue work. Although seen as an opportunity, in many cases it also created budgetary constraints and a tight discipline on project objectives. The luxury of "blue sky" research was not an option for the determined and goal-focused Clark and his team if they were to be perceived as a credible research unit by the external commercial environment. By 1978 it was essential for the team to tackle the difficult process of commercialisation if they were to go to market. For many biotechnology companies at this stage of progressing their invention, the objectives and professional cultures of the two disparate groups (commercial and scientific) have imposed critical constraints for growth strategies. The aim of the university group in this instance was focussed on clinical use, thinking of patient benefit rather than profits. For the commercial team, the focus was on manufacturing issues and the ability to gain sufficient returns on investment without which the investment would not be viable. The ability of the two teams to build on their individual capabilities was crucial to take the project to the next stage of development.

Assessment of commercial viability – proving the science

It was the promotion of the bionic ear through Reg Ansett's telethons that attracted Trainor's attention. The formation of Nucleus, as a holding company for its group of medical device companies such as Teletronics (pacemakers), Domedica, (kidney dialysis) and Ausonics (diagnostic ultrasound) and others, provided access to funds and the ability to raise more funds from consolidating revenue when needed. This gave Teletronics the chance to expand and look for other commercial opportunities. Trainor's interest in the Clark project was part of this diversification process. The Professor wrote to Trainor in September 1977, encouraging him (Trainor) to come and talk more about the project (Clark, 2000).

In June 1978, Dr Mike Hirshorn from Teletronics visited Melbourne University to establish the feasibility of the research. Hirshorn was responsible for the biological
issues for the pacemaker electrode and he wrote in his report to Telectronics “they have not proven anything but is seems like it could work” (Clark, 2000:142). David Money, who, at that time, was the Manager of the R&D Department of Telectronics, with experience in designing circuits for pacemakers says that “he was shocked to learn that Telectronics research department had paid $400 to look at a collection of patents from the University of Melbourne”. On examination Money agreed that the patents did indicate the work that was going on in Melbourne in applied research would provide a variety of different avenues for diversification for Telectronics.

Money was acutely aware of the enormous distance between the prototypes and creating a marketable product that could be commercially successful. Jim Patrick, one of the chief engineers of the Clark team, agrees that the prototype “was never designed to be a clinical device, it was just designed to last a few years and test whether the idea was going to work”. When that was done then the next step had to involve a group that had the technological expertise to commercialise it. Clark also admits that he was “relying very much on their (Telectronics/Nucleus) expertise in sealing packages” (Clark, 2000:147) since the sealing process was of vital importance and his own efforts to develop a seal were far from successful.

Evidence of the accuracy of Money’s fears regarding the reliability of the device was confirmed within a very short time. George Watson was the second person fitted with the prototype and six months after his implant he experienced “odd bangs and hissing sounds in his ear” (Clark, 2000:130). Within another three months the device failed altogether. The third patient also started to experience strange sensations that were quite unpredictable. Her package had developed a leak and needed to be removed. The two halves of the package had been soldered together and this proved to be ineffective in overcoming leakage around the package seals (Clark, 2000). Telectronics was the best firm to refine this aspect of the package.

Money thought that the Melbourne project was an extraordinarily impressive design for a university to have carried through to the prototypes. It was a work of art. However, he worked for Telectronics and he was aware of the reliability needed in implants. He also knew what was needed to make something manufacturable. “The whole of the system needed to be reconsidered to simplify it and make it reliable”. The initial implant had something like 55 or 60 integrated circuits within the hybrid package and to Money that
was not manageable from a manufacturing point of view. The more that could be put into a single unit the more reliable it would be. That is always important when trying to break into a new field. Money thought that there was no way that Telectronics could use the Melbourne University prototype. Research would need to start from scratch focussing on the essentials in a cochlear implant, on those parts that appeared to be effective and building on what the University team had learnt from their device.

Chris Daly, an engineer with Telectronics in the research and development group by 1979 was a very experienced pacemaker engineer. He and Money worked on an entirely different system right from the start of the assessment process. Money says “the whole thing was different. We used one link to convey both power and information. The two original links meant that you could have two links to break down. So we combined them to a single one and then combined the coding into a simple code that was very economical to decode. It was also very economical on power which solved another major problem, how to minimise the power consumption of the implant”. Daly and Money developed a broad-brush functional design that seemed to satisfy all the basic requirements and they patented it. They patented all the new key concepts of the design that made it simpler and cheaper and more reliable than the prototype. The new design enabled the team to prepare a development cost plan. The plan included the cost of actually doing the design, getting prototypes of the integrated circuits and the cost for volume to manufacture forecasted volumes.

Money considered that the first step was to persuade Telectronics that these initial actions were crucial. “You can’t just say no it will not work, because there is obviously a demand but is that demand sufficient to justify the investment? And you couldn’t just say yes because there was certainly a large amount of risk. We really needed to know what it was we were actually in for. The only way to do that was to design a commercially viable product and undertake a market study to determine the level of market demand that would give legitimacy to the development of the concept”.

The idea was conceived and the patent applied for when Nucleus/Telecrhonics were not being supported by government money and the company was only indicating an expression of interest in becoming involved. However the patent came to be quite important in negotiations with the government as to why the contract should be awarded to this Australian company.

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The federal government’s Department for Productivity called a meeting of interested parties in Canberra late in 1978. Money remembers that “it was attended by many people; Graeme was there, federal and a couple of state governments were represented, competing companies like 3M were present and Paul and I were there from Tlectronics/Nucleus. I can remember thinking this was too big a deal for Nucleus to take on because of its very high risk and the very high level of investment required. I thought that this level of risk taking was pretty unlikely and I thought that this was not what you would expect a company like Nucleus to take on. Teletronics and Nucleus were pretty well using all the money they had to expand their other businesses, especially Teletronics. My guess was that the amount of money required to get a cochlear business going was pretty large. I estimated it to be $1 million plus and Nucleus just didn’t have that sort of money”.

“My thoughts were not well received. But I made sure that the meeting understood why I felt it was necessary to have a market survey to determine the market and also to determine an estimate of what was involved in setting up the manufacturing from an engineering perspective. You have got to know what you are buying with limited resources both in terms of human resources and cash. Secondly there was no good basis for determining if there actually was a business for the Cochlear implant. And if there was a market how big it was? How much there was and how much development was needed? We had to work out just what a cochlear implant would look like if we were going to manufacture it. There were so many questions that needed answers”.

**Government support – Public Interest Grant Phase 1**

“On 31 January 1979, the Minister for Productivity, Ian McPhee, announced a Public Interest Grant to achieve commercial development of the Melbourne University implant. The grant was for $1 million to be paid over two years for engineering, medical research and development and for a market survey to see how profitable it would be” (Clark, 2000:143). The Australian Government, seeking to encourage high-tech development, became part of a necessary network in the project’s development and a board was set up under the Australian Industrial Research and Development Incentives Act (AIR&DIB). On February 1, 1979, the Australian Government called for tenders
from companies able to perform a market study and write a development cost plan for commercialisation. Telectronics/Nucleus won the tender. The aims for this phase of The Implantable Hearing Prosthesis Program were threefold. First, the government required that at least two additional patients have the system implanted. Second, the design of the implanted receiver-stimulator needed to be perfected. And finally, the speech processor was to be made portable. The deadline for the program and the market survey was the end of December 1979 (Clark, 2000).

The steering committee set up by the AIR&DIB coordinated the activities of the University of Melbourne and Nucleus/Telectronics. In his book *Sounds from Silence*, Clark acknowledges the outstanding way in which the 'bureaucrats' handled this project. He particularly thanks Paul Schultz, Frank Montgomery, Geoff Tunaley, Nick Sterling and Ted Cowcher (Clark, 2000:144). Money also acknowledges the efforts of the steering committee and comments that apart from providing vital funding, the committee was also useful in managing the relationship between the university and the company, encouraging an additional discipline to both. They were also very constructive in their advice on the project side. For instance Clark admits that making applications for grants to develop an invention industrially, was "all quite foreign to his experience" (Clark, 2000:142). The budget ultimately needed serious revision because costs had been underestimated and the steering committee was able to provide assistance with advice on revising estimates when the university had made obvious omissions such as not including an estimated cost for a project manager.

**Commercial development**

**The market survey**

Telectronics/Nucleus' view was that it was essential that the market be considered as a global context. It was agreed that there was no way that the project could possibly work if the market was seen as that in Australia first and then to be expanded internationally if the local market worked. The government grant provided the means with which to conduct such an expensive exercise.
On July 5, 1979, Maria Yetton was appointed by Teletronsics to undertake the market survey with Mike Hirshorn. Hirshorn’s knowledge of bio-materials meant that he was a natural partner in a number of the areas that Yetton was going to be discussing and they proved to be a very strong team with excellent documentation. Their brief was to assess the market size for the device in Europe and Australia but particularly in the United States. Therefore the survey sought to determine:

- what proportion of the deaf market was made up of pre-linguistically and post-linguistically deaf people
- the distribution of deaf people
- the number of patients a clinic could handle
- if governments were prepared to fund the device (Clark, 2000:145).

From the Nucleus/Teletronsics perspective the trip was required to gather world information and hence to enable the company to evaluate how far advanced other groups researching cochlear implants including strengths and weaknesses compared with Melbourne University. Such market research is clearly very important before a company commits millions of dollars to prototype development; however, it is rarely done because of the cost. Thus Nucleus wanted to know, before it became committed to the Melbourne University team, if there were alternatives that they should pursue. Hirshorn and Yetton interviewed the key surgeons and otologists in all of the major potential markets and also in the places where the development work was being done in an attempt to evaluate the real politics of the situation. This was, after all, a commercial concern and Nucleus had to make the best commercial decision. The Melbourne University group proved to be the most balanced and appeared to be the most advanced in most of the areas of all the groups around the world.

The findings

The study found that there are two categories of deaf people, about equal in size: “post-lingually” deaf (deaf as a result of illness, age or accident after the patient had learned to hear) and “pre-lingually” deaf (deaf at birth). The hearing-impaired market comprised
the profoundly deaf and the severely deaf. Severely deaf people could be helped, to a
greater or lesser extent, by a hearing aid that amplified sound. For a fee of A$1,000 (in
1979), the customer bought this device after consulting a doctor or by going directly to
a hearing aid retailer. The retailers were very commercial and tended to regard Cochlear
as a competitor and therefore, a threat (Vandermerwe, 1991).

People whose hearing problems were not being satisfactorily improved by hearing aids
could have become a market for implants. However, as long as they could hear at all,
such consumers were usually not prepared to risk surgery. Ordinary devices such as
hearing aids were useless for the profoundly deaf as the inner ear had become so
damaged that surgical intervention was necessary. In ascertaining the real size of the
profoundly deaf market, the survey team took into account psychological and medical
factors. Many people who became deaf early in life did not consider themselves "sick"
and, therefore, saw no need for surgery. Many potential users were wary of the concept
of an ear implantation, especially of having an electronic device inside the body and
near the brain. The research showed that over 40% of potential users were against the
idea of "having wires in their head, were afraid of doctors and hospitals, or saw the
procedure as far too risky to justify" (Vandermerwe, 1991:8). This group appeared to
have a strong influence on the profoundly deaf and voiced strong opposition to treating
deafness as anything that needed medical intervention. These groups also had by now
managed to develop strong connections in the political arena and would prove to be a
future source of contention in marketing the implant.

The market study concluded that there was a significant world market for the product,
particularly in the United States and Europe. The study estimated that about 10% of the
profoundly deaf, or about 50,000 patients worldwide, were possible implant candidates.
Apart from this backlog, the data suggested that another 3,000 new cases occurred each
year worldwide (Vandermerwe, 1991). While the total number of potential customers
was small, with an average price of A$10,000 (in 1979) per patient for the implant, the
total value of the market was substantial. The market study therefore justified the further
development of the implant to the stage of clinical trials, at an estimated cost of A$5
million.

By December 22, 1979, the deadline for Phase 1, the market survey and the
development cost plan had both been completed and the university had also achieved all
its milestones on target. The Commonwealth Government awarded the grant for Phase 2 and made a public interest grant of approximately A$3 million to Nucleus Limited in 1980 to start the process and take the product into clinical trials. This was A$2 million short of the estimated cost but was sufficient to continue the development of the project. The estimated shortfall was revised in 1985 and a roadshow was organised by Trainor to obtain the additional funding. This is discussed later in the case study.

Public Interest Grant Phase 2

The second phase of the program required Nucleus to engineer the bionic ear and to make it smaller and more reliable. "They also needed to organise a trial centred in the US to gain FDA approval for its commercial use. The University of Melbourne would be responsible for further developing speech processing strategies, as well as surgical and training programs for the US clinics and biological safety studies" (Clark, 2000:145).

The relationship between Melbourne University and Nucleus went surprisingly well during the second phase of 1980–1983 and the project made enormous progress. The expertise of Telectronics/Nucleus in bio-materials, reliability, hermetic techniques and experience with the regulatory bodies around the world in areas such as patents, were a vital component that established the Cochlear implant company. These attributes had been recognised by the government as being a significant contributing parcel of goods to bring to the table when awarding the grant.

The strengths of the two groups therefore were complementary. The university had strengths in clinical studies, anatomy, psychophysics, surgery, physiology, audiology and statistics, all on biological science. Telectronics/Nucleus on the other hand had major strengths in systems design, reliability, project management, bio engineering, electronics, patents, regulatory authority relationships and a strong focus on manufacturing, QA, marketing, service activities which is then seen in the market. The company had strengths that, the university lacked and the different capabilities greatly complemented each other, enabling each group to extend their networks to increase capabilities of the entire project.
**Location**

The ideal situation would have been to have the research and commercialisation arms of the project close together to allow for ease of transfer of tacit knowledge between the groups. The cochlear implant project is an excellent example of the growth of a high-tech firm across industries built on inter-firm and interpersonal relationships and networks as the need for resources and capabilities changes. Thus, although Clark had really wanted the industrial development to be done in Melbourne so that it would be close to his research team, it was important that initially developments be done in close association with Telectronics/Nucleus which had expertise in implanting micro-electronics into people (Clark, 2000).

**Transferring tacit knowledge**

In describing ‘Cochlear implants: From Idea to Clinical Practice’, William House acknowledges the excellent engineering work that Jack Urban contributed to the design of the team’s implant. House states “no history of Cochlear implants is truly complete without some acknowledgment of the role that this man played” (House & Berliner, 1991:29). Similarly Jim Patrick, described by Clark as an innovative engineer and a lateral thinker who could apply his knowledge to other disciplines (Clark, 2000), has played a major role in the development of the cochlear device that currently makes up the implantable portion of the Nucleus system.

Patrick was responsible for the engineering development of the first functional multi-channel cochlear implant and, as project manager, he assisted PhD student Ian Forster to create groundbreaking knowledge by integrating the original circuit for a Mastermos silicon chip. In addition to leading the design and construction of the university prototype cochlear implants, Patrick played an active role in many related research fields including neurophysiology, psychophysics, electrode design and speech processing. He also played a pivotal role in the early debates on the efficacy of neural stimulation as a method of aiding hearing impaired people and a major role in defining levels within which neural stimulation could be safely used.
Patrick had made particular personal contributions in implications of charge-induced tissue damage to the viability of electrically stimulated implants. He also contributed to miniature multi-electrode arrays suitable for implantation in the cochlea and speech coding strategies for multi-channel cochlea implant systems. These contributions were vital in the realisation of the practical multi-channel cochlear implant system and the subsequent need for improvement of the system.

Once having established the location of the project, Money considered it to be crucial that Nucleus obtain an ongoing commitment from the university in terms of know-how and ongoing research. Therefore he thought that it was essential to at least approach key people, especially Jim Patrick. Money felt that Patrick had all the attributes to be able to carry along the knowledge and prejudices from the university to Nucleus and that such a transfer could maximise the chance for success of the project. Clark has commented that “he was taken aback by the thought of losing some of his special people, but realised that the transfer would be good for relations between the industry group and the research team” (Clark, 2000:147).

Patrick agrees that “a core group of people that have a breadth of experience between them and are totally committed to a project can be the makings of a dynamic beginning of a new company. This then means that things can happen really quickly because you have people who have a common purpose and understand the objectives. They inspire each other. That’s how Cochlear was set up. Paul (Trainor) had this expression ‘tiger team’ that he defined as a small team with one goal and full time commercial commitment”. The strengths of such a group are focus and enthusiasm. There is freedom to use new approaches and not be bound by the conventions of a larger older group. There is freedom to investigate tangents that sometimes really pay off, although there can be risks. With a small committed team the project can survive with only the most essential documentation, “most of us knew a lot about what everyone else was doing which is one of the advantages of a small company” and allows for a lot of flexibility. Weaknesses are the limited resources and the potential for reinventing wheels. David Money considers that in a small team there is not the opportunity to look at all the accumulated wisdom and experience of a larger group operating in a company. However these are minor considerations compared to the possible accomplishments that a dynamic and innovative team is able to achieve.
The new Cochlear Division of Nucleus advertised around Australia for a number of positions and managed to attract Peter Crosby. He joined the group from Royal North Shore Hospital and was very involved in computer systems and building small medical products that were based on microprocessors and related software, an essential skill missing from the team. To take responsibility for the construction of the package, the division also advertised for a mechanical or materials engineer and appointed Januz Kuzma who had recently arrived in Australia. Kuzma was instrumental in finding a practical way to bring twenty-two electrodes out of the package through a ceramic seal. Geoff Lavery also came from Melbourne University a little later. He was the team’s electrode man and he ended up running the production for quite a while. Money acknowledges that as CEO, he saw himself “very much a leader among equals in that small group”.

**Engineering the bionic ear for commercial use**

The time to achieve all the objectives of Phase 2 was extremely short. It was September 1981 by the time the tiger team was in place and by the end of September 1982 the first patient had been implanted with the new system. To have successfully completed so much so quickly for something that was so complex was quite extraordinary. The tiger team managed the critical parts that they had control over. For instance two integrated circuits for the stimulator were carried out in parallel developments to ensure that milestones were met. One was developed in Australia and one was developed in the US in competition with the Australian model. Patrick was sent to the United States to ‘baby’ these integrated circuits through the enormous and complex test procedures. The two integrated circuits were effectively the same but with different layouts and made by different groups. Ultimately they ended up being quite different because the problems each group encountered were different. The first one that worked won the race and it was Amalgamated Wireless Australia Micro-electronics that produced the first working internal circuit. The critical decision to double the effort to design a commercial circuit in an effort to meet the tight deadline would not have been possible without the financial resources provided by the government grant. The new design was based on a novel radio frequency link between the implanted receiver/stimulator and the external speech processor. The data were simple to generate, very simple to decode and capable
of conveying power and data together. The simplicity of the system meant that the team
could achieve the range needed with the accuracy needed without the terrific complexity
that normal digital transmission would have had.

By mid-1982, the Nucleus implant was “going through its final design stages for
implantation” (Clark, 2000:153). The first Australian implant of the Nucleus design was
planned for 12 September 1982. Having achieved successful results with the first
patient, further implants were undertaken and by the end of the year the required
number of six patients had the newly designed device successfully implanted, with very
favourable results. This successful initial trial in Australia gave Nucleus the green light
to start the clinical trial in the US and Europe (Clark, 2000). In 1985 the findings and
histories of 87 patients in three continents (US, Europe and Australia) had been
analysed and presented to the FDA. In October 1985, the FDA finally approved the use
of the Nucleus implant in adults who had hearing before going deaf. “It was the first
multiple-electrode cochlear implant to be approved as safe and effective for clinical use
by any health regulator” (Clark, 2000:161).

Building global networks

Mike Hirshorn, having successfully conducted the marketing survey in 1979, was
allocated the formidable task of establishing and managing worldwide clinical trials,
gaining FDA and other regulatory approvals and creating subsidiaries from which to
market the implant in the US, Europe and Japan. Nucleus had always expected the
company to have three “legs” to their market, estimating that the US would make up
only approximately 40% of demand. Hirshorn went to the US first, the obvious place to
start for a language recognition product. Also at that point the regulatory environment
was more advanced in the US than in other places and Europe looked to the US for
regulatory approval of new products.

Patrick says that Hirshorn “was really crucial to the project”. His medical background
gave him the right kind of expertise for the task. While conducting the world survey in
1979, Hirshorn and Yetton had established and developed successful relationships with
clinics and experts in the ENT field. Many of those who had participated in the study
had developed very favourable impressions of Hirshorn and reported to the US
government giving impressive reports on the survey team. One of the people to have made a significant contribution to the project was Dianne Mecklenburg. Dianne was an audiologist who had completed a PhD in the US and was on sabbatical at the University of Melbourne in 1976. Mecklenburg had always believed in the technology and was instrumental in the design of the clinical trial ensuring that patients were fitted to the correct protocol that was an important aspect of the design.

From early in 1982, it became necessary to determine where the trials should be carried out in the US and Europe and who would be the appropriate ear surgeons to conduct these trials. It was also necessary to decide if the centres should be in cities where there would be a larger population of deaf people, or in special centres in smaller cities. In Australia all the centres were in big cities but this was not the case in the US. Would teams be able to manage people for lengthy rehabilitation sessions when they came from other parts of the US? It was Mecklenburg's and Hirshorn's contacts that finally determined some of the centres and developed the processes for determining criteria to assess the reputation and skill level of surgeons and their multi-skilled teams.

The process of access to contacts was made easier by networking strategies that had been established some time ago. In the years leading up to the trials, Clark had gathered an impressive list of disciples in the ENT field. As early as 1977, he had strategically invited Dr Jim Jerger from Baylor Medical College, a pioneer in audiology, to be guest of honour at Melbourne University's inaugural audiology workshop. “Baylor had two outstanding ear surgeons in Dr Bob Alford and Dr Herman Jenkins” (Clark, 2000:158) and Clark considered these to be ideal future contacts. Such thinking proved to be absolutely correct and Baylor was one of the first centres in the US to trial the Nucleus device. Similarly Dr Brian McCabe, Professor of Otolaryngology at the University of Iowa had been invited to present a paper at the University’s annual audiology conference in 1981. On hearing Clark speak at the conference, he became very enthusiastic and wanted to use the Melbourne device to do a comparative study he was planning to undertake. Iowa, under the supervision of lead surgeon Dr Bruce Gantz, was also one of the first to undertake US trials of the new device (Clark, 2000). Once the FDA gave its approval for the trials to begin, Iowa and Baylor were the first centres in the US to implant the Nucleus bionic ear in May 1983. Other surgeons to participate in the US clinical trials were Dr Charlie Mangham from the Mason Clinic in Seattle; Dr Noel Cohen at New York University; Dr George Lyons from the Louisiana State
University, New Orleans; Dr Owen Black from the Good Samaritan Hospital in Portland and Dr Julian Nedzelski from the University of Toronto.

From 1982 to 1984 Mecklenburg worked to bring the pivotal study to a successful conclusion. Hirshorn joined Mecklenburg in mid-1982 and was charged with the responsibility to promote the Melbourne/Nucleus device to a market that did not always recognise or necessarily trust Australian scientific excellence. Selling the concept of the multi-channel device and its benefits to the US market was difficult due to American competition. Specifically because the 3M/House device was promoted by the very eminent and respected Bill House, who spoke at conferences and had personally trained many of the ENT surgeons. Clark, however, refused to travel to the US thus constraining the Cochlear team's promotional efforts. An even bigger challenge was to develop the protocol that all the surgeons, audiologists and clinics would adhere to for the equivalent of phase III trials, a pivotal study that would provide data for the ultimate FDA approval.

In October 1984, Ginger Minelli, Hirshorn's assistant, and Judy Brimacome, an audiologist and Mecklenburg's assistant, also joined the team. Certain personality characteristics were necessary for this kind of successful outcome. Colleagues described Hirshorn as very bright, sincere and with a very high level of integrity but very much the opportunistic business entrepreneur driven to succeed. Although working as a consultant, Mecklenburg was very committed to the project. Her task was to organise the protocol, collect the data, run training workshops and run around the country trouble shooting technical problems. She gave workshops and wrote papers. "I thought it was important to start giving papers so that we could talk about Cochlear implants although without data, which was still being collected, it could be embarrassing. I would just pop up at conferences all over the place and thank God I had the freedom to do that, and just ask questions as an opportunity to talk about multi-channel Cochlear Implants and the Melbourne device".

She and Brimacome were always there for the first programming of a patient. They trained every single clinician who had ever programmed any patient in the US and slowly built up a team of audiologists. She flew to where ever there were any problems and phoned "Jim Patrick if anything wasn't working to work through various strategies to make the technology work. Jim flew over for some of these cases and so this is how
wonderful the service was”. Nucleus offered the service at no cost to the patient, and they would go anywhere that was needed, using whatever man-hours were required. Replacement units would arrive as special delivery with no expense spared. The Cochlear team was very professional, very confident and fast responders. This kind of service made their chief competitor look very sluggish and slow. It also proved to the American specialists that there wasn’t anything to worry about a device not being made in America. In addition, the team was very strict about the protocol to ensure that FDA approval was not held up due to unreliable data.

In December 1984, Ron West was recruited as the CEO of the US subsidiary. Hirshorn was very careful to choose the first CEO of a subsidiary company. One of his perceptions was that he needed someone who understood the medical professional culture as well as someone who could relate to the technology and not just focus on sales. West had come from Johnson & Johnson, where he worked for the ultrasound section of the cardiovascular business. He was interested in running a business but at Johnson & Johnson Ultrasound his only opportunity to run a business was on the East Coast and he didn’t want to do that. He had decided to stay in Denver and began to do some consulting work while looking for an opportunity to run a business. In late July of 1984 he was contacted by a recruiter for the CEO position. Hirshorn asked West to draw a heart as part of the interview. West says that “I knew a little bit about cardiology so when he asked me to draw a heart, I thought that was fair. The interview went pretty well but I didn’t think much about it. Cochlear was a start up company and I wasn’t sure I was really interested in all the issues that go on with a start up company especially fund raising”. But Hirshorn was very thorough, checked all West’s references and thought the best way to start was by getting to know each other better. So he hired West initially to do some consulting work. That strategy fitted with West’s plans “because that’s what I was doing at that point in time anyway and I wasn’t in a big hurry. He left me to help him with positioning the firm and some marketing work associated with The American Academy of Audiology conference that was to be conducted in the fall”.

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Problems for the American president of a new Australian subsidiary

As the new leader of the new subsidiary, West was charged with growing sales for the company to meet its current business plan objectives. Experienced in the US medical devices market, he was a crucial element in the business plan for the firm by providing a solution to its problem of not having the business know how in the US market. However, there were a number of serious problems for him in taking on this role.

West had very little experience with firms outside the US and he was sceptical that the Cochlear device could be dominant in the US market place, "after all Australia is not where you expect to find the best technology". But he had experience with some other Nucleus technology and "knew that they had some fairly sophisticated design tools". On the other hand when he saw the business plan numbers they were staggering. "They had the price going down 5% every year for the first ten years and the demand going up dramatically and I just couldn't convince myself it was possible to move a business so fast". He was also worried that the company as a start up would be undercapitalised but was again pacified in that the start up was part of the Nucleus Group. Trainor refused to give him options and he had to renegotiate his contract to include a bonus scheme. When he tried to employ senior staff who needed to be paid US salaries, Nucleus did not see the need initially leaving him with less qualified people. Also his board was not always cooperative. One member who had been part of the Nucleus group of companies for many years, was described by West as "hostile".

Several events did, however, provide him with solutions. David Money, the new CEO of the Australian Cochlear company, strongly believed that nationals knew their own market best and as long as they were producing the results he did not interfere with their procedures. West believes that "under David's entire period we had a good working relationship and I think all the executives would really have struggled without his support". Another beneficial factor was that 3M had been in the market already for a year so the concept was no longer new. He and Brimacombe were the first US sales team and being very opportunistic, they visited all the firms working with the 3M device because these people "at least knew what the heck we were talking about". They developed a video showing how the patient received speech recognition and this proved to be very effective. This first sale, produced desperately needed revenue that was equivalent to the entire income for the previous year.

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Penetrating the US market

Rae Reynolds was hired by West in late 1985 to develop a market for Cochlear implants. She notes that although the company had now received FDA approval for adult implants, and was running classes for surgeons, there “weren’t any people volunteering for implants and the doctors were saying they would love to do the surgery but had no idea where to find the deaf people”. Reynolds, therefore, saw two barriers to meeting the budget targets that the Australian Head Office had set for them. The first was that they had no customers and secondly there was a major competitor in the House device that was sold through a highly respected US corporate giant, 3M, with a wonderful reputation. House, as noted earlier, had trained many of the surgeons and they mostly felt a loyalty to him. He also made sure that he was at all the surgeons’ meetings promoting his device. However, his single channel device was not as effective as the Cochlear multi-channel device and patients who had been implanted with the 3M device were not getting speech recognition and were not recommending others to follow in their footsteps. Furthermore, surgeons and audiologists did not understand that there was a significant differentiation between the two products and were reluctant to recommend either of them.

The solution was multi-tiered. First West and his team needed to train the surgeons and audiologists to understand the issues and benefits of the Cochlear system to begin recommending it. They then had to begin to market to the deaf community with original strategies. Finally they had to convince the medical insurers, in both the government Medicare system and the private systems, to reimburse patients who had received the implant. This was difficult. As with any new technology, until the agencies were educated in the difference, the implant was seen as a hearing aid and the insurers had written exclusions in their policies that did not cover hearing aids. To complicate the matter further, when the government did finally start to reimburse implants, it was at a very low level so that doctors and hospitals were not covering their costs and excluding Medicare patients from surgery. The problem was quite tricky in that many of the hospitals did not know just how much they were losing. Furthermore, some hospitals were spreading their costs to paying patients and this was illegal. If the Cochlear team was to advertise these facts in attempting to get government support they would potentially lose that market. The first major problem for the new subsidiary therefore was how to stimulate the market to generate more surgery and make more people
became aware of the fact that it was potentially beneficial to them while keeping doctors and hospitals and government agencies on side.

Organisations of the deaf were the first to be approached. PR campaigns were generated with advertisements in newspapers announcing forums to show case studies of people who had benefited. A hot line was established to explain the device to the public. Advertisements were placed in audiology magazines to try to draw distinctions about why this device was an improvement over the single channel device. Thus the company became the first to promote their device direct to the consumer, but that brought its own problems. Reynolds notes that "the deaf community was against us. We were challenging their economic basis since many of them were sign language interpreters and teachers of the deaf and administrators of deaf institutions and we were undermining their whole economic potential. But it wasn’t till we received approval to implant the device into children that it really got ugly. These people would attend forums and became quite vicious in their attack on the device”. She laments that many of the arguments regarding the debate of an implant vs sign language are still continued today. This is despite the fact that the technology has been much improved and the benefits have been accepted to the point where not only the profoundly deaf but also the hearing impaired are receiving implants.

Problems for West were also extended by the lack of understanding of the US environment by the Head Office. For instance Reynolds felt that the people in Australia were quite foolish in not providing any funds to lobby government bodies. “It is just one of those things that you have to do to get attention is be politically active. One of our major competitors has had a couple of product recalls but these were not at all widely publicised or as devastating as they could have been without the connections that company had in Washington”.

Production problems were also an issue. The patient would be ready, surgery was scheduled and there would be no delivery of product. Sales reps would be sent out to borrow a back up implant from somebody else so that the scheduled patient had an implant. This was very embarrassing for the sales team. In addition the busiest time for child implants was during the Christmas break but that is when the Australian office would shut down for three weeks. Mecklenburg laments that “we would have parents screaming down the phone because they had carefully rearranged their lives so that their
child could get an implant during this brief window and the Australians were going on vacation. We were just going nuts”.

Australians also did not understand the market in terms of cosmetics. There was one colour that the product came in and that was beige, which was fine if the patient was white. Being manufactured in Australia, West felt that he had no control over even cosmetic changes to the device. He felt that “living a long way from the suppliers became a convenient excuse and was used exhaustively”. Additional problems noted by the American team included the inability of the Australians to see the need for an extension of products such as their competitors had established and the acquisition of groups that could extend their market. The major advantage for the company was the superiority of the product and the lack of aggressive marketing by their competitors. A further competitive advantage has been the dedication and solutions driven focus of their staff. This was not always easy to handle.

West notes earlier in the chapter that Mecklenburg was very strict about the protocol to ensure successful FDA approval. He notes however that “that kind of control can be justified because the study has to be done according to the protocol. We had a very interesting study as a result of Dianne’s commitment and her control orientation but once we got through the clinical trial we no longer needed that kind of control”. West had a lot of trouble with Dianne as he tried to put commercial systems in place and build up customer relationships. Mike Hirshorn also had difficulty in letting go. West gave him three going away parties before Hirshorn finally moved onto his next assignment setting up a European subsidiary. West suggests that “Mike found it difficult to let go of what he had so brilliantly started”.

The European subsidiary

In Europe Hirshorn repeated the process of finding an office, hiring a CEO and establishing a market. As in the US, he visited surgeons that Cochlear had made contact with earlier, specifically Professor Ernst Lehnhardt who was operating in Hannover. Hirshorn and Money had earlier made several visits to Hannover to talk about the Nucleus system. A presentation had been made to Lehnhardt and his engineer Dr Ralph Battmer in Australia who then championed the cochlear implant program in Hannover
in mid-1984. The Nucleus system provided treatment where there was none before, providing surgeons with great satisfaction. Lehnhardt then drove the project in Hannover since it would have been considered to be inappropriate for the company to do so. "Within a year, the European professor had created the largest implant centre in Europe through using the Cochlear Device" (Clark, 2000:159).

Due to language difficulties Hirshorn set up a office in London, but eventually established a Head Office in Basel, Switzerland to meet three criteria. First, to suit his replacement executive; second, to be able to reach German and other markets; and third, to avoid an extremely high German tax regime. He hired Dr Monika Lange (later Lehnhardt) to lead the new subsidiary. She proved to be the perfect candidate speaking five languages fluently, stylish with a strong presence and a knowledge of the medical industry. These traits provided the basic characteristics to overcome many of the cultural issues that Hirshorn anticipated. He introduced her to Professor Lehnhardt who she later married. In 1984 Mecklenburg joined Lange and her assistant, Ulrike Trautmann and "we literally hit the ground running".

The job for this team was the same as it was initially in the US. They travelled to centres in different hospitals and trained staff in all aspects of rehabilitation and programming, giving lectures and workshops where ever possible. Mecklenburg did not have a language problem as "most of the work was done in English, and most people who are European have some English". She also had some German and French, so she understood what patients were saying. Her main problem was working with cultural issues. In the US she was able to bring the various disciplinary groups together to determine a protocol that everyone agreed to. In this part of the world, disciplinary systems were considerably more hierarchical and Lehnhardt was not impressed that he should be told to adhere to what some audiologist had agreed to. Considering the relationship between Dr Lange and Professor Lehnhardt, the relationship between Mecklenburg and Lange very soon broke up and Dianne reluctantly went to work for the opposition.

Sue Roberts joined Hirshorn in the UK and colleagues speak of her as "fantastic". She was very spontaneous and jumped in and took a risk at everything – get on a plane and go to another opportunity. Roberts established the market in the UK, France and then began to sell to customers in the Middle East often taking serious risks being a woman in
Moslem countries. Given the drive for success that this team had, sales continued to grow despite the strong competition in Europe. Hirshorn was careful to introduce the European to the US group and “there was quite a lot of camaraderie between the two Cochlear groups”.

The problem that began to seriously impact on the two groups was the lack of coordination between the production team in Australia and the sales that the subsidiary teams had made. Roberts laments that one half of the Head Office was demanding higher sales figures but production figures in Australia were not keeping up with what was ordered. Eventually Hirshorn moved back to Australia and took over the manufacturing. The manufacturing function was carried out by two parts. One group was responsible for that part of manufacturing that made the implant. The other group was responsible for the non-implant parts such as the speech processor but they shared common warehousing, transport and administration. The heads of the two groups were at ‘war’ with each other.

Hirshorn’s task was to bring about harmony. There was a serious need to coordinate all the elements and the important thing for him was the shipping schedule and he made that clear to everyone. Roberts says that “it made a huge difference to us because HO just didn’t understand what it was like in the field. Australian customers accepted anything. There was no competition. We had competitors were prepared to sell their implant for half the price of the Nucleus device”.

Objectives within the impossible business plan, as West had seen, were in fact eventually achieved and Cochlear continued to grow into Garnsey’s next growth reinforcement phase by developing new products and markets.

The Japanese market

Mike Hirshorn visited Japan for the first time in May 1985 as part of a medical lecture tour with the United States Veterans Administration on Rehabilitation Medicine. After the tour, he took the opportunity to do some exploration to determine what the next action would be. It is a testament to Hirshorn’s skills that towards the end of that year he had identified Tokyo Medical College as an interested participant. In line with earlier
strategies, the chief surgeon was invited to visit Australia for an International Cochlear Implant Conference, and in December 1985, Professor Funasaka, of Tokyo Medical College, implanted the first patient in Japan. In early 1986, audiologists were flown to Japan from Melbourne University to train Japanese staff. Fortuitously in 1987 Telectronics decided to close down its Tokyo office and Cochlear was able to purchase the subsidiary, Nihon Telectronics Company. The name of the subsidiary was changed to Nihon Cochlear Company thus giving Cochlear a direct presence in Japan and the necessary governmental import license to operate in the Japanese market.

**Financing the project**

A common factor facing many new Australian biotech firms is the constraining problem of funding for the early growth stage. Although the Australian Government had been very generous with seed and early stage funding for developing the Cochlear product, in 1983 the company was still several years from projected cash flow break-even, which was not expected till 1986. By 1982 the government had contributed $4.4 million, providing Nucleus with most of the funds to take the product through clinical trials, gaining US FDA and other regulatory approvals, and to begin sales in major markets. However more commercial sources of funding would be essential to get to that point (Smith, 1999).

The Australian financing community until the mid 1980s had been subject to a tightly regulated financial system and was very conservative and inexperienced in sophisticated financial markets. They were particularly risk averse with respect to technology based investing. There were few venture capital investors, and very few precedents that investors could use to determine appropriate value of the company, and the related risks involved in Australian companies that planned to dominate global markets based on novel technologies. The federal government's Management Investment Company (MIC) program, was initiated to promote the development of a venture capital industry in Australia as a means of fostering young, Australian technology-based companies (Smith, 1999). Fortuitously, this initiative created a new pool of possible investment funds for Cochlear.
Nucleus Limited was unwilling to bear the burden of funding the entire period from 1982-1986. Cochlear Pty Limited was established in part to facilitate external fund raising in 1983. "A revised estimate of $5 million would be required to take the company through to cash flow break even, and Trainor was determined that at least $3 million of this would have to be raised from external sources" (Smith, 1999).

As none of the funding so far had been in the form of an equity investment, there was no previous round of funding to refer to. A net present value of projected cash flows was calculated and verified by Price Waterhouse, yielding a value of $20 million (Smith, 1999). Paul Trainor, therefore, led a global road show to ascertain what the market would pay for a company at this stage of development. Trainor understood that overseas, particularly the US venture capital industries, were experienced in best quality science, particularly in the biotechnology sector. To establish a real value for the fledgling company he would need to go outside the Australian financial community that was unfamiliar with this type of company. He also determined that Cochlear would only accept Australian financing if the financial terms were almost as good as those that he could establish with players from the global market. However the availability of further government grants and other non-dilutive government funding would need to be considered if the ownership of the company went off shore.

**Global search for funding**

"In the second half of 1983 Bear Sterns New York was retained to help the management team identify international venture capital investors for a $3 million first round financing. Trainor selected a New York based merchant bank to lend credibility to a small Australian company as it met with experienced finance groups in Europe and the USA. The team spent several weeks visiting investors in the United Kingdom and on the US East and West Coasts. The road show met expectations, with considerable interest shown by many of the investors. By December 1983 the team had secured an offer of A$3m to buy 27.5% of the equity in Cochlear Corp, a US based company that would own the rights to Cochlear Pty Ltd’s technology, from Fred Adler. Adler was renowned for his successful venture capital investments in the computer industry" (Smith, 1999).
The offer set a value for Cochlear by an international player with expertise in high technology investment. Accepting this investment had several attractive features. The offer was on the table. The investor was US-based and could do much to support the establishment of US operations and the US regulatory process. If the planned exit from the investment was a NASDAQ listing, the support of US based venture capital investors was essential. The price recognised a significant improvement on the funds attracted to date, a factor that would satisfy Nucleus Ltd and the Commonwealth alike. Surrendering significant ownership of the company to a non-Australian party, however, would be less attractive to the Commonwealth.

**Australian investors**

Concurrent with the international fund raising effort, Trainor also courted Australian investors. By mid-1984 three independent venture capital groups, two with funds raised under the MIC scheme, had expressed interest in investing small amounts in Cochlear Pty Ltd. Trainor advised these investors that he would prefer a syndicated investment, led by Nick Callinan of Western Pacific in Melbourne.

Western Pacific had raised a $10 million fund in May 1984 under the MIC scheme, which provided investors in the government-licensed fund with a 100% tax deduction for the capital they committed to the fund, as long as they maintained their investment for a minimum of four years. This was enough time to take Cochlear to break-even point. The MIC fund was constrained to invest only in early stage, technology-based Australian companies with a strong export orientation. Government approval was required for each investment. The MIC scheme was the government’s attempt to generate in Australia a similar surge in the formation of start-up high-tech companies as was being seen in the US, particularly in the biotechnology sector and perfect for Cochlear.

Western Pacific had recently formed an association with Advent, a global venture capital group based in Boston USA. Nick was able to draw on his network at Advent to assess what was the strength of interest in Cochlear by US investors, and to understand the valuation that was appropriate for a company at this stage of development. He understood that the US venture capital industry was known for seeking the best quality
science and particularly in the biotechnology sector, science with a lead-time over its competition. While it became clear to Nick from his discussions with colleagues at Advent that Cochlear had other financing options, he believed that Western Pacific as an Australian investor would have a “home ground advantage”.

With a total fund of only $10 million, Western Pacific could not prudently invest the full $3 million required by Cochlear. It assembled an investment syndicate, itself committing $1.25 million, with a further $1.25 million coming from another MIC company, BT Innovation, and $0.5 million from Citicorp Capital, the venture capital operation of the international bank. Negotiations on the terms of an investment ensued with Bill Thomas, Nucleus Limited’s Chief Financial Officer.

In late 1984 the Australian syndicate made an offer to buy 27.5% of Cochlear Pty Ltd for A$3 million. Cochlear now had a choice of two offers. Accepting the Australian investment would have a number of attractive features. Cochlear Pty Ltd would remain Australian operated and owned and would have the support of local venture capital with a strongly commercial approach. This was clearly important to the Australian staff, to the Australian Government who had provided the early stage funding and to the Australian management team. Control of the future and the location of manufacturing and other operations would be linked to the nationality of the investor group. The Australian syndicate of investors also provided some capacity for future financing, if this was necessary due to longer than anticipated clinical trials or other regulatory procedure. The Cochlear Board decided that a locally based investor rather than a US based investor would be easier to deal with from a logistical standpoint, and would be able to provide more hands on support (Smith, 1999) and it accepted the Australian investment offer.

Thus by 1985, Cochlear Limited had the funding, the technology, essential capabilities, subsidiaries and FDA approval for taking the bionic ear, “the new miracle in sound” to a proven market. The major actors had also managed to embed the company in essential networks on a global scale. The journey from Clark’s bench top to global market had been difficult but all those involved refer to it as very exciting time with a great sense of achievement. As the returns continue to show annual increases in sales of around 20%, it would appear that a very solid foundation had been established through the early growth of the firm.

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Growth enforcement phase

The impressive growth of Cochlear from 1981 to 1986 moved the company into what Garnsey calls the growth reinforcement phase of a firm’s growth. “A strategy that many technology-based firms must undertake in this stage of their development is to produce a stream of new innovative products to keep ahead of the competition.” (Garnsey, 1997:13). Patrick agrees that Cochlear’s current products are very different from those of the 1980s in both performance and cosmetics. He concurs with Garnsey’s sentiment that the company could never have achieved continued growth without continued product improvements.

Therefore as soon as the Nucleus designed device was successfully implanted in the first six Australian trial patients in 1982, Clark was keen to attempt the development of a device to help children born deaf. “The thickness of the device meant that it could only be implanted in the skull of a teenager or adult. Another problem in using the bionic ear was that the transmitting radio aerial had to be aligned accurately over the receiving coil on the package using a headband” (Clark, 2000:166). This was problematic in that children would have trouble adjusting to it and it would almost certainly be dislodged when they played games. A smaller improved package using magnetic alignment and attachment was developed by Nucleus and approval from the US FDA was sought for a worldwide trial to begin. Approval for the trial came in 1986. Despite a long time in being able to collect evidence to prove that children benefited from the implant, and some strong criticism from the deaf community, approval was granted in June 1990. “No health authority from any country had sanctioned a bionic ear for children before. The bionic ear was now being called the first major advance in 200 years to help profoundly deaf children communicate” (Clark, 2000:181).

Cochlear’s system is now composed of an extensive range of products. They include the Nucleus® R24; the newly launched ESPrít™ 3G BTE; the SPrint™ bodyworn processor; Nucleus® R126 software and the Neural Response Telemetry™ (NRT). The company continues to develop newer and better designs and win Medical Design Excellence Awards around the world demonstrating why they continue to hold a very strong position in the cochlear implant market. Alliances with capability building partners such as Phonak FM products to expand the use of miniaturised FM
communication technology with cochlear implants, demonstrates the relevance of Garnsey's theory and continues to underpin Cochlear's consistent growth.

Sadly in 1988, the "heart of the Nucleus Group" Paul Trainor suffered a personal tragedy with the death of his son, which led to possibly devastating consequences for Cochlear. Teleconetics at that stage dominated the Nucleus Group with an approximate $350 million turnover, compared with Cochlear's $10 million. Even so, they were running sufficiently short of cash that they "needed a big brother" to assist with further expansion. Trainor sold his share holding to Pacific Dunlop on the undertaking that he would have no more to do with the business. Between 1988 and 1995 a sequence of events then followed that brought down Teleconetics and could have also destroyed Cochlear Pty Limited.

In direct contrast to Trainor's innovative management approach, Pacific Dunlop had a financial orientation to the business with tight financial controls. When Teleconetics acquired one of its pacemaker competitors Cordis and its factories in Florida, Pacific Dunlop decided to move all of Teleconetics' head office activities such as finance, marketing etc., to the USA. Some of the manufacturing and R&D was already being done in Denver and that was now expanded. Therefore, the centre of activity and decisions went to the US and Money considers that the move was short-sighted.

Shortly before this move, approximately 40,000 patients were implanted with a Cordis designed pacemaker lead. A small number of patients died because the lead could break or crack and then poke through the side of the heart. A recall was made. The FDA came down very heavily on Teleconetics. Teleconetics, unlike Cordis, was a foreign company and the biggest pacemaker competitors such as Medtronic Inc. were American. Pacific Dunlop had no experience in the health sciences business where deaths do occur. Joe Shaw, CEO of another company within Nucleus has said that under such circumstance, the "standard procedure for a company earning much more than they need to pay out in damages claims, is to keep trading. The company pays out claimants, suffers losses for a few years but keeps going. In doing so it keeps FDA on side by paying out liabilities and learns from its mistakes". Pacific Dunlop it seems did not understand the business. Money agrees that "Pacific Dunlop should never have bought (Teleconetics) in the first place. Or if they did buy, it should have been essentially as a shareholder and allowed the business to be run by someone who knew it". It wasn't very long before Pacific
Dunlop decided to sell Telectronics and move out of the medical devices business altogether. At this point Cochlear was floated.

As a listed company, Cochlear moved out of its early growth phase into the maturity phase of its growth and by 1995 a new champion Catherine Livingstone led the company to new strategies and structures that were required for this next phase. Livingstone had been the CFO of Telectronics and she took the company through the listing process in December 1995 and led the company to its current 20% annual growth rate. Cochlear now faced the challenge of a mature firm in the global market, a challenge that the 2002 annual report suggests was met with Cochlear’s continued success. However this stage of its growth is beyond the case study’s frame of reference.

Conclusion

Professor Graeme Clark received an AO for his contribution to science. His ability to extend the problem solving capacity of his research team to a level of operations that could expand into commercial development was critical given the opposition to his original concept and the many constraints that stood in his path throughout the project. His positive perception of the need to harness the resources of the commercial world was developed early in life and provided an incentive to take the science out of the laboratory to the real world.

However, as quoted above, the wonderful work at Melbourne University would have gone nowhere if Clark and his team had not been able to leverage their knowledge resources to form a partnership with the entrepreneurial Paul Trainor and his “tiger team”. Together the scientist and the entrepreneur were able to extend operations out of the research institution and tap into a very diverse range of networks to obtain necessary resources to achieve growth.

The early growth of Cochlear has been an evolutionary process involving an accumulation of knowledge unique to the new firm. The concept of the multi-electrode implant and its prototype developed by the Melbourne University team was taken by David Money and his team and redesigned to meet commercial standards. The commercial product could have easily remained on the shelf without the “link to the
world market" that Mike Hirshorn and Dianne Mecklenburg were able to achieve. The whole team continually linked into networks to inspire surgeons, clinicians, audiologists, engineers, governments and investors worldwide.

Throughout the early growth process learning took place through shared knowledge and action and the competence building that the two teams were able to achieve has extended the firms productive opportunities to global proportions. Jim Patrick's strategic move from Melbourne University to the Sydney-based Teletronics was an essential transfer of tacit knowledge and clearly demonstrates that in a country with a small and dispersed population, proximity between research institution and commercial activity is not always necessary. Furthermore, by moving into major growth markets in the US, Europe and Japan and allowing nationals to conduct the marketing and operational strategies in those markets, the company has established a strong worldwide base.

The story of Cochlear's early growth is an inspirational tale of an amazing group of people. Together they are responsible for the improved quality of life for over 50,000 people who would have surely remained in a world of silence had it not been for their implant. Also, the commercial benefits to investors and national growth in the form of exports, highly skilled employment and R&D cannot be overlooked. Furthermore, ex-employees such as Mike Hirshorn, who is now a venture capitalist, provide experienced mentoring for other potential global players in the biotechnology industry. The Cochlear story is one where a small Australian biotechnology company achieved the right combination between scientific vision and excellence, entrepreneurial flair, visionary and strong government support, and a global market perspective. Cochlear Limited provides a sterling example of the critical characteristics that make it possible for small Australian biotechnology firms to access, mobilise and generate resources for sustained growth in global markets. A world-class company is the clear result.
Novogen Limited was founded in Australia and is now an international biotechnology company involved in drug discovery and product development for disorders that are commonly associated with aging. Currently the company is based in Australia and the USA. Its technology platform is based on isoflavonoid compounds that the company aims to convert into products that will successfully treat and prevent the major human degenerative diseases.

In 2003, new evidence appeared to confirm that the company’s drug phenoxodiol promotes programmed cell death in cancer cells by inhibiting the activity of key regulatory proteins and enzymes. Trials in Australia and the US have been able to show that phenoxodiol is able to selectively inhibit an enzyme expressed by all cancer cells but not by healthy cells. In effect normal, healthy cells become injured innocent bystanders during a drug’s attack on cancer cells and, based on recent findings, phenoxodiol may be the first drug to selectively target all cancer cells while leaving normal cells largely unharmed. This is an unprecedented achievement. If this is proven in subsequent experiments, it would be a revolutionary development and position phenoxodiol as the breakthrough drug in the prevention and treatment of cancer.

Furthermore, the company is shortly expected to sign a commercial agreement with a yet to be specified cosmetic company for the development of another of its drugs NV-07a, a drug that restores immune capability and corrects DNA damage. The drug’s cosmetic value is its ability to inhibit wrinkles and thickening of the skin providing the potential to gain enormous income from the cosmetic market.

Novogen is similar to most firms in the biotechnology industry, which is characterised by small entrepreneurial firms spinning off from public research institutions. Difficulties encountered by such firms include lack of commercial awareness by the founders, technology development and environmental constraints. The difficulties of commercialising Australian biotechnology innovations, however, have additional institutional obstacles to growth and commercialisation of their products and these obstacles are not always recognised. This Novogen story attempts to provide a
qualitative study to explore the “forces that changed the firm’s productive opportunity” (Hugo and Garnsey, 2005:141) as it began to commercialise its technology platform.

**The technology**

The basis of the Novogen technology platform is the naturally occurring plant compounds known as 'flavonoids' which are the dominant bio-regulators of plant survival functions such as plant cell growth, division and survival. Plant cells and human cells have little difference in the mechanisms within the cell that control basic behaviour such as growth and survival. Large amounts of flavonoids naturally occurring in human blood contribute in a significant way to human health, preventing the onset of degenerative disease processes. Novogen has identified the most powerful flavonoids, isoflavones, and selected them for the development of therapeutic products since they show the most promise in terms of preventing degenerative disease. Isoflavones have also been shown to be estrogentic, suggesting that they have promise in preventing degenerative diseases such as osteoporosis that are associated with oestrogen deficiency.

The company's research into isoflavones has created a considerable amount of scientific understanding and intellectual property that has created the Novogen Technology Platform. This platform has developed along two separate but closely related pathways of Consumer Health Products and Prescription Drugs. A strategy of international development and distribution of three over the counter (OTC) products has been pursued in an effort to establish significant brand equity and the development of operational skills in international markets. The second pathway manipulates the basic isoflavone molecule to obtain new compounds and then synthesises them in the laboratory. These new compounds appear to be making a significant contribution to the prevention and treatment of a wide range of common degenerative disorders such as cancer, heart disease, osteoporosis, rheumatoid arthritis, and inflammatory bowel diseases. They are disorders for which there are currently few options. The company’s drug phenoxodiol, for instance, promotes programmed cell death in cancer cells. Trials by Novogen in Australia and the US have been able to show that phenoxodiol is able to selectively inhibit the growth of rNOX, an enzyme expressed by all cancer cells but not
by healthy cells. Furthermore there appear to be no toxic effects on healthy cells with the use of phenoxodiol, a major problem with the use of most drugs currently used in the treatment of diseases such as cancer.

External environment

The market: size and growth

Novogen’s technology focus is on cardiovascular, anti-cancer and dermatology therapy. The market for these therapeutic areas is substantial, providing the company with lucrative opportunities. Alternate health therapies also enjoy strong consumer support.

Cardiovascular disease (CVD) refers to heart and blood vessel disease, and stroke. The underlying causes of most CVD is a gradual clogging of the arteries (atherosclerosis) that supply blood to the heart, brain and other vital organs. Cancer is a group of more than 100 different diseases but they all affect the body’s basic unit, the cell. Cancer occurs when cells become abnormal and divide without control or order. Plant flavonoids as bio-regulators in humans assist in preventing the onset of both of these diseases. The evidence from trials already undertaken supports this intellectual property and suggests that Novogen’s proposals are sound and its drugs will be able to target diseases for which medicine currently has few effective therapeutic options.

Mortality rates demonstrate the lack of options to effectively treat these diseases. The US National Centre for Statistics in its latest report noted that the two leading causes of death in the US are heart disease and cancer (NCHS, 2001). More than 10 million people are diagnosed with cancer every year. It is estimated that there will be 15 million new cases every year by 2020 (WHO website). Similarly, the Australian Institute of Health and Welfare (2002) estimates that cardiovascular disease is also a major health burden throughout the world, especially in developed countries. The Institute predicts that cardiovascular disease will become the single leading public health problem for the world by 2020.

The commercial benefits of a life-saving drug are substantial. Once a drug is licensed by the FDA there is nothing to stop doctors using it for other conditions so phenoxodiol’s
apparent multi-cancer application would make Novogen and its subsidiary MEI a very lucrative partner. The Merck licence of Inclone’s drug Ebitux demonstrates how lucrative such associations can be with an estimated deal of US$1,900 million (Aegis Equities Research Pty Limited, 2003). Royalties ranging from 5–30% are also payable.

In the dermatological market Novogen’s commercial compound NV-07a, an anti-aging compound, also has valuable cosmetic potential. NV-07a has demonstrated an ability to undo the underlying damage to skin from exposure to ultraviolet light, even when applied to the skin after the damage was inflicted. Sun damage to skin can cause premature aging, but also causes a reduction in the immune response in the skin which increases the susceptibility to development of various types of skin cancers. Both of these effects were reversed by topical use of NV-07a and this was reflected in reduced incidence of skin cancer in long term pre-clinical studies. NV-07a has commercial potential for use as an after-sun skin repair agent in cosmetics and skin care products. The current total skin care market for the world is around US$30 billion annually, of which about US$6 billion is spent in the US (ASX press release, 18.9.02).

Currently Novogen’s major revenue generator remains the OTC business that involves the sale of isoflavone dietary supplements. Although these compounds have earned significant revenues for the company, they are subject to ongoing conflicting publicity and conflicting professional opinions about the safety and efficacy of Hormone Replacement Therapy (HRT) and natural alternatives for women after the age of 45. However, despite various debates, the global market for this alternative form of hormone treatment continues to be firm.

**Overview of Novogen’s competitive position**

Novogen’s ultimate test in being able to grow into a international pharmaceutical company hinges on its drug phenoxodial. New drugs such as Novartis’ Gleevec™, AstraZeneca’s Iressa™ and Genentech’s Herceptin™ have been notable successes in the treatment of cancer. Drugs of this type appear to work because cancer cells rely, at least in part, on growth hormones for survival. The demonstration of efficacy and tolerability of these types of drugs in clinical trials and their subsequent commercial success following FDA approval constitute a proof-of-concept that drugs such as
Novogen’s phenodoxiol that target signal transduction pathways operating in tumour cells are effective in slowing disease progression and prolonging life.

However, it would appear that drugs that target a single mechanism may have limited application because other mechanisms remain functional in sustaining the cancer. This is one reason there are so many drug combinations used in chemotherapy and why pharmaceutical and biotechnology companies are always interested in evaluating other drug targets. Experimental evidence and preliminary results from clinical trials are suggesting that Novogen’s phenodoxiol is unique among anti-cancer drugs in two important aspects: 1) phenodoxiol’s principal target, tNOX, is present only in cancer cells and (2) tNOX is absolutely essential for cancer cell growth and proliferation in all cancers. These findings may explain why the drug is effective against a broad range of human cancers while maintaining a negligible toxicity profile. No other anti-cancer drug appears to have the potential of selectively killing cancer cells while having no effect on normal, healthy cells. Phenodoxiol appears therefore to hold a very strong competitive advantage against all other drugs designed to fight cancer.

But although there are many things going for phenodoxiol, they are still in Phase II studies. It is estimated that there are currently over 300 cancer drugs in development (AER, 2003). Many drugs have passed Phase II only to fail when given to a broad spectrum of patients in the more extensive Phase III trials. In Phase III a drug’s efficacy needs to be shown over a longer period, usually in multiple sites. These studies are the definitive tests for drugs as they must contend with many more variables coming into play like drug resistance, interactivity with other drugs, etc. Previous positive results don’t necessarily guarantee success in later stages. For instance “Novartis’ Gleevec has not proven to be quite the magic bullet it has been proclaimed to be...Several leukaemia patients relapsed and died as cancer cells acquired mutations that protected them against the drug” (Branca, 2003). Also AstraZeneca’s Iressa proved to have serious side effects not initially perceived in earlier trials and “a rash of unexplained pneumonia cases occurred in Japan, where the drug was first approved” (Branca, 2003). Therefore although the company’s competitive position is very promising, the maintenance of that position is dependent on further trials and the speed with which its competitors are able to emulate that competitive edge.
Company foundation

The founder, Graham Kelly

Kelly confesses that he has always been fascinated by ideas; a different way of doing something and he never rejects anything until he has evaluated it. His science is based on the philosophy of the professor of surgery with whom he trained. "He (Shiel) would take these big leaps and if they didn’t work out then (he would) back off and go somewhere else. And that was my personality and that is the way that I do my science". Therefore among the most formative of Kelly’s experiences in developing a commercial perspective at the university, was the respect that he developed for surgeons. "Surgeons are heroic. They just go in where angels fear to tread". Developing a disregard for the faint hearted is perhaps fundamental to the future founder of a company whose whole science is based on something that is totally unconventional.

The second major influence on Kelly’s entrepreneurial perceptions is the commercial experience he gained through the operation of a small veterinary practice. Throughout his time as a researcher at the university, Kelly operated a veterinary practice from home in the evenings and weekends. It was only a small practice, but it kept him in touch with the world outside of academia. By the mid-1980s he started to think about opportunities outside the university and one of those was the production of veterinary therapeutics that were currently unavailable to his practice.

Kelly had an additional, and he feels, probably more educative, early commercial experience. This came about as a result of a chance meeting in 1986 with John Clark, who had made his name as the first manufacturer of aluminium dinghies in Australia. Although Clark was uneducated and a ‘knock-about guy’, he appealed to Kelly who marvelled at Clark’s limitless ideas and the ability to speedily organise action around those ideas to bring them to fruition. With Kelly providing the academic credibility to the partnership, they formed a company called Clarkel Holdings in 1987. The first commercial exercise of the company was to supply specialty feed for laboratory animals. Kelly’s experience in the supervision of laboratory animals gave him essential insight into this very lucrative market. They began to manufacture a range of products. These products included such things as specialty feeding and bedding material. Goodman Fielder eventually licensed the bedding from the young company. Kelly acknowledges
that "it was a very useful learning experience for me to see that if you had an idea that was good enough, and if you researched it properly so that you could develop it properly, you could make it work". But eventually by 1992, Kelly was beginning to lose interest. The ideas were small and the association became a drain on his time in a period when he was on the edge of a revolutionary discovery.

Kelly completed his PhD in 1972, after 4 years' research into the manufacture and use of an experimental drug to overcome tissue rejection. He went on to be appointed as Senior Research Fellow within the Department of Surgery and to become Director of the Transplantation Laboratories. His research over the next 20 years focused on the problem of increased risk of cancer development in transplant recipients.

By 1988 Kelly had spent almost 20 years focused on cancer research, but was becoming disenchanted with the general direction being taken by medical research in finding an answer to the cancer epidemic facing Western communities. This disenchantment led him to seek alternative approaches to provide answers that to date were not forthcoming through conventional approaches. This was the start of the isoflavonoid technology. However, he found it difficult to gain interest from the university on the isoflavone research. "I applied twice to the National Health Medical Research Council (NHMRC) and they just laughed at the project. The notion that isoflavones could be beneficial to human health was just that alternative stuff''. But Kelly was convinced that although the hypothesis was very simplistic, there was a great opportunity for anybody that wanted to research it. "When I couldn't get any funds and they declined the opportunity to patent it, I just ran with it and for the next three to four years we did an enormous amount of work on it while still at the university. We had to beg borrow and steal equipment and funds to do the work, but at that stage there was no thought of commercialising it''.

By 1993, the research team was desperate for additional funding. Kelly had established that there was an enormous opportunity for the isoflavone research but to advance the research, the continued ability to access resources of a commercial nature was now essential. Through his research and commercial activities, he had built up networks both in the science and business communities. Both networks were critical to commercialising the science. Access to these networks provided him with the capability to develop the Novogen isoflavone technology platform and turn it into a viable
operation. Later, by building on these capabilities, he was able to progress the growth of the firm.

The founding process

The founding of Novogen Limited (originally Norvet Limited) clearly demonstrates the evolutionary aspect of knowledge acquisition that can eventually lead to the development of crucial capabilities. Novogen’s founding process may be traced through three stages of Kelly’s commercial experience. The first involves the founding of his company Norvet Pty Limited and the development of his early veterinary products. The second incorporates the change in direction of the company as new opportunities opened up through its research and development program. Finally was the development and on going stage, which includes the evolution of the original business plan and the expansion of the company into global markets.

Commercial foundations

Concurrently with his company Clarkel Holdings, Kelly was the co-founder of a small veterinary manufacturing company. He notes that while running his small veterinary practice, he was “concerned that there was a lack of certain therapies, creams, lotions and that sort of thing. I thought, why haven’t we got these things? It seemed obvious ... so I started to develop these products and formed a company to manufacture them”. His immediate social network included Mal Logan, a retired businessman, and Kelly approached Logan for initial capital to develop veterinary products. Logan offered to put his own money into the venture and the two partners subsequently formed a company called Norvet Laboratories Pty Limited in 1987 in order to manufacture veterinary therapeutics. Kelly notes that originally “we had vet products, we had vet glucan cream, animal husbandry applications for glucan, and we were in discussions with C.U.B. for using their waste yeast. So the whole thing looked top heavy ‘vet’. That’s how we called it Norvet ... the whole idea was that we would become a vet pharma company”.

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Thus Novogen Limited was an extension of its predecessor, Norvet Laboratories Pty Limited whose focus was on the “vet” part of its name. Peter Bradfield describes the origins of the company as very small. “We started in Northbridge (a Sydney suburb) in an old shack with one employee called Bryan Palmer and Graham (Kelly) still at the university” with no intentions of growing to global scale. Kelly agrees,

“the notion that I had at the time, was that I would leave the university and I would have a practice and I would have the laboratory that produced its own products. The idea was to distribute these products and become the manufacturer. There were no big ideas, just something that would tick over and provide a nice little income. Nothing extraordinarily entrepreneurial about it but they were good products and they are still selling today”.

By 1992-93 the isoflavone project had become all consuming and it had become obvious to Kelly that nobody else was pursuing this line of research. Having been turned down by the university, Norvet Laboratories Pty Limited filed the patent and “did a deal with a multinational herbal therapy distributor, Blackmores Ltd, with the idea that Blackmores would commercialise the isoflavone product”. Blackmores offered to buy Kelly out but he declined the offer, agreeing to work in partnership instead. An agreement was reached where Kelly and his team would provide the isoflavones and Blackmores would commercialise the product. However, at that stage the research had not yet discovered how to efficiently extract the isoflavones out of plants. R&D costs were rising dramatically and although the university continued to provide modest facilities, “by 1993 the spending was starting to get out of control. That’s when we decided to go public”.

**Going public: the initial public offering**

The scientist didn’t know much about shares at that stage of his commercial career, and his commercial partners became a key influence. Kelly’s friend Mal Logan was an accountant and he introduced Kelly to other investors such as Peter Bradfield, among others. These men had experience in financial matters and complemented the capabilities of the scientist in the prospecting phase of the firm’s growth. Bradfield’s social network included a Sydney underwriter. The underwriter, uncertain of the firm’s prospects, initially withdrew his offer until Bradfield through his own social network was able to renegotiate the underwriting.
"That was a major problem ... we had to sign guarantees with the solicitors that we would pay them, Mal and myself. Mal and I were the venture capitalists lending the money and Graham was the genius".

Even though Kelly notes that it was an opportune time to list the company since the financial environment was "pretty bullish. As someone who had 'crawled over hot coals' before a NHMRC committee to get a pitance in funding", he was astounded at the ease of raising millions of dollars through the stock market. Bradfield admits that "one of the most important reasons why I put money into Novogen was because I backed the man. I always back the man if I think he is right – it is not the concept that I backed but rather Graham Kelly".

Kelly, as a recent Fellow in Experimental Surgery in the Faculty of Medicine at NSW's oldest university, was highly credible. Twenty-five years in medical research involving drug development, immunology, surgery and cancer added to the impressive reputation. Kelly had also drawn on his own social network and asked Professor Marshall J Edwards AO to be the Chairman of the Board. Edwards was the dean of the faculty when Kelly graduated and he knew the professor "as a man of honour, who was incredibly well liked and was well regarded and well respected". Professor Edwards had recently retired as Dean of the Faculty of Veterinary Science and Professor of Veterinary Clinical Sciences at the University of Sydney where he held board positions with the J D Stewart Foundation, the Birth Defects Research Centre, and the Postgraduate Committee of Veterinary Science (Chairman). Professor Edwards was also a consultant to the World Health Organisation, the Australian Department of Foreign Affairs, the World Federation for Ultrasound in Medicine and Biology and the Agent Orange Royal Commission. This was a very impressive list of references and would have made a significant contribution to the acceptance of Norvet's prospectus by the investment community. Furthermore, Kelly's powers of persuasion had been developed over many years and he was well able to convince prospective investors of the merit of his technology.

Working part time in the company was no longer a viable option for Kelly. Commitment of time and effort to the new product range was required for the start-up of the new venture. It was at this point that Kelly chose to change direction and move into the growth market of a new industry. Kelly was now in a very competitive and uncertain market, but considering his earlier perceptions of risks and his disposition to
new ideas it could be expected that this is exactly the kind of market where Dr Kelly would thrive.

Graham Kelly had overcome some critical difficulties in accessing critical resources for the development of his technology by 1994. The intellectual property he created was demonstrably unique. He had established a social network of associates that provided a broad range of expertise in business, marketing, accounting, product development, medicine, biology and veterinary science. The public flotation raised $6,500,000 in financial resources (1994 annual report). Physical resources at 160 Sailors Bay Road, Northbridge were leased and additional laboratory/manufacturing facilities were leased from the University of Sydney to take the company through its initial growth stages. On 18 March 1994 Norvet Limited became a registered company and on 1 September 1994 Norvet shares and options were listed on the Australian Stock Exchange.

**Identifying appropriate directions**

**A changing focus**

In a new start-up, the resource conversion process has to be set up without precedents or accepted ways of proceeding (Garnsey, 1998). In its initial report, Norvet stated that it had embarked on a wide-ranging R&D program to exploit four areas of research. First was its β-1,3-Glucan that was described as potentially being able to provide many therapeutic benefits in both veterinary and human medicine. Second was the protection for humans from the development of a range of cancers and modulation of reproductive hormone functions through research on isoflavones. The third area of research to be exploited was a focus on a paralysis tick vaccine which would ultimately isolate the respective gene leading to the development of a protective vaccine using recombinant DNA technology. The final area of research for the company was the agreement with Venom Supplies and Medvet Science Pty Ltd for the cooperative development of the next generation of anti-snake venom.

Kelly reflects that he "had scouted around and found a few opportunities that had come about like the snake venom. I look back now and realise that I was behaving then like a scientist - which is just gee it must be commercial. Where as now, I am a businessman"
with a science background and I can look at a project and say is this even worth worrying about. I think that is a fault line that is common to many biotechnology companies that because they have a product they think it must be able to become commercialised”. Bradfield had originally been inspired to invest in the company by its tick vaccine. “I thought the tick thing was something Australian, something that was killing a lot of cattle on the eastern seaboard, but the only vaccine available at the time was a pretty rough sort of thing. Eventually we found the gene but the money that was needed to pursue it would not bring the return on it, so we gave it away”.

“What turned out to be the big thing was the isoflavones. But in 1997 we had a dispute with Blackmores. We were not going to get much of a return from them and they were mucking us around and setting deadlines about when we were going to start and things like that. But we only had $6m and so we broke away from Blackmores and went out on our own”. The dispute with the distributor proved to be beneficial to the fledgling company in changing its veterinary focus. With lack of returns from its tick and snake venom research and worldwide scientific interest in phytoestrogen research expanding rapidly, the company redirected its resources towards the development of its isoflavone technology platform.

The company’s glucan research appeared for a time to be headed in the same direction as the snake venom and the tick vaccine. Initially research into glucans was prompted in the early 1990s by interest in immunostimulants drugs which could safely and effectively promote wound healing despite the increasing emergence of strains of bacteria resistant to antibiotics. Studies by Norvet had been able to concur with overseas research that β-1,3-Glucan was a potent and safe immunostimulant in both animals and humans. Bradfield says that “it cleared it (the wound) up but the trouble was we couldn’t get the QA formula to see how it works” so research was stalled for quite a few years. It was not until 2003 that reliable results were achieved and Glycotex Inc., a US subsidiary was specifically established by Novogen to develop its glucan technology to continue trials in the treatment of ulcers and it was not until 2003 that reliable results were achieved.
Over-the-counter product development

In 1995 an important technical development led to the company's first generation isophytoestrogen product Pratensil, which was expected to provide the basis for various over the counter (OTC) products. This was a herbal product, as distinct from a pure drug, and, being derived from an approved human foodstuff, red clover, Pratensil was able to be registered for sale in most countries without undue delay. In 1996, Professor John Eden from the Royal Hospital for Women, Sydney, reported to a scientific conference in Europe that studies had provided evidence for the first time that these compounds had a therapeutic effect in menopausal women in reducing both the frequency and severity of their symptoms. These trial results opened up the way for Promensil the first of the company's OTC products, to be presented to the market as a safe and alternative therapy for those women who chose not to use the traditional hormone replacement therapy (HRT) in 1997. Building on this technology, the company released Trinovin for maintaining prostate health in men in 1998 and Rimostil for the maintenance of health of women after menopause, in 1999.

The OTC products provided the company with some major opportunities. Receiving regulatory approval in 1997, the company was able to launch Promensil in Australia that year and the USA in the following year. Sale of the product generated much needed cash and the company now had the opportunity of establishing its commercial brand in the global market and simultaneously gaining international experience with which to promote future products. In line with its new direction the company name was changed from Norvet Pty Limited to Novogen Limited to reflect its change from a veterinary to a now largely human focus. An additional opportunity to be realised a few years later, were the associations and networks that the company was able to establish during the promotion of its OTC products. These associations are dealt with later in the case study.

Physical solutions to production problems

The company's therapeutic products are based on isoflavones from the red clover plant, which it identified as the richest source of isoflavones in nature. The R&D team developed its own strains of red clover that have specific ratios of the different
isoflavones. These plants were grown in Australia and New Zealand under contract. The technology to extract isoflavones from the clover was also eventually developed and became the subject of an international patent.

In November 1996, the company opened its large-scale manufacturing facility in Wyong, New South Wales to extract iso-phytoestrogens from plant material. Its extraction technology ensured a highly efficient and cost-effective extraction of isoflavones in a non-destructive manner. The scale of the state-of-the-art facility in Wyong was designed to have sufficient output capacity to produce approximately 600 million tablets per annum, the quantity anticipated as the demand for the world-wide commercialisation of Promensil. The facility also began to manufacture a range of isoflavone products for future clinical trials.

The Wyong factory was built with the initial intention of supplying Blackmores in Australia and fulfilling the company's offshore plans. Following a dispute with the Australian distributor, Novogen launched the OTC products without the assistance of a distributor. Increased production at the Wyong facility was accompanied by the expansion of the Company's clover production. Additional New Zealand contract clover growers and consultant agronomists were appointed as the company's demand for the product expanded. Contracts in NZ had been expected to provide cheaper costs of production but as problems with NZ producers developed, production was eventually centralised at Wyong and clover was grown only in Australia. Significant efficiency improvements also became possible with increases to scale of production. The expansion of raw material production and handling capacity continued to be progressively updated to meet forecasted market demand. In 1997 Novogen appointed Sigma as the licensed contractors to tablet and package sufficient product to meet projected worldwide demand for finished goods. The tableting and packaging of products for world distribution has now been extended and is performed under contract in Australia and the USA.

However, to realise the opportunities that these resources provided, several major problems needed to be addressed. First, although efficient manufacturing facilities had been established to fulfil expected demand, major financial outlays were required to market the product and subsidiaries established to distribute it overseas. Furthermore, if the company was to undertake global operations, it required extensive international
commercial skills. These skills included knowledge of international legal regulations, financial understanding in areas such as international exchange rates, and the ability to establish and coordinate organisational functions and routines in order to facilitate growing activity within the firm. Also the research program itself established a problem as the pipeline of products grew and products at different stages of development and trial needed coordination and documentation routines established. Finally, but perhaps one of its major hurdles, Novogen had now become a major competitor to giant companies such as Novartis and Wyeth who saw their HRT business being threatened by the therapeutic products. Thus although after many years of R&D, Promensil was launched onto the market, Novogen faced some major obstacles threatening its goals for global growth.

Managing an expanding company

Financial resources for initial survival and expansion

In mobilising resources, the company faced difficulties that can be categorised under two major headings. Manufacturing risk and financial risk are the two categories of problems that have underpinned the commercial viability of the firm in its attempts for global growth. Managing that process efficiently was critical not only for growth but also for survival.

To ensure that the company had sufficient working capital to meet the cost of establishing its manufacturing facility in Wyong, the Directors authorised a placement on September 1995, of 2,690,000 fully paid ordinary 25 cent shares and 1,299,000 options exercisable to 31 December 1998 at 50 cents. The placement raised $3.27 million. Similarly on 28 August 1996 the shareholders agreed at an EGM to issue an additional 6 million shares at $2.50 in order to accelerate the company’s isoflavone technology, which had progressed to a commercial stage substantially faster than originally anticipated (1996 annual report). This placement raised A$15 million. Further private placements raised A$24.4 million in 1999, A$17.9 million in 2000 and A$21 million in May 2001. Each placement had the objective of facilitating the progress of R&D to reduce manufacturing risk.
In November 1997, Novogen entered a licence agreement with DuPont Protein Technologies and its subsequent joint venture with Bunge now called Solae LLC, to make regular milestone payments and to pay royalties on sales of its products covered by the Novogen patents. DuPont Protein Technologies obtained the worldwide rights (other than for Australia and New Zealand) to certain Novogen soy isoflavone technology. In the deal, Novogen retained all rights to its own red clover-based isoflavone technologies and the licence related specifically to Novogen patents or patent claims relating to soy applications. Novogen received initial consideration of A$15.7 million, and an additional payment by way of equity placement of A$3.6 million in November 1998. Later in 2002, Novogen received the first milestone royalty payment under the licence of A$1.6 million and in January 2003, a further A$2.3 million milestone royalty payment was paid.

These are substantial amounts of finance and clearly demonstrate the financial obstacles that small biotechnology companies face in taking their invention through the supply chain to the final customer. Alan Husband has said that “it is investor confidence that makes or breaks a company” and Novogen has been able to source very strong investor support throughout the 1990s. Government support in the form of grants would also assist Novogen meet its growth objectives, but this is referred to later in the case study.

**Commercial expertise**

By 1996 the company was seriously in need of international commercial expertise to take its OTC products to international markets and the legal knowledge to undertake sophisticated patents and company restructures to facilitate planned growth. Therefore in August 1996 Chris Naughton joined Novogen as Commercial Director. Naughton had degrees in Economics and Law. He had completed the program for Management Development at the Harvard Business School, and had been an Attorney in New South Wales. As well as working as a merchant banker, he had spent eleven years in the pharmaceutical industry including worldwide business development with the Wellcome Foundation Limited in the UK. Kelly acknowledges that “the business was beginning to grow by leaps and bounds and we needed someone who had strong financial capabilities. Chris returned from the UK so that his children could finish their schooling in Australia. I still remember interviewing Chris and within a minute into the interview I knew who was
going to be CEO”. It is perhaps telling of Novogen’s success that it has a founder that understands that “the greatest talent you can have as a company founder is to know how to align yourself with people who can plug the (information) gaps”. Kelly admits that this was no easy task. “Chris has had to make a lot of hard decisions that I couldn’t have made, like getting rid of certain key people or taking certain directions, some of which I didn’t agree with”. Bradfield agrees saying that Novogen was “very lucky to get Chris Naughton who is still the CEO and to me he is the driving force of the company. Had we not got him we would not be where we are today … Maybe we would have even folded”.

Marketing issues

Initially Paul Macqueen, with qualifications in veterinary science, accounting and marketing, was also part of the Board. He subsequently stepped down from the Board and focused full time on developing sales and marketing of Promensil. The marketing team oversaw a campaign covering press releases and subsequent extensive media coverage, which set the pace for the introduction of Promensil. Distribution of the product was determined to be most effective through pharmacy and health food outlets nationally. Advertisements were placed in leading women’s magazines and informational lectures were conducted across the country. An extensive program of advertising to the medical profession was also conducted through journal advertising, direct mail, staff training, trade shows and an isoflavone plant hormone lecture series.

In addition, a New York public relations firm was hired who put together an aggressive marketing campaign. The agency was able to secure a slot on the Oprah Winfrey show using Cybil Shepherd, a famous actress at the time, to tell the story. Marketing in America however, was a very expensive business. Alan Husband, company Chief Scientist laments that “we have always had this tension between what you need to spend in America to make a product successful and what we can afford to spend. Our product in America is not nearly as successful as it could be if we spent the sort of money that companies like Pfizer or Wyeth or some of the big companies would if they launched a dietary supplement on the American market”.

Building on the promotional campaign to commercialise the company’s OTC products internationally, subsidiary companies were formed in the UK and the USA and an
American resident Warren Lancaster was appointed as Vice President-America. Thus Novogen Limited was established in the global market place, with overseas nationals at the head of its subsidiaries.

**Research coordination**

Kelly had met Professor Alan Husband during his veterinary practicing days while tending to Husband's cat. Later because Novogen was looking for people to do research for them, Kelly approached Husband and asked him to do some work on contract for the company. Husband, a leading world authority in mucosal immunology, headed a research team in collaboration with Novogen to investigate the biology of oral glucans in animals. While working on the project, it became clear to him that this company had potential. "Everyone was trying to do too much but no one had the time to organise the research. Graham was flying off on a lot of different ideas and I became involved on a consulting basis to look after the company's research program. Initially it was only one day a week but eventually by 1996, I came in full time".

Husband strategically maintained his university appointment to benefit from what he saw as real advantages for both the university and the company from the retained association. To this day he is still the professor of veterinary pathology at Sydney University. "Although they accept that I only have a fractional appointment and they accept that I spend most of my time with the company. But it is in the university's interests to see that they try and meet the obligations of government policy and work more and more with industry. And the company has benefited greatly by having access to university facilities that the company pays for. Because the two groups understand each other and I have a foot in both camps, it has worked very harmoniously. Also if we want work done in other parts of the university, I can open doors which might otherwise be more difficult. Universities are very complex because there is no pyramidal structure or hierarchal control. University groups tend to operate more as satellites than a strong organisation. So often its knowing the technician in the lab will get you further than knowing the chancellor". The ability to transfer knowledge from the public research institution to the company is a major resource that many Australian
biotechnology firms do not have access to although it may be crucial to their growth prospects.

Professor Husband, therefore, provided the executive arm of the company with additional balance and strength in the important area of research leadership and was able to further focus the company’s scientific resources and extensive network of international collaborators that had been used to contain direct costs and expedite its research. The company research strategy was to build a core level of ‘in house’ skill to support an active drug discovery program, but continued to rely on a growing alliance with major universities and research institutions world-wide to support its R&D activities.

External threats to growth

Despite accessing and mobilising a formidable number of valuable resources to facilitate strong growth, Novogen faced a major threat from the external environment soon after launching its dietary supplement products. Pharmaceutical companies saw Novogen’s products threatening their HRT business. Bradfield and Husband refer to a “campaign being waged against Promensil, where medical academics were given funding for projects in return for comments that interpreted research results of the supplement as being no more effective than a placebo. We have not the clout to sufficiently rebut a lot of the stuff that went on. So there will be doctors who mouth what they have been told or heard by people who represent that HRT lobby. But if you look at the scientific data, it is true that there have been a couple of studies where we failed to reach statistical significance from placebo effects. There has been an effect, but because of the high variability, and because not all women respond the same, across the board the statistics were not strong enough to show a difference to a placebo. But there have been other studies where the statistics have been quite clear about it being better. So if you are on their side of the fence, they don’t mention the ones that work, only the ones that don’t work. On our side of the fence, we make the most of the ones that worked. What we did do was to commission an independent meta-analysis to be done by an expert in meta-analysis from the University of Exeter in the UK. He came out with the final conclusion that Promensil does work. That has been done very recently and not published yet. It
will be ignored by people that don’t want to believe it and there will still be people from the drug companies who go around to doctors showing them the old paper that said it didn’t work and that is what the doctor will remember. We can’t afford to pay representatives to go to all the GPs around town. Although ours is a good story, we can’t promote it as effectively as the big companies do”.

Novogen’s OTC products continue to generate substantial revenues and in 2003 contributed an amount of $19.6 million in sales. However, ongoing conflicting publicity and conflicting professional opinions about the safety and efficacy of Hormone Replacement Therapy (HRT) and natural alternatives continues to impact with varying degrees of intensity on various sectors of the market

Restructuring the original business plan

Phenodoxiol: a revolutionary concept

Naughton has commented that in “Australia generally the hospitals, the research houses and universities have gone from a publish or perish attitude to thinking more strategically about where their science is going and what value can be added”. He adds that although that is a positive step, it is not an easy path to take. “You can’t just say, we have invented this new idea, now lets go and commercialise it. The business world outside the scientific arena is set up to inhibit that process. It is a very competitive environment, and not all inventions are right for the right time. Various drugs get superseded very quickly and manufacturing issues or trialling issues or toxic issues get in the way. Great inventions often succeed by exception. But the mechanics of how you structure the company or the institute to allow the commercialisation process to take place, now that’s a real problem and that’s why many companies are forced to go off shore”.

In 2000, Novogen’s new cancer compound phenoxodiol (NV-06) is an example of the above discussion. The question of how to fund the program became paramount. The program was moving from Phase I trials to the next phase which is much more expensive. But how to get the finance? Because it was a new idea, it was like a new company. It was a part of Novogen but there was no point in financing it through
Novogen which is a combination of ideas and projects. Novogen's consumer (OTC) business generates revenue and thus gives analysts a basis on which to measure the business but this means that they could ignore the research and development of the new idea. "By having a consumer business we effectively relegated our intellectual property value of the new idea to zero. We had to take that new intellectual property out of Novogen and deal with it separately and thereby establish a value for it which had nothing to do with the consumer business".

Therefore in preparing the commercialisation strategy for phenoxodiol, the company established a new subsidiary Marshall Edwards Inc (MEI). The directors saw two imperatives that the commercialisation of phenoxodiol highlighted. The first imperative was to access sufficient cash to complete the clinical program to the point where licensing to a major pharmaceutical company was the preferred strategy. The second imperative was to have phenoxodiol in a corporate vehicle that enabled a licence to be undertaken without affecting the rest of Novogen's intellectual property or other compounds in development.

The directors agreed that in this case, the price of Novogen stock did not recognise the underlying value of phenoxodiol within the company and previous strategies for raising funds through share placements were inappropriate on this occasion. An independent expert valuation of phenoxodiol undertaken in the USA clearly showed that such a disparity existed between the price of Novogen shares (or market capitisation) and the current value of phenoxodiol.

In order to facilitate the listing of MEI, a prospectus was lodged with the Australian Securities and Investment Commission in April 2001. The prospectus envisaged floating approximately 10% of MEI with a priority offer for participation by existing Novogen shareholders. "We actually went to ASIC before we lodged our prospectus and showed it to them and asked them for their opinion. This is generally not possible but Ernst & Young had a study group working with ASIC and they used us as a case study. But unfortunately Ernst and Young were using the people who wrote the ASIC guidelines in Melbourne. That group made some comments and we made changes in response to those comments. We lodged the prospectus in Sydney but unfortunately there was a turf war going on between the two groups. The Sydney group asked us why did we go to Melbourne? Made us look suspicious in their eyes, from the start. We wrote the
prospectus in line with the guidelines as written in Melbourne but in Sydney they had no respect for those guidelines. It was very bad timing”.

The Novogen prospectus waited throughout 2001 for an appeal to go through the Administrative Appeals Tribunal. There were three matters that formed the basis of the delay. Firstly, the assumptions used by the expert valuer produced a value for phenoxodiol that was greater than the market price of Novogen. Secondly, the valuer’s independence was questioned as the words “we” and “us” were used in a few of the extensive information exchanges that were a necessary part of the valuation process. And lastly, the opinion of the accounting firm Ernst & Young included in the prospectus had been questioned. MEI, its legal advisors Blake Dawson Waldron and Ernst & Young, all consider that the delay has been unfounded.

Due to the delay in the MEI prospectus in Australia, and in order to ensure that there was no consequent effect upon the expedition of the phenoxodiol clinical program, Novogen raised US$10 million in May 2002 by floating MEI on the London Stock Exchange’s Alternate Investment Market (AIM). “We would have preferred to be here in the local market using local resources and facilities, but our experience means that this local business has gone off-shore”.

Kelly anticipates that the company expects to stay offshore. “Novogen will always remain an Australian company, but you have to be listed where your main shareholders are”. To demonstrate the accuracy of Kelly’s statement, MEI was listed in the US on the NASDAQ national market in 2003. The stock was priced above the indicated range and was three times oversubscribed with the price doubling upon listing. The US stock market capitalisation of MEI remains greater than the Australian listed Novogen despite Novogen owning 87% of MEI. Naughton considers “there isn’t the experience or the willingness to take the big picture approach needed for biotechnology in Australia. There is good intent but the whole regulatory environment looks at the past, tries to regulate what has happened when the whole point of biotechnology and innovation is to do what has not been done before. Therefore we expect to keep the property here but move the financial infrastructure offshore. Novogen perceives this as a fundamental step to global success”. Kelly agrees that “Australia will be our home in terms of our R&D but MEI is clearly American and our subsidiaries are all over the world and none of us
ever want to go through what we had to face with (the Australian attempt at) listing MEI again”.

**Changing company structure**

As of 2003, the Novogen Group is managed through four divisions that include Pharmaceutical R&D, Marshall Edwards Inc (MEI), the commercial vehicle for phenoxodiol, Glycotex Inc., the commercial vehicle for Novogen’s glucan (skin care) technology and its Consumer Health Division. The Pharmaceutical Research and Development owns the Group's intellectual property and manages the laboratory and preclinical activity across each therapeutic area that has compounds under development. The company's portfolio has a significant number of compounds in laboratory testing to ascertain suitability to carry forward into preclinical studies and augers well for its future.

Recognising the importance of this research for national health, Novogen was awarded a A$3.74 million START grant on 12 October 1999. In 2000 the company was able to obtain further funding from the START fund for A$2.79 million to assist in the development of phenodoxiol. By 2001 the company’s profile was such that the Prime Minister said that he was pleased to announce that the R&D START grant had offered Novogen a further A$3.7 million to develop its promising experimental anti-inflammatory drug, NV-07. A total of A$10.23 million dollars has been obtained from government programs between 1999 and 2001. Husband reflects that although he feels that it is investor confidence that makes or breaks a company, “the government (grants) were certainly very helpful to us because they helped us do things more rapidly and spread our focus a little wider than perhaps we could have otherwise”.

**Strategic alliances: resources through association**

Naughton acknowledges that “in biotechnology it is essential for the start-up (company) to become embedded in industry networks both in a local (Australian) and global sense depending on their stage of development. These networks include research institutions, hospitals, and partners and alliances that have the capacity to provide the infrastructure
to take the product through to the final stages of commercialisation”. Such associations have been entered into with a view of allowing some larger R&D projects to be accelerated while reducing the cost of the research and to also enhance both the likelihood and the rate of entry of the company’s products into the marketplace. The collaborations also provide transfer of difficult to obtain tacit knowledge and thus provide an important additional knowledge asset with which to extend growth plans.

Significant research projects have been undertaken jointly with various groups both in Australia and overseas. In Australia, anti-cancer drug trials have been conducted at the Royal Prince Alfred Hospital (Sydney), St George Hospital (Sydney) the Royal North Shore Hospital (Sydney) Royal Women's Hospital (Melbourne) and Sir Charles Gardiner Hospital (Perth). Overseas, anti-cancer drug trials have been conducted at Cleveland Clinic (Ohio, USA), and Yale-New Haven Hospital (Connecticut, USA). Research collaborations are in place in the USA with the National Institutes of Health, Medical University of South Carolina, Yale University, Purdue University, John Wayne Cancer Institute, and the University of Birmingham at Alabama. In Australia, research collaborations are in place with the Hansen Institute (South Australia), University of New South Wales (NSW), Wollongong University (NSW) and Newcastle University (NSW).

That the legitimacy of the company’s key drug has been noted on the world stage is reflected in the prestigious boost the company received by its collaboration with US researchers from Yale University’s School of Medicine (Yale Group). This association is a long term beneficial outcome from the company’s OTC promotional exercise. Kelly notes that “while trying to launch Promensil in America, we got together opinion leaders to help us launch the dietary supplement into the US market. One of the guys we contacted was the chairman of the Department of Obstetrics and Gynaecology at Yale Medical School who happened to be Professor Fred Naftolen. He really liked what we were doing and was very supportive. He had a post doctoral fellow working for him called Gil Mor. I talked to him a few times but there was a mismatch between what Mor wanted to do and what we needed to be done at that time. Because we wanted to launch women’s health products and this guy was more interested in immune regulation, signal transduction. But when phenoxodiol came along we realised that we needed signal transduction work, and he was working with ovarian cancer. So Graham (Kelly) went to see him and the association has been extremely rewarding”. The Yale Group has
isolated the mechanism of action of the drug, an important step toward understanding the drug and gaining regulatory approval. Having a high profile respected US cancer researcher as a collaborator should also help phenoxodiol achieve FDA approval, a critical pre-requisite for sales to commence (Aegis Equities, August, 2003:1).

There are additional benefits to this association. Yale University gets a number of public grants, endowments and large donations and to continue receiving and increasing these, it needs to keep on producing good news, especially high profile news. The positive announcements delivered by the Yale medical team regarding their outstanding research on phenoxodiol makes the achievements appear to be even more impressive. Yale is a powerful organisation; it has graduates in all fields of business and their connections with all facets of industry are of superior quality. It is reasonable to surmise that they are well represented in the US Government and will be recognised by powerful interests. Securing ties not only with Yale but also with the other universities, research institutes and hospitals has significantly improved the company’s credibility on the global stage. Once these connections have been established, they can be used in future projects. American connections secured now are important particularly if any trial successes are declared later and the company seeks FDA approval for the sale of its drug.

Naughton, for instance, acknowledges that there has been little peer-reviewed data released on phenoxodiol so far, but says “we have managed to start new trials before the results of the old ones have been finalised. There has been a bit of a tail but in the hospitals they’ve been comfortable with that. ... some drugs have been approved without the standard Phase I, II and III trials where they have shown results”.

**Expanding with cultural change**

The skills and personalities that form the legendary team as it struggles against adversity during the firm’s emergence and early growth, is very different to the skills required for a structured company running on organised routines and reporting procedures. Bradfield left the company shortly after the listing of MEI. He considers that the Board now needs to be able to provide solid scientific and financial advice that he as a property expert, is unable to contribute. Similarly other founding members of the Board like Mal Logan,
Paul MacQueen and others left the company having made substantial contributions to the success of the company in its early days but in some cases unable to agree with the growth strategies of the new culture. In later years Mr Phillip Johnston, who had extensive experience in the pharmaceutical industry, was elected chairman of the Novogen Group. Also the distinguished Professor Paul Nestle AO, MD, FTSE, FRACP, FAHA, Senior Principal Research Fellow and Head of the Cardiovascular Nutrition Laboratory at the Baker Medical Research Institute in Victoria, was a highly skilled and valuable addition to the Novogen Board. Mr Geoffrey Leppinus adds economic perspectives and in 2003, Professor Leanna Read, chief of TGR BioSciences with experience in leading and managing commercially related research organisations was appointed to the board as non-executive director to further enhance the profile of the company. Thus the company has managed to successfully combine its network structure to support both commercialisation networks by importing appropriate management skills while simultaneously supporting scientific networks through its board and collaborative research projects.

**Conclusion**

In 2004 Novogen’s major revenue generator remained the OTC business. Despite the impressive success of these products, the company has not yet achieved break-even point. Although the operating loss for the financial year 2002/2003 showed a distinct 29% improvement on the previous year, the company still faces an operating loss after providing for minority interests and income tax of $10.5 million. Among its major hurdles in achieving the full benefit of its resources are Phase III trials of its phenoxodiol drug and the ability to find an appropriate cosmetics partner for the commercialisation of its drug NV-07a. Other hurdles depend on the success of trials in the company’s extensive pipeline of drugs. Success or failure of these trials will inevitably impact on Novogen’s ability to reach resource generation or the next phase of its growth.

To date, however, using size of assets (capitalisation value) as a measure, Novogen has achieved substantial growth in its productive capacity since its IPO in 1994. Dr Kelly’s initial research into isoflavone technology has provided the company with intellectual property to progress the growth process. Acquisition of capabilities to commercialise the
science have been demonstrated through the company's OTC products which have also established a market base and global exposure to the company brand. The Novogen team has achieved a high level of credibility with its many influential alliances and the maintenance of its network of high profile associations.

The demonstrated tenacity, experience and credibility of the company's founder, Board of Directors and Management Team augers well for this small Australian biotechnology company. Novogen may still prove to ASIC and others that it really is possible to be successful as a biotechnology drug discovery and development company in Australia.