CSL, from blood stock to blue chip

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Abstract. From its modest beginning in 1916 with a staff of 20, CSL has grown into a major company, which now employs more than 25,000 people, operates in more than 70 countries and has a market capitalization of over A$130 billion.

Few Australian companies survive for 100 years let alone survive and thrive. CSL, by constantly adapting to changing circumstances, is one of the few to have done so. Its history has three phases: a lengthy period as a Government business enterprise producing a range of biological products for the local market; a period of diminishing importance when the organization became uncompetitive with the private sector; and a renaissance following its transformation into an independent company supplying innovative products to the world.

At the beginning of the 20th century, infectious diseases were responsible for approximately half of all deaths in industrialised countries. In Australia, one in 10 children died before the age of 5 and the average life expectancy was about 50 years. Due to the pioneering work of Louis Pasteur, Emil von Behring and Robert Koch, the germ theory of disease had been established and the possibility of active and passive immunisation demonstrated. Once passive immunisation was found to dramatically improve the survival of patients with diphtheria and tetanus, Government funded organisations in Paris, Marburg and London began to produce antiserum in horses and to provide these products to local physicians and in some instances, to countries without local production facilities.

The advent of WWI, with its dramatically increased requirements for tetanus antiserum to treat battlefield wounds and the disruption of traditional supply lines, caused a problem for remote countries like Australia, creating a demand for national self-sufficiency. In 1915 the Australian Government established the Federal Serum Institute (now CSL Ltd) funding the purchase of a farm on the outskirts of Melbourne, construction of laboratories, stables for the horses and a house for the Director – the Edinburgh trained bacteriologist, William Penfold. By the time that Penfold took up his position a year later, similar organisations had been, or were being, established in Russia, Scandinavia, Japan, Canada and the US.

With a staff of 20, the Institute soon began producing horse antiserum to diphtheria and tetanus toxins as well as tuberculin and smallpox vaccine. One of CSL’s first challenges was to respond to the devastating pandemic of Spanish influenza. As the viral aetiology of the disease had not yet been demonstrated, a mixed bacterial vaccine was developed in the hope that it would reduce the incidence of severe pneumonia, which, to some extent, it did.

In the early 20th century, as Australia was extremely dependent on exports of beef and wool, the company established a veterinary division, subsequently producing a wide range of vaccines against economically important diseases of livestock and later of companion animals. For the first phase of its existence the organisation was led by microbiologists or public health experts (Penfold, Frank Morgan, Val Bazeley, Bill Lane, Ron Greville) whose aim was to harness scientific advances being made overseas, to improve the health of the Australian community. During this period CSL and its sister organisations in other countries thrived and fulfilled a vital role in public health.

Advances in microbiology provided the basis for development of vaccines against important childhood diseases such as diphtheria, whooping cough and tetanus as well as diseases encountered by travellers, such as cholera, typhoid and paratyphoid. None of these products required access to intellectual property rights. As oversight of the production process was minimal and the clinical data required to support use of new products, modest, the investment required to develop and introduce a new product for Australia was within the means of a Government funded entity. Because of its mission to safeguard Australian’s health, CSL was able to respond rapidly to new developments overseas. In 1923 it was one of a handful of organisations to license the process for extracting insulin from animal tissue from the University of Toronto and continued to provide this product to the Australian community until 1990.
It was similarly opportunistic in benefiting from the discovery of penicillin by Alexander Fleming. Once the significance of this work was recognised and Florey and Chain had demonstrated that it was possible to produce penicillin at scale, the eminent public health worker, Bill Keogh convinced the War Cabinet that Australia needed to be self-sufficient and that Val Bazeley, a CSL veterinarian, then serving in the army in New Guinea (with a reputation for being able to get things done), should lead the effort. Bazeley flew to the US in September 1943 and after visiting major manufacturers, returned in December, setting CSL the ambitious target of producing penicillin within six weeks which he achieved.

By February 1944, 10 weeks after his return from the United States, sufficient penicillin had been produced to save the life of a soldier with septicaemia and, by April that year, Australia became the first country in the world with the capacity to provide penicillin to both soldiers and civilians. World War II triggered a dramatic growth in the use of blood transfusion and certain products such as albumin, which could be extracted from plasma by the newly developed process of Cohn fractionation.

In 1949 the Australian Government authorised the Australian Red Cross to provide unused plasma from volunteer blood donors to CSL and funded the organisation to extract a range of plasma proteins and clotting factors which could then be provided to the public, free of charge. It was a far-sighted initiative which was later copied by many countries. CSL was soon able to supply albumin, a range of immunoglobulins and a number of clotting factors to the community.

In the 1950s cell culture technology enabled scientists in the US to develop an inactivated vaccine against poliomyelitis and later, live attenuated vaccines against measles, mumps and rubella. In 1952 Bazeley, who would later become Director, was sent to the US to work with Jonas Salk, who had developed a candidate polio vaccine. Bazeley established large scale production techniques which, on his return in 1955, he replicated at CSL so that the organisation was soon able to supply Australia’s needs for the vaccine. The late 1950s, when it was manufacturing polio vaccine, a wide range of human and veterinary vaccines, antisera to some of Australia’s most venomous snakes and spiders, insulin, penicillin and a suite of blood products, was probably the peak of CSL’s period as a Government owned entity. The organisation and its staff were widely admired and Bazeley became a national hero.

From the early 1970s CSL encountered strong headwinds because the circumstances that had allowed publicly funded producers of therapeutic products to thrive were changing. If I had to choose a date that the winds of change began to blow, it would be almost 20 years earlier, on 25 April 1955, when a child in Chicago, who had been injected with polio vaccine 9 days previously, developed paralysis. The so called ‘Cutter incident’ (because the vaccine was produced by a small US manufacturer, Cutter laboratories), in which 94 children who had been immunised and 166 close family and community members, developed paralysis as a result of an inadequately inactivated batch of polio vaccine, threw a spotlight on the lack of rigour around vaccine manufacture and regulation and the need for careful monitoring and oversight of all aspects of production. It also drew attention to the inherent conflict of interest when the government was simultaneously the producer, regulator and major purchaser of therapeutic products. Independent Regulatory authorities were established and provided with significant resources and powers and manufacturers were required to demonstrate that their production processes were reliable and their products safe and effective.

For public sector manufacturers, complying with these new requirements to produce a suite of generic products, required major investments in plant and equipment, which Governments were loath to provide. Additionally, development of novel vaccines required major investments in research and development, large and expensive clinical trials and construction of dedicated production facilities. Oversight of the development process required sophisticated management skills, a tolerance of risk and a willingness to wait a decade or more for the outcome. None of these sat comfortably with Governments faced with tight budgets and short electoral cycles.

From the 1960s, while the Australian Government, continued to support CSL, it failed to do so at a level that would have enabled the organisation to develop new products and remain internationally competitive. As a consequence, the organisation became a relic of a bygone era, a biologics museum producing a limited number of generic products.

The factors which were affecting CSL had a similar impact elsewhere; from the 1970s many comparable organisations in the developed world were closed, while others limped along with Government support until they could be sold to industry or transformed into institutions with a different role. By virtue of Australia’s geographical isolation and a respect for the organisation’s historical role in national security, CSL escaped scrutiny longer than most. Management changes in the 1970s including the appointment of a Director (Neville McCarthy) with pharmaceutical industry experience who introduced a more commercial approach, extended the organisations life, but failed to deliver the new products essential for long term survival.
In 1990, when Brian McNamee became CEO, although the organisation was still producing human and veterinary biologicals and had a biosciences and blood products division, its future was in doubt. When the Government announced its intention to sell the enterprise to a multinational pharmaceutical company, McNamee was able to persuade the Minister of Health, Brian Howe, that privatising CSL would not only provide the Government with a greater financial return but give the organisation a chance to flourish.

The initial public offering in 1994 returned A$300 million to the government and gave the company control over all of its plant, including an uncompleted plasma fractionation facility at Broadmeadows, which was based on a novel and at that time unproven technology, large scale chromatography.

The opportunity to complete the construction of the facility and validate the new technology was a turning point for CSL, while its release from Government control gave the CEO and Board the opportunity to respond rapidly to new opportunities. As the local market is too small to sustain a pharmaceutical company, McNamee’s genius was to find a way for the organisation to expand internationally and to develop a suite of new products to meet unmet medical needs. While he considered human health, specifically plasma products and human pharmaceuticals as the company’s core business, McNamee gave each division a chance to succeed, initially focussing on expanding the animal health and biosciences capabilities through modest acquisitions in New Zealand, the UK and the US. In each case the head of the relevant division and their family relocated, to run the newly acquired business and in each case CSL’s knowledge, insight and commitment was able to add value. Some years later, these businesses were sold for almost 20 times CSL’s original investment.

With this success, the organisation recognised that it had the knowledge and skills to operate internationally, which provided the confidence to attempt transformative transactions. In addition to expanding overseas, McNamee recognised that new product development was the key to long term success and began investing a significant proportion of the company’s profits into Research and Development. This emphasis has seen the organisations direct spending on R&D rising from around A$10 million in 1990 to over A$30 million in 2000 to over A$1 billion in 2020.

The area of business in which CSL had the deepest skills and the only area in which it had world leading technology, was plasma fractionation. In 2000, armed with the knowledge provided by Jack Wood, a Canadian executive with a long history in the industry, the analysis of a team from the London School of Economics and his engaging personality, McNamee was able to persuade the owners of the Swiss fractionator ZLB, that CSL was a suitable acquirer. The transaction, which was sealed after McNamee, who had been severely ill, travelled to Bern to present his case to the ZLB board, has become part of company folklore.

When coupled with the acquisition of NABI’s plasma collection facilities in the US, a year later, it was truly transformative. On each occasion it proved relatively easy to raise the funds to support the acquisitions because the market was able to see their logic and how they would create value. The subsequent acquisition of Aventis - Behring’s plasma business in 2004 and its successful integration, enabled the company to operate internationally and at scale. The integration of these businesses has enabled CSL to extract the maximum number of therapeutic proteins from each unit of plasma at the lowest cost and to invest in developing a range of products generated by recombinant DNA technology.

This approach has been very successful; whereas in the period 1974–1990, only a single new human product had been developed by CSL, (exclusively for use in Australia), since 1990 more than 20 new products have been licenced for International markets. The acquisitions provided CSL with production facilities in Europe, the US and Australia, staff with world class technical skills, a suite of interesting research projects and sophisticated marketing capabilities.

With access to major markets in the Northern Hemisphere and recognition of the potential provided by the emerging market in Asia, Paul Perrault, a senior executive with extensive marketing experience was chosen, on the retirement of McNamee, to lead the company into its second century.

CSL has designated its Melbourne laboratories, which are located in the Bio21 Institute on the campus of the University of Melbourne as its primary source of innovation, whilst conducting most of its clinical development in the US. Plans are underway to move its administrative headquarters and laboratories to a new site adjacent to the University and Parkville precinct.

The acquisition of a research-based company, Zenyth therapeutics, has provide additional technical depth and a pipeline of recombinant products and monoclonal antibodies, while the acquisition of Calimmune has provided an opportunity to enter the exciting field of gene therapy.

By ceasing production of generic childhood and travellers’ vaccines to focus on influenza vaccines, through its new business
unit Seqirus, CSL has adopted a similar strategy to that it employed in plasma fractionation. The recent acquisition of Novartis’s worldwide influenza vaccine business has provided the company with considerable scale, production facilities in three continents capable of producing both cell culture and egg derived vaccines and a suite of products designed to meet a range of public health needs.

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Given the importance of acquisitions to its strategy and the success that CSL has had with its acquisitions, when so many others in the pharmaceutical industry have been value destroying, it is interesting to ask why? There were probably a number of factors involved. First, CSL has developed a deep understanding of what have been relatively unfashionable areas (plasma fractionation and influenza vaccines) and recognised the benefits that consolidation of production activities and R&D pipelines could provide. Second, it has generally acquired businesses that were small parts of much larger organisations and not receiving the management attention or resources that would enable them to flourish. Third, it had a clear understanding of how it could add value to any business it acquired and quickly put in place plans to unlock this value. Fourth, being based in Australia and relatively unknown, the company was able to fly under the radar and thus able to make acquisitions at reasonable prices. Fifth, it had great respect for the skills of the personnel that it acquired and the culture that they brought with them and sought to create a situation where $1 + 1 = 3. Last, and perhaps most importantly, as the company grew it retained the ability to act swiftly while maintaining an appetite for risk. Clearly, while all these ingredients were necessary, they would have been insufficient for success without outstanding leadership and a laser like focus on outcomes.

Despite its transformation over the past 30 years, CSL has retained fidelity to its original mission and culture. It is fascinating to see an organisation whose first major challenge was responding to a pandemic of influenza now turning its formidable skills and resources to combat the challenge of COVID-19.

Conflicts of interest

Ian was the R&D Director of CSL from 1990–2000 and continues to hold shares in the company.

Acknowledgements

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Biography

Professor Ian Gust AO is a medical virologist with a distinguished career in public health including the development of vaccines against hepatitis A and human papillomavirus infection and membership of the International Task Force for Hepatitis B Immunisation which accelerated the introduction of HB vaccine into routine immunisation programs. During his 20 years at Fairfield Hospital he built an internationally renowned research team, founded and directed the Burnet Institute, established the National HIV reference laboratory and directed the NHMRC special unit for AIDS virology. During his subsequent period as R&D Director at CSL Ltd, he reorganised the research division and laid the basis for the company’s new product portfolio. Ian is the author of three books, more than 300 papers and has received several major awards for his work. Since ‘Retirement’ in 2000, he has been appointed a Professorial Fellow in the Department of Microbiology and Immunology at The University of Melbourne and has been a board member of several biotech companies and a number of non profits including the International AIDS Vaccine Initiative, International Vaccine Institute, ICDDR,b and the Human Vaccines project.

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