# CSL Submission to the Senate References Committee Inquiry into Australia's Innovation System

31 July 2014

## Summary of comments and recommendations

CSL develops, manufactures, and markets pharmaceutical products to treat and prevent serious human medical conditions. CSL is Australia's largest biotechnology company and a global leader in plasma-derived therapies and their recombinant analogues, and a leading developer of antibodies. The CSL Group, headquartered in Melbourne Australia, operates globally while maintaining a substantial research and development ('R&D') presence in Australia. As such, CSL is an important part of Australia's innovation system. Accordingly, CSL welcomes the opportunity to make a submission to the Senate Inquiry on Australia's innovation system.

The matter of Australia's innovation system was referred to the Economics References Committee for inquiry on 18 March 2014, framed in the context of 'the challenges to Australian industries and jobs posed by increasing global competition in innovation, science, engineering, research and education'. CSL makes the following observations and recommendations concerning the Australian innovation system.

1. ***Australia is a relatively unattractive location for entrepreneurial manufacturing or as a base from which to commercialise locally developed intellectual property ('IP') into global markets***. CSL is not saying that Australia is unsuitable as an entrepreneurial manufacturing location – indeed we have several significant operations in this country. The observation is a comparative one, based on CSL's direct experiences and observations as a global corporation. This is principally a function of Australia's uncompetitive corporate tax system, but is exacerbated by declining access to some important specialised skills, high overall labour costs, location, terms of trade (resulting in a sustained strong currency) and the complexities of dealing with Australia's system of government and regulation.

   Developing IP, as an activity in itself, brings gains to the economy. If Australia's biotechnology innovation earns royalties on 'invented here' but does not earn returns on 'made here' it will not secure the full range of benefits from its innovation system. The largest gains from innovation, in terms of sustainable industries, and high value jobs that are secure, derive from the manufacture and global sale of goods and services that have a substantial innovation component. New biological medicines fall clearly into this category.

   In CSL's view, Australia will find it difficult to secure this economic growth unless it is willing to emulate some of the policies of other sovereign nations. Australia should learn from those who have been successful in attracting entrepreneurial investment, such as Ireland, Singapore, the UK and Switzerland.

   CSL observes that Australia's competitors are increasingly offering concessional tax treatment for the development and commercialisation of IP through so called 'patent

boxes'. The patent box recently adopted in the UK is a notable example. CSL envisages that a similar scheme in Australia would offer the prospect of narrow and targeted support for genuine IP development and its follow-on, new entrepreneurial manufacturing, both of which would stay in Australia and drive economic growth.

2. ***Direct government support can bring important R&D infrastructure to Australia and be influential in attracting investments that embed Australia into global supply chains.*** Direct government support can be helpful in attracting important R&D infrastructure to Australia. CSL has made a number of substantial investments in projects, such as the Biopharmaceutical Formulation Centre at Parkville and the Biotechnology Manufacturing Facility at Broadmeadows, which have strengthened Australia's innovation system and delivered benefits to the wider medical research and biotechnology communities. Direct government assistance was helpful in stimulating these investments.

   In CSL's experience, there are often opportunities to develop manufacturing which makes use of existing know how or IP, for example in extending existing global manufacturing at new sites. If these investments take place in Australia, they can help embed Australia more securely into global supply chains. While these investments might not add as much value as new entrepreneurial manufacturing, they can nevertheless deliver secure high skilled jobs and significant multiplier benefits to the broader community. Government help can be instrumental in securing these types of projects.

   Investments such as these, that strengthen Australia's technology clusters, are likely to deliver social benefits beyond the private returns that investors can earn from the investments. The importance of clusters to sustainable innovative industries is demonstrated by highly productive technology clusters in, for example, Boston and San Francisco in the US. This was recognised in 2008 by the Pharmaceutical Industry Strategy Group ('PISG') when it recommended that the government establish a strategic investment fund to contribute to such projects. CSL continues to support this.

3. ***Australian governments' expenditure on basic science is likely to remain highly productive and should remain a priority.*** Although Australia is currently a relatively unattractive location for entrepreneurial manufacturing, it is at the world forefront in a number of areas of basic research in biological science and human health. This expertise has developed in part as a result of State and Commonwealth Government funding of basic science through the university system and research institutes over many years.

   This type of basic science gives rise to substantial knowledge 'spillovers,' which can be inter-generational in nature. These spillovers mean that the benefits of the basic research extend far beyond those involved in the research itself, into many other

spheres. By way of example, the work of Crick and Watson on the structure of DNA had no immediate commercial application, but was the foundation of modern biotechnology. Private companies would not normally be willing to invest in this type of landmark basic research because they would not expect to make any immediate commercial returns from it; they cannot capture for their shareholders all the potential economic benefits. As a result, the private sector will (in aggregate) invest less in basic research than is socially optimal. Accordingly, basic science would be under-supplied if left to the private sector without government support. Australian governments' expenditure in this area should therefore remain a priority.

4. ***Australian universities and medical research institutes, supported by Government, are the foundation of Australia's innovative biotechnology sector.*** Australian universities and research institutes are central to Australia's biotechnology ecosystem. They are located at the heart of the developing Australian clusters such as the biotechnology hub in Melbourne. They provide an environment in which scientists are trained either for research or the workforce. They attract eminent scientists to the clusters, bring with them important skills and experience; and the researchers who develop through these institutions generate the early IP that larger firms can go on to commercialise.

   CSL maintains its centre of excellence in early stage R&D in Australia in large part because of this ecosystem and the high quality of IP that it generates. This is not simply prospective new patentable targets and molecules, but also technologies independent of these such as new experimental processes and paradigms. CSL also relies upon the Australian universities and medical research institutes for its skilled Australian workforce.

   CSL would welcome further government support for university science and technology and the research institutes in order to increase the supply of these essential cornerstones to the sector: knowledge spillovers; IP that can be developed into commercial products; and a large pool of highly skilled scientists and researchers entering the work force.

5. ***Australia lacks resources and capabilities in translational research that would complement its high quality basic research base***. Translational research intersects academic research and business R&D, which progresses early stage clinical research to establish proof of concept. Translational Research should ideally link together academic research with business, including companies like CSL and start-up and small biotech companies. Its role in the R&D process is to lower the risk associated with later stage and costly clinical development. In CSL's view, the level of translational research in Australia is inadequate given the high quality of our scientific community and basic research. Few of these translational activities currently occur within the academic research sector in Australia.

There is a compelling rationale for further support in this area beyond CSL's private interests. Translational research occurs in the early stages of the R&D process and therefore delivers, in relative terms, larger knowledge spillovers than later stage developments. Furthermore, this component of the R&D process benefits from close collaboration between academia and business, further enhancing these benefits.

CSL recommends that the government, through the National Health and Medical Research Council ('NHMRC'), increase funding of this research through Translational Grants similar in form to the grants provided by the National Institute of Health ('NIH') in the US. CSL notes the announcement of the new Medical Research Future Fund in the May budget and that it will be used to fund medical research priorities, including through payments to the National Health and Medical Research Council. CSL considers that, should the legislation pass, this could provide an effective mechanism for increasing support for translational research.

6. ***Government support for basic research and R&D should provide greater incentives for private investment in R&D, in order to deliver a higher overall level of R&D expenditure in the economy.*** CSL notes that Australia sits somewhere close to the average of OECD countries in terms of the proportion of GDP spent on R&D. Although CSL does not suggest a particular economy-wide target for R&D; if Australia is to attract new investment in innovation to secure high skill, high wage jobs and industries, the proportion of its GDP spent on R&D will need to increase. This will require increased contributions from government that, in turn, stimulate higher R&D expenditure from business.

7. ***The Commonwealth R&D tax concession is effective***. The Commonwealth tax concession is a valuable source of support for Australian R&D, particularly in the area of new product development. CSL understands that the 45% tax offset available to smaller firms is similarly valuable. CSL's view, which is widely echoed in the economic literature, is that private sector R&D also produces knowledge spillovers, if perhaps fewer than basic research. Accordingly, there is a strong rationale for government support of business R&D, and CSL believes this is best delivered through the tax concession.

   The reality of biopharmaceutical development is that late stage clinical development, the most costly R&D stage, has to take place in overseas markets (particularly the US and EU), even if the products are developed in Australia. In CSL's view, Australia would benefit if more of this overseas R&D was eligible for the tax offset, provided that the IP related to the product being trialled is held in Australia at the time. This would tend to prolong the amount of development that takes place in Australia, thereby increasing the likely returns to the Australian economy.

8. ***Smaller biotechnology firms can struggle to attract investors, even when continued support would deliver benefits to the economy.*** There are market failures in the Australian innovation system as it applies to the biotechnology sector. As already noted, these include inadequate translational research and early clinical research, often the province of small biotechnology firms, given the spillover benefits they generate. These spillover benefits are particularly difficult for small firms to capture as they lack the complementary assets (such as later-stage development skills, managerial skills, portfolios of projects etc.) necessary for their appropriation.

   Therefore there is a strong case for further government intervention to support small biotechnology firms, particularly when the support enables more of these firms to develop their IP to the proof of concept stage. Understanding the nature of the market failure that limits investment in small, early stage technology firms is important in designing the best form of support.

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# 1. Introduction

CSL develops, manufactures, and markets pharmaceutical products of biological origin to treat and prevent serious human medical conditions. CSL is Australia's largest biotechnology company and a global leader in plasma-derived therapies and their recombinant analogues. The CSL Group, headquartered in Melbourne Australia, operates globally while maintaining a substantial research and development ('R&D') presence in Melbourne, Australia.

CSL has a successful track record in the development of innovative medicines for global markets. CSL is both an important part of Australia's innovation system, and is reliant upon it. CSL's innovation efforts and ability to take products from early research to market from an Australian base depend upon our links to the rest of the bioscience community in Australia. In short, the health of the national innovation system is an important driver of CSL's continued growth and development. Accordingly, CSL welcomes the opportunity to make a submission to the Senate Inquiry on Australia's Innovation System.

CSL views Australia's innovation system from the perspective of a pharmaceutical company dedicated to the supply of medicines of biological origin to treat and prevent serious human medical conditions. Fulfilling this role involves substantial expenditure on R&D to develop new medicines, with the large risks that this entails. It also requires substantial R&D to maintain, develop and improve the existing portfolio of therapeutic products for global markets.

To address the terms of reference from this perspective, we first provide an overview of CSL and the importance of R&D to the organisation. CSL has the second highest R&D expenditure of any Australian firm and is one of only six Australian firms within the top 1,000 firms globally, as measured by their R&D spend. As a growing company, CSL continues to make substantial investments in manufacturing. CSL's global footprint gives the company a unique perspective on Australia's position in the global competition between nations for these valuable assets

R&D in the pharmaceutical sector is complex, costly and uniquely risky. In order to assess the role that governments should play in the innovation system as it impinges on this sector, we set out the costs and risks involved.

Governments play a significant role in Australia's innovation system through the provision or funding of many of the building blocks of the innovation economy. We therefore briefly review the case for government support for innovation, and set out in very broad terms where it is likely to be most beneficial.

Having established this context, we then review Australia's innovation system having regard to the Inquiry's terms of reference.

## 2. Innovation at CSL

CSL was established in 1916 to provide the Australian community with human vaccines and sera that could not be guaranteed in the event of war. CSL continues with that proud tradition, supplying products of national interest such as seasonal influenza vaccine, pandemic influenza vaccine, plasma products made from Australian plasma, antivenoms and other vaccines.

CSL was incorporated in 1991 and sold by the Commonwealth Government in 1994. CSL's evolution into a global speciality biopharmaceutical company involved the acquisition of the Swiss Red Cross fractionator ZLB (2000), US blood collection centres from NABI (2001) and Aventis Behring (2004). Since then, CSL has consolidated its position as a leader in the global market for plasma-derived medicines and as an innovator in these products, vaccines, and recombinant proteins. Throughout, CSL has continued to increase its R&D expenditure, which remains a cornerstone of CSL's growth plans. CSL Limited now has a market capitalisation of around A$32bn,[1] employs over 12,000 people globally, has major operations in 27 countries with manufacturing facilities in Europe, USA and Australia. CSL is currently Australia's 10th largest public listed company by market capitalisation.[2] In 2012/13, CSL Limited's consolidated group revenue was US$5,130m.

CSL has a successful R&D track record. For example, CSL successfully advanced[3] research relating to a potential HPV vaccine to the stage where it was ready for development into the global product Gardasil® by Merck, as a result of which CSL earned a royalty stream flowing back into Australia of US$134m in 2012/13 alone.

### 2.1. CSL's R&D activities and expenditure

CSL has extensive R&D activities across all its global sites. However, CSL continues to maintain its largest R&D centre in Australia, co-located with its global corporate headquarters in Melbourne. This reflects the strategic importance of R&D and of Australia to CSL. In 2012/13, CSL's Australian operations comprised total sales of A$849 million, including A$154 million in export sales; $254 million paid in wages and salaries to Australian workers; A$609 million in goods and services bought from other Australian and overseas businesses; and 1,851 full-time equivalent employees.

CSL's largest centre for R&D is Australia. Of the 1,851 Australian staff, almost 400 are involved in R&D functions across the Melbourne sites, of which in excess of 80% are

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[1] As of 23 July 2014.

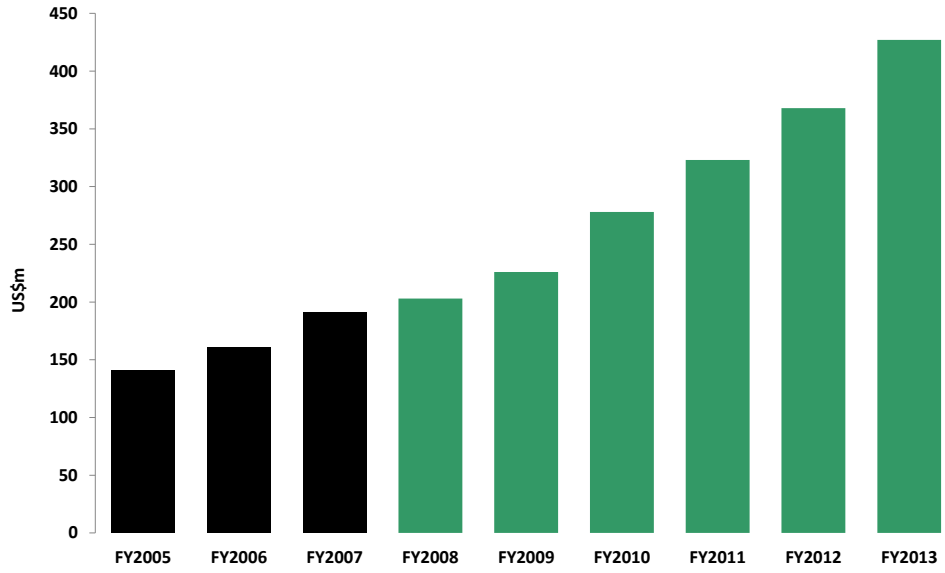
[2] ASX 2 July 2014. http://www.asx200list.com/ (last viewed 17 July 2014).

[3] This was done through its collaboration with Professor Ian Fraser at the University of Queensland.

graduate scientists. This does not include graduate scientists and engineers working in other Australian CSL divisions.

CSL has increased its R&D at a compound rate of approximately 15% per annum, from A$141m in 2004/05 to US$427m in 2012/13 (see Figure 1), and is planning further growth in the future. CSL's total R&D expenditure represents approximately 8.3% of global revenues.

**Figure 1. CSL's global R&D expenditure**




FY2005-FY2007 in AU$m. FY2008-FY2013 in US$m.

CSL has consistently ranked in the top two or three Australian companies in terms of its global R&D expenditure. By way of example, according to PwC in its 2013 Global Innovation 1000 Study[4] CSL ranked second to Telstra in its global R&D expenditure followed by Aristocrat Leisure, OneSteel/Arrium, Cochlear and Amcor; only these six firms ranked within the global top 1000. According to the 2013 EU Industrial R&D Investment Scorecard[5] CSL ranked second to Telstra amongst the Australian non-financial firms;[6] on these measures, CSL ranked 329th in the global list. These figures do not,

[4] PWC (2013) *The Global Innovation 1000: Navigating the Digital Future* http://www.strategyand.pwc.com/global/home/what-we-think/global-innovation-1000 (last viewed 16 July 2014).

[5] European Union (2013) *2013 EU Industrial R&D Investment Scoreboard* http://iri.jrc.ec.europa.eu/scoreboard13.html (last viewed 16 July 2014).

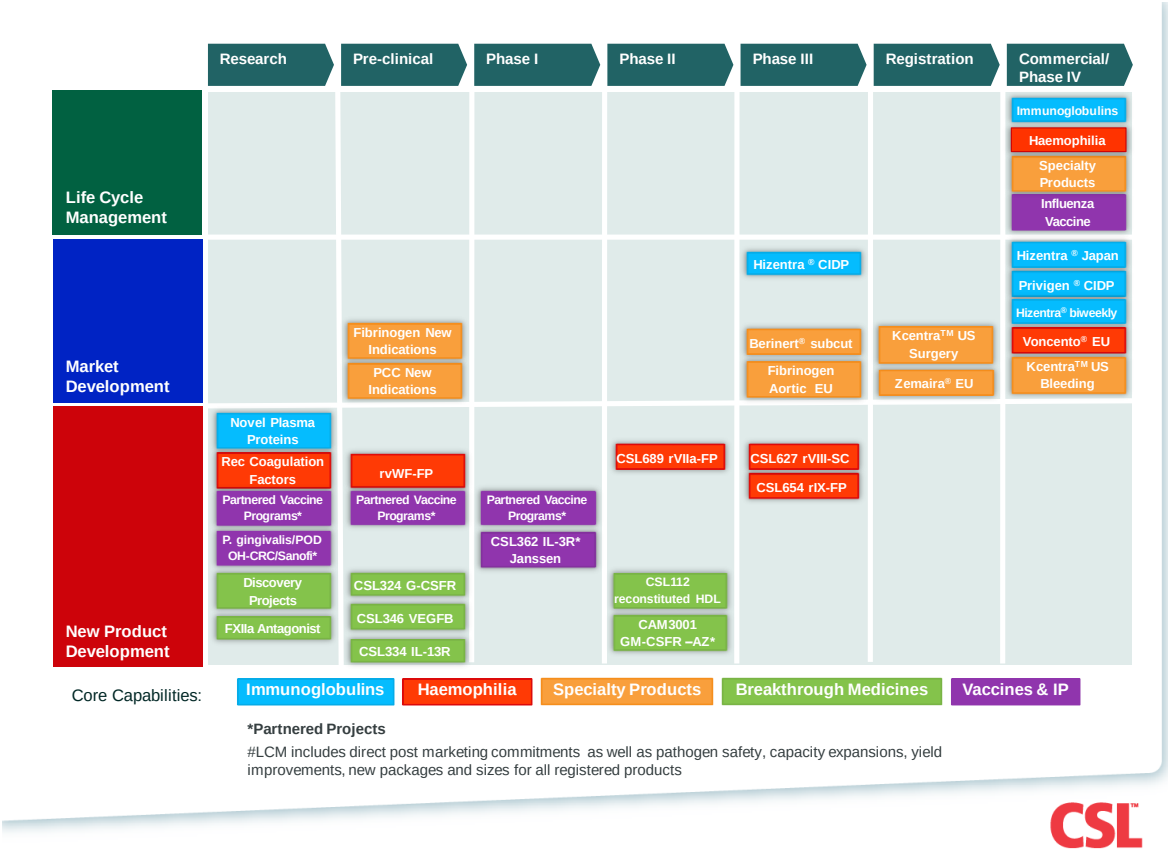
[6] The *2013 EU Industrial R&D Investment Scoreboard* (*ibid*) characterisation of Telstra and CSL expenditure on R&D is consistent with reports by other commentators. However, it places three of Australia's largest banks above CSL, indicating that it has adopted broader definition of R&D expenditure.

however, detail the character of the R&D expenditure. Considerably in excess of half of CSL's R&D expenditure is on high risk potential new products (see section 3.1 below).

## 2.2. CSL's current R&D portfolio

CSL currently has multiple innovative products undergoing clinical trials and in preclinical development. In addition, CSL's R&D pipeline includes partnered projects, many projects still in the research phase, and market development activities on existing products which nevertheless encompass considerable technical risk. By way of example, CSL is currently developing a quadrivalent influenza vaccine to supplement its existing trivalent formulation. CSL's current and future R&D activities are summarised in Figure 2, which shows CSL's global R&D pipeline as of December 2013.

**Figure 2. CSL global pipeline (December 2013)**



## 2.3. Government support for R&D received by CSL

CSL currently benefits from the Australian government R&D tax incentive scheme. The benefit is a 40% tax offset for all eligible Australian R&D expenditure. Of the US$427m of R&D expenditure in 2012/13, approximately A$97.5m million was eligible for the tax concession, a figure that is somewhat lower than our R&D spending in Australia.[7] This generated an additional A$9.75m tax benefit. At first glance, the Australian Government's support for CSL's R&D contributed about 2.3% of CSL's total R&D expenditure in 2012/13. The practical impact on CSL's real cost of R&D is somewhat less than this suggests, an issue discussed in more detail below (see section 5.2 below). In 2012/13, CSL also received valuable State and Commonwealth grants (A$11.1m) for the construction of facilities at Broadmeadows.

## 2.4. Co-location of R&D, entrepreneurial risk and manufacturing

CSL now has sufficient resources, skills and global reach to take innovative products from the discovery phase through to the market. That process is best exemplified by CSL's portfolio of recombinant extended half-life coagulation (clotting) factors (referred to by their R&D project codes - CSL627, CSL654, CSL689). Development to proof of concept and subsequent preclinical development of these products took place in various locations around the world. For one of these products, CSL's specially constructed Biotechnology Manufacturing Facility ('BMF') at Broadmeadows[8] is capable of supporting the product through to early commercialisation. While a government contribution to CSL's investment in the BMF was helpful in the final choice of location, there was also a compelling R&D rationale: Broadmeadows was an existing manufacturing facility with many of the skills necessary for ensuring its success, including regulatory and quality compliance skills.[9] It was also important to maintain close links between the R&D team that developed and optimised the recombinant proteins and cell lines, and those charged with its initial small scale manufacture for late stage clinical development and launch. The clinical trials for the recombinant coagulation products are being conducted at a number of global sites.

The BMF is principally an R&D facility, not suited to full scale commercial manufacture. CSL, after an extensive search, recently determined that commercial manufacture of the portfolio of recombinant coagulation products should take place in Switzerland. A broad range of considerations impinged on that decision including closeness to market, closeness to CSL Behring's commercial and clinical support centres, closeness to existing CSL Behring manufacturing facilities, access to and cost of skilled staff and financial factors such as the level of government support and taxes.

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[7] Not all Australian R&D expenditure qualifies for the tax concession.

[8] For which CSL received both Victorian State and Commonwealth support.

[9] Tailored to the TGA rather than to US and European regulatory requirements.

CSL's operating paradigm, which has been in place now for many years, establishes manufacturing sites as entrepreneurial centres that hold the IP alongside the manufacturing and R&D resources necessary to maximise commercial value. In CSL's view, the model is commercially efficient in that sites are then responsible for the maintenance of the value of that IP (through appropriate lifecycle management and market development R&D), exploiting the scope economies that arise from co-location of biological manufacturing, R&D and IP. Under this model, the necessary IP for CSL's novel recombinant coagulation products will be held at the new manufacturing site, purchased on an 'arms-length' basis through a once-off payment of US$100m to be followed by a series of technical and commercial milestone payments and an appropriate royalty rate on commercial sales.

From the perspective of this Inquiry, these arrangements will enhance Australia's pharmaceutical R&D capabilities through late stage clinical trials and early commercialisation of recombinant biological medicines, and will result in a flow of payments to Australia (should the products prove clinically and commercially successful) reflective of the value of the IP that was generated in Australia on which they rely, qualitatively similar to the royalty stream from Gardasil®. These payments will contribute substantially to the Australian economy, however, Australia will not benefit from the high tech manufacturing jobs, spillovers (such as regulatory competencies) and profits that will arise from full scale commercial manufacture.

## 2.5. CSL decision making - from development to market

CSL is a A$32bn company with global revenue of US$5.130bn and an attractive R&D pipeline. Accordingly, CSL is increasingly called upon to make decisions over where best to locate sites for R&D, development and manufacture. Choice over location materially impacts the returns that CSL can expect to make for its shareholders. To illustrate:

- in 2010, CSL determined to locate the Biotechnology Manufacturing Facility at Broadmeadows to support manufacture for clinical trials and early commercialisation of its pipeline of potential new products;

- in 2010, in anticipation of growing global demand CSL determined to locate a second site for the manufacture of Privigen® at Broadmeadows[10] using the technology that was developed and is continually refined in Bern, Switzerland;

- in 2014, CSL decided to locate its manufacturing facility and entrepreneurial centre for its recombinant coagulation products in Switzerland;

[10] The Turner Facility.

- CSL will shortly have to decide the best location for the commercial manufacture of CSL112 (reconstituted component of plasma-derived High Density Lipoprotein – known as 'good cholesterol' – for the treatment of acute coronary syndrome), should this product succeed through clinical trials; and

- CSL will shortly have to decide on an additional site for the manufacture of an existing plasma product, Alburex®, in anticipation of growth in global demand.

All of these projects involve substantial new investment. Most are the result of considerable investment in innovation. They will secure high skill, high wage jobs and further innovation at the chosen locations, and help sustain industries at those locations. The implications of CSL's decision making processes for Australia's innovation system is discussed in section 6.

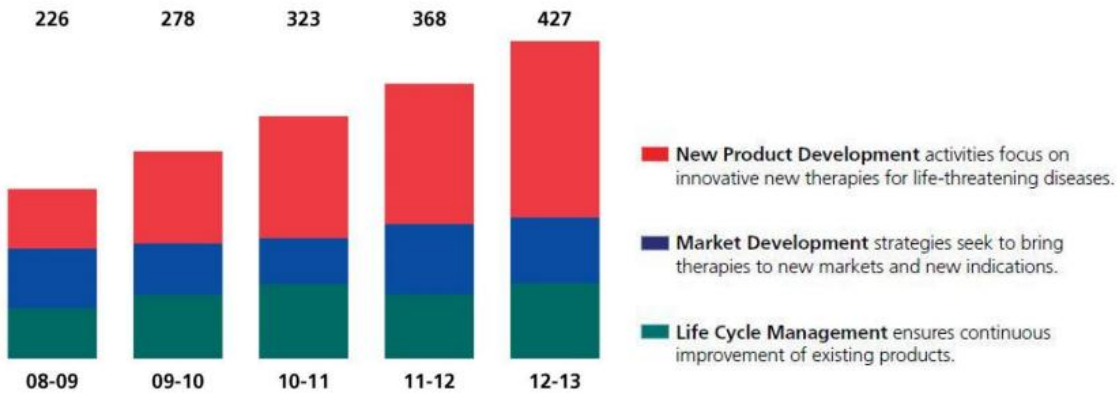
## 3. The costs, risks and architecture of biotechnology innovation

R&D in pharmaceutical sector is complex, costly and uniquely risky. In order to assess the role that governments should play in the innovation system as it impinges on this sector, it is helpful to understand the different types of R&D, the different stages of the drug development cycle, and the costs and risks at each stage.

### 3.1. Types of R&D

Figure 3 shows CSL's R&D expenditure over the last 5 years broken down into three classes of activity: new product development; market development; and lifecycle management.

**Figure 3. CSL's R&D investment by type (US$m)**




Lifecycle management R&D is essential to maintaining biopharmaceutical product sales. It includes activities ranging from ongoing clinical and regulatory support (e.g. maintaining product registrations, dealing with adverse event reports, labelling requirements) to changes in product formulation, storage and administration aimed at improving the utility of the product for both patients and clinicians. Market development R&D is primarily directed at maintaining and improving the sales of existing products, by extending products into new geographical markets, and researching and developing new indications where existing products are clinically beneficial.

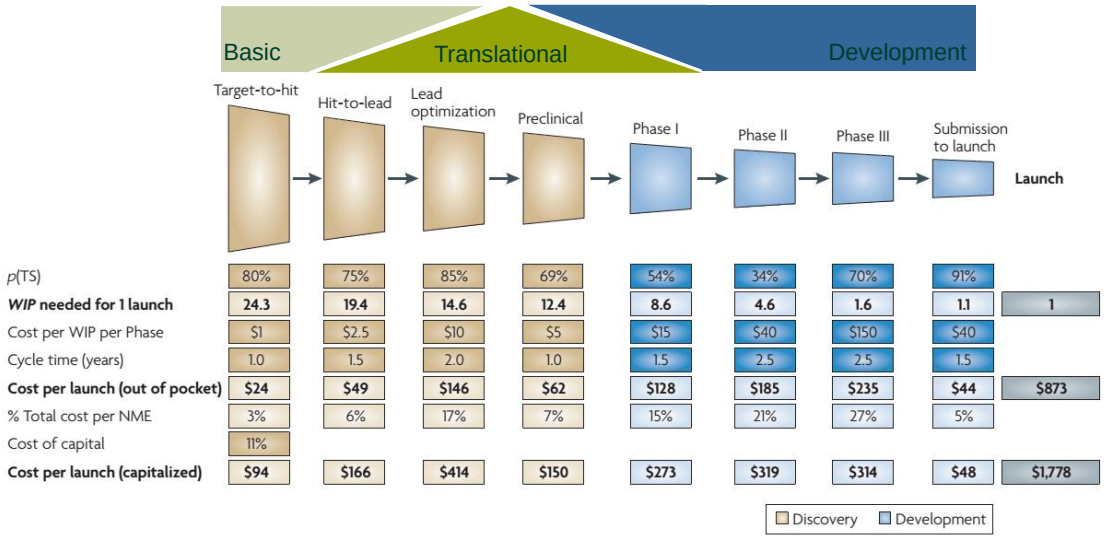
In CSL's view, life cycle management and market development are largely non-discretionary. Successful firms in every type of market will carry out analogous activities although the appropriate level will vary across firms and sectors. The strictures of the biopharmaceutical market, such as the need for clinical trials, render these activities somewhat more risky than for most other industries.

In contrast, companies including pharmaceutical companies exercise considerably more discretion[11] over new product development. New product development R&D involves researching new products that target unmet medical needs. This entails very high risks of failure (technical risk) because the research is often at the borders of existing scientific knowledge.[12]

## 3.2. The development process for new products

Developing new biotechnology products targeted at unmet medical need is expensive and risky. Whilst it differs significantly depending on the type of therapy being developed, Paul SM *et al* estimate a development cost for a new drug of approximately US$1.8bn[13] (see Figure 4) and cites previous estimates by other authors ranging between US$800m and US$1.7bn. Of those that enter clinical trials, only 1 in 9 will result in a product launch.

**Figure 4. Pharmaceutical development pathway and costs**




*Source:* Paul SM et al (March 2010) *amended by CSL*. In the stylised typical pathway, 'target to hit' represents the first stage of discovery after the identification and validation of a target for drug action, both of which are the province of basic research. It involves the identification of compounds that are active against the target. These are then refined to a lead compound ('hit to lead') which is then optimised in anticipation of preclinical development. WIP refers to 'works in progress.

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[11] In the sense that the capital employed in new product development could instead be applied to other purposes, for example mergers and acquisitions or expansion of manufacturing capacity for existing products.

[12] The distinction is not hard and fast. For example, researching the use of existing products for new conditions (such as the use of CSL's coagulation products to control surgical bleeding) can involve substantial technical risk necessitating expensive clinical trials and a high attendant risk of failure.

[13] Paul SM, Mytelka DS, Dunwiddie CT, Persinger CC, Munos BH, Lindborg SR, Schacht AL, 'How to improve R&D productivity: the pharmaceutical industry's grand challenge', *Nature Reviews Drug Discovery* 9, 203-14 (March 2010).

Typical failure rates for a project might be 46% in phase 1, 66% in phase 2, 30% in phase 3 and 9% at the stage of submission to launch. These yield an overall success rate in clinical development of around 12%. The capitalised development costs per compound (whether it successfully transitions or not) typically increase by between 2 and 3 fold across each of the clinical development stages. Hence in capitalised terms, phase 3 costs are, on average, around US$200m per compound, while phase 1 costs are around US$32m per compound. The costs of resolving technical risk[14] therefore rise through the development cycle.

## 3.3. The private and social rewards from innovation

While innovation and R&D are not synonymous, CSL believes that well managed and targeted R&D is an essential and substantial element of any innovation system. Innovation is not an end in itself, but rather a means of delivering social benefits. In so far as those social benefits are economic in nature they can include: more, and more valuable, research; high skill, high wage jobs that are secure; and more value adding industries located in Australia. They can include royalties on IP or the proceeds of sale of IP, if Australian IP is developed and commercialised elsewhere, or they can extend further into the value chain if Australian IP can be developed and commercialised (including manufacture) in Australia for global markets.

The private rewards of innovation are those that can be captured by investors. The social rewards include the private rewards, but also include spillover benefits (see section 4.1) from, for example, the dissemination of knowledge.

### 3.3.1 Private rewards

Typically, in innovative industries the extent of value added increases as new products proceed through the development cycle. This is certainly the case with biotechnology, where the market value of IP rises dramatically as the product passes each pre-clinical and clinical development stage, and by considerably more than the development costs. Of course, most projects fail on the way.

The majority of the financial risks of development are incurred late in development, particularly in phase 3 and, commensurate with this distribution of risk, the bulk of the returns from successful products accrue to firms that undertake this late stage development. This is well illustrated with Gardasil®; CSL helped develop the IP on which the vaccine is based, and licensed the IP to Merck who undertook the extensive and very

[14] Technical risk is the risk that the product will fail to work as intended. This may be for a variety of reasons including low efficacy or unacceptable adverse events. This is distinct from commercial risk whereby a product works as intended but fails to make an acceptable return. This could arise, for example, if development costs are too great, if market prices are forced down through regulation or monopsony purchasers, or through competition that diminishes price and/or market share.

costly late stage clinical trials. CSL receives an appropriate royalty on all Gardasil sales, but Merck will realise most of the rent from the project.

In this context, it is instructive to compare and contrast two of Australia's greatest contributions to modern biopharmaceuticals: G-CSF, a growth factor used to treat cancer patients, and Gardasil®, the HPV cancer vaccine. G-CSF was lost to Australia early in its development and the multi-billion dollar rewards from its success stayed overseas. The HPV vaccine technology on which Gardasil® is based was taken further along the development path in Australia by CSL, resulting in substantial royalties flowing back to Australia.

### 3.3.2 Social rewards

Social gains from innovation in excess of these private gains are typically largest in the early stages of R&D and arise even if projects fail. They accrue principally from knowledge spillovers from research. As the R&D process proceeds, these spillover benefits typically diminish as development focuses on single products and as firms seek to limit spillovers through patents, trade secrets and corporate specialisation and expertise.[15]

## 3.4. Requirements to develop and commercialise new biotechnology products

Even now it is questionable whether CSL would choose to undertake the full clinical development of a product like Gardasil® given the size and nature of CSL's global activities. CSL has, however, decided to take its recombinant coagulation pipeline to market itself. CSL's ability to do so is based on acquiring and developing the necessary strategic assets:

- the financial resources to fund late stage R&D expenditure;
- global commercial operations capable of marketing a global product;
- integrated clinical, regulatory and quality functions that can support the product in international markets;
- the scientific skills to invent, develop and improve products; and
- the skills and facilities to manufacture products at both developmental and commercial scale.

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[15] Oxera Consulting. (2005). Innovation market failures and state aid: developing criteria. Report prepared for Directorate-General for Enterprise and Industry, European Commission. http://www.pedz.uni-mannheim.de/daten/edz-h/gdb/06/innovation_market_failures_and_state_aid.pdf (last accessed 14 July 2014).

Biotechnology firms seeking to commercialise their products from Australia, and to retain the bulk of the returns from doing so, will require a similar set of endowments.

## 3.5. The efficient market structure

Biotechnology is fiercely competitive. That competition manifests itself through competition (and prices) for ideas, competition for skilled staff and competition for funding. The sector requires proliferation of ideas (which spring from basic and translational research), and a culling process that filters out the unsuccessful projects and funnels genuine prospects to the firms that can develop them.

The industry structure therefore comprises a large number of small firms, each of which is seeking to develop a few possibilities, often just one, in which the inventors or scientists typically hold equity.[16] This business model is the single minded development of their IP, to the point at which it is of value to the next firm in the chain, a firm capable of the next stage of development. If the ideas they are working on fail, then the companies themselves fail. If their IP does prove to be of value, many companies will be swallowed up by larger firms with the necessary endowments to develop and commercialise the products.[17] Very few small biotechnology companies will successfully grow to a global scale.

The fact that many companies will fail and that very few have a long-term future should not be seen as a sign of market failure or a signal for the government to intervene. This Darwinian model is efficient in that it gives the strongest possible incentives to develop IP, but is ruthless in cutting off funding when they are shown not to work. It allows scale economies to develop where they are important — in the costly later stages of clinical development and in commercialisation — without lumbering the early stage with scale diseconomies. The successful intermediate and large pharmaceutical companies that commercialise the IP have to be 'intelligent receptors'.

CSL is the only globally scaled pharmaceutical company headquartered in Australia at present, and is mid-sized by international standards.

### 3.5.1 The importance of structure, networks and markets

While few globally scaled firms can be expected to develop in Australia, it is important that there are at least one or two that can operate internationally. There are substantial spillovers from the integration of basic research, a number of small biotechnology companies and one or more large biotech companies.

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[16] This structure is also important in reducing information asymmetry that would otherwise impede investment in this level of research. Investors struggle to determine whether the IP in these small firms is valuable. When inventors 'invest' by working for, investing in and taking on the risks of these small biotech firms, they signal to outside investors that insiders believe the IP is valuable.

[17] CSL's acquisition of Zenyth is an example of this.

Lord Sainsbury, Minister for Science in the UK[18], identified the importance of such biotechnology clusters to successful biotechnology innovation, and noted the presence of a large firm alongside a strong science base (amongst other factors) as key components of a successful cluster. The evidence of biotechnology clusters in the US, such as Boston and San Diego, supports this.

Technology clusters agglomerate a critical mass of know how across the range of activities needed for the development and commercialisation of innovative products. Hence typically, they arise around universities (which generate basic research and skills), they contain one or more large companies with commercial reach capable of resourcing the most expensive elements of the development process, and a large number of smaller companies that both generate IP and support the activities of the other cluster members.

Governments play a fundamental role in developing and supporting innovation, even in the most vibrant biotechnology markets such as the US. In designing government support, these architectural imperatives, such as the importance of clusters, need to be recognised.

[18] See Biotechnology Clusters. 1999. Report of a team led by Lord Sainsbury, Minister for Science http://www.dti.gov.uk/files/file28706.pdf

# 4. The case for government support of innovation

The Productivity Commission in its review of public support for innovation[19] concluded that government support for business innovation was justified when it gave rise to positive spillovers, and when it also gave rise to additionality. That is, public support for R&D should increase the amount of R&D undertaken, and the social value of that R&D to Australia should be in excess of the private value to the firms that undertake it. CSL, as articulated in a number of prior submissions related to Australia's innovation system, concurs with this view.[20]

## 4.1. Spillovers

Government support for research is desirable when there will be too little investment[21] by the private sector as a result of market failures. One of the central market failures in R&D is the existence of spillovers whereby third parties benefit from private investment in innovation, but the innovator cannot capture these benefits in the form of a contribution to the return on investment. There is an extensive literature that shows that the social rate of return on investment in R&D exceeds the private rate of return.[22]

CSL's own R&D activities result in knowledge spillovers[23] into the broader economy. For example, 88 of CSL's research scientists work at the Bio21 facility in the University of Melbourne. Their research work is part of CSL's R&D program, but their contact and collaboration with other users of Bio21 and the broader University of Melbourne and Parkville science community results in considerable knowledge spillovers. CSL also has an extensive network of links[24] to the biotech community through collaborations, licenses, research contracts, clinical trial agreements and grants. The majority of these involve considerable interaction and exchange of information. They foster active research projects,

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[19] Productivity Commission Research Report (9 March 2007) *Public Support for Science and Innovation*.

[20] See for example CSL (December 2006) *Submission to the Productivity Commission Research Study into Public Support for Science and Innovation in Australia;* CSL (April 2008) *Submission to the Review of the National Innovation System;* CSL (September 2008) *Response to the Review of the National Innovation System,* CSL (September 2009) *Response to Treasury's Consultation Paper "The new research and development tax incentive"* and CSL (March 2012) *Submission to the McKeon Strategic Review of Health and Medical Research*.

[21] An inefficiently low level of investment from a societal perspective.

[22] This is extensively reviewed by the Productivity Commission (2007) *op cit* at n 19.

[23] Knowledge spillovers arise when the knowledge generated from activities is used more widely than those who create it (since most knowledge can and is freely disseminated). The acquired knowledge then generates additional and valuable economic activity. One of the benefits of networks, such as biotechnology clusters, is that they facilitate the development of the knowledge spillovers.

[24] In previous submissions on R&D, CSL identified more than 120 of these network links.

provide an excellent training ground for scientists involved in basic research, and generally foster vibrant and effective research. This is precisely the type of activity that generates the knowledge spillovers. Few of these collaborations will lead directly to a finished commercial product — a simple reflection of the technical risks. CSL cannot capture (in the form of returns to shareholders) the broad range of benefits that accrue to partners, universities, institutions or to the researchers working on the projects. CSL does benefit from the extensive contact with the basic research community which can provide insight into potential new research areas, but that is probably only a fraction of the overall gains to the community.

### 4.1.1 Spillovers and clusters

Section 3.5.1 noted the importance of clusters in maximising the value of innovative industries. There are noted biotechnology clusters in Cambridge UK, Boston and San Diego. Clusters enhance the knowledge spillovers that are generated from R&D, and can reduce the transaction costs that cluster members face, for example, reducing the costs of identifying and acquiring skilled staff or IP to develop. These benefits cannot typically be captured by private firms investing in infrastructure aimed at developing the clusters. Accordingly, government support is important in ensuring a socially efficient level of investment in cluster development. In CSL's view, Melbourne is a developing cluster that could, with further investment and support, become a highly effective biotech cluster by global standards.

## 4.2. Additionality

The Productivity Commission[25] stated that government support for business R&D should result in more R&D, the 'additionality' criterion. It should not be directed at R&D that efficient firms would undertake anyway. CSL concurs with this view. The balance of the evidence shows that measures which reduce the cost of R&D result in more than proportional increases in the amount of R&D undertaken. To the extent that government support for innovation, such as tax offsets for R&D, results in lower costs of R&D as is generally intended, it is likely to result in additionality. There is broad consensus that this is the outcome in both the short and long term, but there are cautionary factors. There is evidence that some government funding of R&D can reduce or 'crowd out' other industrial R&D[26] or can result in changes in the location of, rather than additional, R&D.[27]

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[25] *Op cit* Productivity Commission (2007).

[26] See, for example, Mamuneas T, Nadiri M (1996) Public R&D Policies and Cost Behavior of the US Manufacturing Industries. *Journal of Public Economics* 63 1 57-81 and Wilson D (2005) Beggar thy Neighbor? The In-State vs Out-of-State Impact of State R&D Tax Credits. *Federal Reserve Bank Of San Francisco Working Paper Series*

[27] *Ibid* Wilson (2005).

## 4.3. Other sources of market failure

R&D knowledge spillovers are a form of market failure. If they are not resolved they are likely to result in socially inefficient underinvestment in innovation. These spillovers are pervasive in basic research. However, they are also substantial in translational and early stage research which, for reasons of efficiency (see section 3.5 above), are in large part the province of small biotech firms. While there are benefits from this architecture, small firms lack the complementary assets (e.g. late stage and commercial development capabilities) to appropriate the gains from their R&D,[28] with the result that the benefits spill over to other parts of the economy.[29] Government support of such firms is therefore important in ensuring socially efficient levels of investment.

### 4.3.1 Capital market failures

Capital market failures are sometimes identified as impediments to achieving the socially efficient level of investment in the innovation economy. Reluctance to invest because expected returns are inadequate given the anticipated risk, a common problem for small biotech firms, is not capital market failure *per se*. Rather, capital market failures typically arise from information asymmetry, adverse selection and moral hazard. Information asymmetry arises when the information necessary to appraise the investment risk is held within the target firm, sometimes diffusely across a number of staff, and cannot be determined by outside investors. Adverse selection arises because insiders are most likely to seek investment (to replace their own contributed capital) when they ascertain an increased risk of failure that external investors cannot perceive. Moral hazard arises when insiders are encouraged to take extra risks (or commit insufficient effort) because the risks are borne by external investors. The structure of the biotech industry has evolved in response to these issues.

Until the 1970s, pharmaceutical R&D was solely done by vertically integrated large firms that could manage the risks across the whole development path so these problems did not arise. Since that time, a complex architecture has emerged to allow the development path to be segmented, a process that has involved the monetisation of IP. Consequently, a large and sophisticated system involving basic science, patents, small, medium and large companies and the capital markets has emerged to support biotechnology development. The most successful examples are based around clusters, the most advanced in the US. Hence for example, the development of a new idea emerging from basic science might go through a grant funded stage, patenting, transition into a small company supported by

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[28] Teece DJ, Economic Analysis and Strategic Management, *California Management Review*, 26:3 (Spring 1984), 87-110.

[29] Griliches Z (1998) The Search for R&D Spillovers in *R&D and Productivity: The Econometric Evidence*.

FFF[30] investors, angel investors,[31] venture capital, IPO and then through to later stage development typically enabled through acquisition. Venture capitalists in this chain are typically closely integrated into their target firms and provide sequential investments as a means of minimising information asymmetry, adverse selection and moral hazard, before exiting upon acquisition.

Australia has made some progress in developing similar structures over the last decade, particularly with the emergence of biotechnology venture capital funds. Nonetheless, Australian capital markets, particularly at the very early FFF and angel fund levels which fund projects before they are of interest to venture capital, are noticeably less vibrant than in the US.

This should not, however, lead to the immediate conclusion the lack of vibrancy is simply a manifestation of capital market failure. The vibrancy of the US could well be a feature of its unique research, commercial and educational environment. Outside the US, government attempts to 'fix' the lack of vibrancy by supplying increased venture capital have not been obviously successful (in the sense of being seen to emulate the US model); evidence from the UK suggests that this lack of success is in large part due to 'thin' markets for investment quality IP,[32] which make it difficult for venture capital to assemble portfolios of investments with manageable risk characteristics. This manifests as a reluctance to invest in individual projects. That is, government intervention aimed at raising translational research to increase market depth may be more effective.

The case for increased support for small biotech firms operating in the translational and early clinical phases of development is strong, and does not rest primarily on there being capital market failures in need of correction. In CSL's experience, valuable IP that is generated in Australia can find investors. That is not to say, of course, that the IP attracts domestic capital that ensures ongoing development in Australia. Acquisition of domestically generated IP by foreign investors for offshore development is not *prima facie* an indication of market failure even if, as a result, valuable late stage development, commercialisation and manufacture for market do not take place in Australia.

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[30] The three Fs, "friends, family and fools"

[31] Wikipedia describes an angel investor thus: An angel Investor or angel (also known as a business angel or informal investor) is an affluent individual who provides capital for a business start-up, usually in exchange for convertible debt or ownership equity. A small but increasing number of angel investors organize themselves into angel groups or angel networks to share research and pool their investment capital, as well as to provide advice to their portfolio companies.

[32] National Endowment for Science, Technology and the Arts (2009) 'From funding gaps to thin markets UK Government support for early-stage venture capital,' Research report: September 2009 available at https://www.strath.ac.uk/media/departments/huntercentre/research/researchreports/NESTA_Report_Thin_Markets.pdf (last viewed 17 July 2014).

# 5. Implications for government support of innovation

The contextual background set out in the previous sections is important in understanding how governments can and should influence the innovation economy in order to generate sustainable industries in Australia and high value jobs that are secure. In this section we narrowly focus on governments' involvement in R&D. In the following section, we address the factors that impede innovation and R&D from translating into these goals.

## 5.1. Aggregate levels of government support

Australia, broadly speaking, sits somewhere close to the average in respect of the proportion of its GDP spent on R&D, at 2.21%.[33] CSL's view is that Australia is seeking (and should seek) to establish an education and basic research environment that is towards the top end of the OECD spectrum. It should also encourage the development of a business sector that can derive value from it. On that basis, the Commonwealth Government should assess the benefits of greater government support, which would likely move Australia up the OECD rankings. While we do not advocate a particular level of government support for R&D or a target economy wide R&D intensity, the balance of the evidence suggests that increased government spending in this area will bring significant social benefits.

## 5.2. The R&D tax offsets

R&D tax offsets provide the primary means of government support for private sector R&D in Australia. The 40% offset, for which CSL is eligible, is a valuable source of support for CSL's Australian R&D, particularly in the area of new product development.

Government support for R&D should ideally meet the additionality requirement and should target areas that produce spillovers. It should not support R&D that firms would undertake without support. However, we recognise that most R&D produces some spillovers benefits, but these are typically smaller as the development moves close to market. The 45% refundable R&D tax offset for smaller firms and the 40 per cent non-refundable tax offset to larger firms represent a reasonable balance that avoids overly proscriptive definitions of the R&D activity.[34]

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[33] OECD (2011) *OECD Science, Technology and Industry Scoreboard 2011*. The figures for Australia were from 2008. The average share of GDP spent on R&D was 2.33%. Israel, Finland, Sweden, Korea, Japan, Denmark, Switzerland, United States, Germany, Austria and Iceland were ahead of Australia in the ranking.

[34] CSL believes that increasing the quantum of overseas expenditure eligible for the offsets would enhance the effectiveness of the concession by increasing incentives undertake later stage development and commercialisation from Australia. This is addressed in section 6.

### 5.2.1 Imputation credits

Australia has an imputation credit system that treats corporate tax as a pre-payment of personal tax. Hence, a person liable for personal tax in Australia who receives franked dividends from a firm that pays corporate tax in Australia can reduce their tax by the amount of the franking credits. While the effects on the cost of capital of the firm are complex, there is no doubt that imputation credits dilute the value of the R&D tax concession to listed Australian firms that make profits in Australia. In contrast, the dilution on foreign firms is much less and perhaps negligible.[35] The government has an opportunity to ensure Australian companies' shareholders receive the full benefit of the R&D tax concession by eliminating this dilution effect.

R&D undertaken by foreign firms in Australia generates spillovers,[36] so there is a legitimate case for government support for their R&D activities. However, CSL would not expect the R&D undertaken by foreign firms in Australia to be as likely to generate the same level of secure high skill, high wage jobs and industries in Australia because overseas firms are likely to move the IP offshore at an earlier stage of development.

## 5.3. Direct support for investments

Given the complexity of the effects of imputation credits on the value of R&D tax offsets, CSL does not recommend specific changes. However, CSL notes that dilution is problematic only for firms that make substantial Australian profits. For these firms, direct government support in the form of co-investment or support for specific investments may be an appropriate means of delivering enhanced benefits from Australia's innovation system.

In 2008 the Pharmaceutical Industry Strategy Group ('PISG'), chaired by the then CEO of CSL, recommended 'a strategic investment fund program that would provide Government co-investment in strategic industry projects that transition the industry to a sustainable position and deliver enduring net benefit to Australia.[37]

CSL has received substantial support from State and Commonwealth governments that are similar to the support arrangements recommended by PISG, for example the Biotechnology Manufacturing and Privigen (immunoglobulin) Manufacturing facilities at

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[35] For a more detailed exposition see CSL (April 2008) *Submission to the Review of the National Innovation System*.

[36] There is some evidence to suggest that spillovers from foreign R&D investment in a country are lower than those from domestic R&D investment, but CSL does not doubt that there are, nevertheless, positive spillovers. See, for example, Higon, 2007, 'The impact of R&D spillovers on UK manufacturing TFP: A dynamic panel approach', *Research Policy* 36(7) 964-979.

[37] *Pharmaceuticals Industry Strategy Group Final Report/December 2008* (Commonwealth of Australia 2009).

Broadmeadows and the Biopharmaceutical Formulation Centre at Parkville. Some of these projects were 'footloose' in the sense that CSL had options to locate them at overseas sites (discussed in more detail in the following section). Collectively, these facilities enhance the Melbourne biotech cluster with enhanced R&D, biological manufacture and enhanced regulatory compliance skills, all of which can be expected to deliver significant spillover benefits over and above the benefits that CSL itself derives from them.

### 5.3.1 A single point of reference

In CSL's view, these types of direct support mechanisms can deliver significant spillover benefits and are therefore appropriate avenues for governments. However, in CSL's experience they are excessively complex to argue and secure. In particular, in presenting the case for support for the Biotechnology Manufacturing Facility at Broadmeadows, CSL liaised with two levels of government, State and Commonwealth, and multiple departments at each level.

In contrast, in CSL's dealings with other governments, notably Ireland, Singapore and Swiss Cantons, there has typically been a single point of contact capable of managing the manifest complexities involved with securing assistance with major investment projects. CSL is Australia's largest biotechnology company with considerable knowledge of the workings of Australian governments, and by these means was able to secure support. CSL doubts whether foreign firms or smaller Australian firms could do so with such facility.

## 5.4. Growth in the provision of basic science

Australia is at the world forefront in a number of areas of research in biological and human health research. This expertise has developed in part as a result of State and Commonwealth Government funding of basic science through the university system and the research institutes.

Basic science gives rise to substantial spillovers, which can be inter-generational in nature. Accordingly, basic science is likely to be under-supplied in the absence of government support. On that basis, government expenditure targeted at basic science is likely to remain highly productive and should remain a priority. The primary value of basic science derives not from the commercial value of individual projects, but from the foundations it lays for future research.

### 5.4.1 Skilled scientists

The biotech sector relies upon Australian universities and medical research institutes for its skilled Australian workforce. CSL would therefore welcome funding models for university science and technology that ensure the sector has a rich source of highly qualified scientists and engineers for both research and the work force. We also believe that Australia benefits from Australian trained scientists working in overseas markets, particularly the US. Most

Australian scientists that work overseas choose to return to Australia at some stage in their career (often for family or lifestyle reasons), and return better trained and with valuable experience.

### 5.4.2 Access to IP and technology

CSL maintains its centre of excellence in early stage R&D in Australia in large part because of the high quality of IP that these institutions generate. By way of example, CAM3001 (GM-CSFR antibody), CSL362 (IL-3R antibody), CSL334 (IL-13R antibody), CSL324 (G-CSFR antibody), CSL346 (VEGFB antibody), P gingivalis vaccine and a number of discovery projects in CSL's R&D portfolio all emerged from Australia. CSL does not just benefit by acquiring patentable targets and molecules, but also from technologies independent of these such as new experimental processes and paradigms.

Continued and enhanced government support for Australian universities and medical research institutes would, in CSL's view, increase the supply of these essential inputs to biotechnology innovation, generating further knowledge spillovers, and further enhancing Australia's innovation system.

## 5.5. Translational research

CSL has previously identified[38] that Australia lacks resources and capability in translational research, and this inhibits the potential for Australia's health and medical research investment to be fully maximised.

Translational research includes: preclinical studies in relevant animal models of disease; *in vitro* and *ex vivo* studies using relevant tissues sampled from the target patient population; and toxicology studies, manufacturing and scale-up activities. They are fundamental steps before proof-of-concept studies can take place in patients. Translational research then extends into early stage human clinical trials. These R&D activities lie at the transition between the academic research sector and business R&D, but few of these translational activities currently occur within the academic research sector in Australia.

Because of the complexity and expense of translational activities through to proof-of-concept, many potentially valuable projects fail to attract the level of resource required to progress further. For example, at CSL we look at over 100 new product opportunities each year. Of these, we choose 5-10% for full evaluation and then fewer still for licensing. CSL has no doubt that greater government support for translational research would increase the pool of high quality projects, helping to address the 'thin market' problem described in section 4.3 above.

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[38] CSL (March 2012) *Submission to the McKeon Strategic Review of Health and Medical Research*.

There is further compelling rationale for supporting translational research. It occurs early in the R&D process and therefore delivers, in relative terms, larger knowledge spillovers than later stage development. These spillovers can be expected to be greater still if government support encourages them to take place in collaborative enterprise between the academic research community and biotech firms. CSL has suggested that the government, through the NHMRC, increase funding for this research through Translational Grants similar in form to the grants provided by the National Institute of Health ('NIH') in the US.[39]

Although basic research should remain largely government funded, and later stage commercial development should remain private, there are considerable benefits from close links between the scientists working in the two sectors. The Translational Grants assists with this by requiring that the translation research is undertaken with a credible industry partner.

From an Australian perspective, these initiatives will increase the likelihood that the large investments that governments make in tertiary education and basic research will translate into projects that can be taken through to market (or closer to market) by Australian firms, with all the concomitant benefits this would deliver including high skill, high wage jobs.

CSL notes the announcement of the new MRFF in the May 2014 budget and that it will be used to fund medical research priorities, including through payments to the National Health and Medical Research Council. CSL considers that, should the legislation pass, this could provide an effective mechanism for increasing support for translational research.

[39] *Ibid* at 6.

# 6. Australia as a location for commercial development

Section 5 set out mechanisms whereby governments could increase R&D undertaken in Australia in the biotechnology area particularly. While there are specific mechanisms that would deliver superior outcomes to the Australian economy, such as Translational Grants and support for small biotech firms in the translational research space, and there is a case for increasing the overall level of Australian support given that Australia ranks no higher than average in global terms, CSL does not advocate dramatic changes to government support for R&D. Subject to the foregoing considerations, these initiatives should ensure a robust and secure stream of biotechnology research capable of development into commercial products.

The terms of reference are framed in part in terms of high value industries in Australia, which connotes productive industries, making use of Australian innovations, exporting products and services to global markets. If Australia's biotechnology innovation earns royalties on 'invented here' but does not earn returns on 'made here' it will not secure the full range of benefits from its innovation system.

## 6.1. CSL's own experience with CSL627, CSL654, and CSL689

CSL's own experience with CSL627, CSL654, and CSL689, our three recombinant coagulation (clotting) products currently in development, illustrates the challenges that Australia faces in realising all the benefits from its innovation system. CSL went through a comprehensive evaluation of different locations for the large scale commercial manufacture and supply of these products, should they succeed through clinical trials. Australia was not preferred. There are a number of reasons for this: closeness to market; integration with CSL's global clinical support and commercial teams; the cost of skilled staff; available financial incentives; and Australia's uncompetitive tax system.

CSL's entrepreneurial model, in which IP is held at the manufacturing facility to provide the correct incentives for ongoing development and exploitation of the IP, has necessitated the license (on and arm's length basis) of the IP for these projects from Australia. The innovative effort that has taken place in Australia will be remunerated through an up-front payment, a series of milestone payments and a stream of royalties (should the products succeed to market). However, Australia will not secure the several hundred skilled staff that the manufacturing plant may eventually employ or, beyond appropriate royalties, the additional returns available from manufacture, commercialisation or further development of these products.

CSL is confident that State and Commonwealth governments would have been willing to support such a development in Australia. However, the reality is that the level of support needed to offset the operational and financial advantages available at other sites, but particularly the tax advantages, were untenable.

## 6.2. Manufacturing for global supply chains

CSL determined to expand its Privigen® manufacturing facility at Broadmeadows in order to increase supply in the face of growing global demand. This investment further cements CSL's Australian operations into its global supply chain. The entrepreneurial site for Privigen® is Bern in Switzerland, which has undertaken all the risky development of the process and product. The intellectual property in Privigen® was developed and is located in Bern, which bears the product market risk. Broadmeadows is, in effect, a lower value-added manufacturer of Privigen® making use of Bern's IP. This is reflected in the arm's length commercial arrangements.[40]

As the level of value added in manufacturing rises, for example by taking on entrepreneurial risk or earning a return on IP, so to do the profits that accrue to the manufacturing process. As a result, Australia becomes increasingly uncompetitive relative to locations such as Singapore, Ireland and Switzerland as the value added increases.[41]

In the pharmaceutical sector, Australia is likely to be more attractive in the lower value added aspects of manufacture, such as fill and finish, and less attractive for higher valued added aspects of manufacture, such as manufacture of active ingredients and/or development and exploitation of novel manufacturing processes. The lower value-added activities can nevertheless be of considerable value to Australia, helping to strengthen biotechnology clusters through the greater presence of complex manufacturing, through skilled employment, and through significant multiplier benefits to the broader community. In so far as this type of manufacturing is footloose, the level of support that might influence location is probably within the co-investment range contemplated by the PISG.

## 6.3. International competitiveness

In CSL's view, there are three main impediments to entrepreneurial manufacture: ease of access to government support; human capital and IR; and taxation.

### 6.3.1 Facilitation

CSL's experience in identifying potential locations for the manufacture of CSL627, CSL654, and CSL689 is that most jurisdictions, including Singapore, Ireland and

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[40] State and Commonwealth support was influential in attracting this footloose project, but was not the sole consideration. Other factors, such as the importance of diversifying sites of production were important considerations.

[41] There are examples of other medical companies that undertake high value added manufacturing in Australia, for example, Cochlear's manufacturing operations are primarily located in Australia. CSL also has high value added manufacturing in Australia, for example Intragam-P® and Fluvax®. However, in CSL's view firms would, today, be less likely to locate production for *new* innovative products in Australia.

Switzerland, provide sophisticated and tailored assistance packages through a single state agency. This makes the evaluation and comparison of potential sites for footloose manufacturing simpler. Australia, with its mix of responsibilities across levels of government and different departments, has no such equivalent. This does not obviously comport with the message that Australia is open for business.

### 6.3.2 Skills, capabilities and IR rules

In comparison with CSL's global sites in Switzerland, Germany and the US, CSL's Australian sites have higher operating costs driven, for the most part, by high wage rates and, particularly, inflexible labour rules. These are exacerbated by the high level of the AUD relative to the Euro and USD.

While Australia has a high level of skills in some biotechnology areas, notably R&D and some manufacturing processes, it is less well endowed with personnel with experience of global markets in areas such as FDA regulatory compliance and clinical support. In so far as CSL develops and commercialises products from Australia, it often has to rely on recruitment from the US and Europe to fill these critical roles. CSL does not expect this reliance on overseas skills to change in the short term. Continued ease of skilled migration is therefore important if Australia is to become a base from which to access global markets.

### 6.3.3 Taxation

Australia has a comparatively high corporate tax rate. As a result, there are large differences in the net present value of products if they are manufactured and commercialised from Australia as opposed to other jurisdictions with which Australia has tax treaties. Ireland, for example, has a 12.5% corporate tax rate; Singapore has a 17% tax rate but concessional rates and tax holidays are also available; and Switzerland has a range of effective tax rates available below the statutory rate of around 25% for limited periods, depending on canton and commune.[42]

CSL has previously endorsed Medicines Australia's recommendations that Australian governments should provide globally competitive incentives to encourage major investment by pharmaceutical companies in Australia, and that such incentives could include either lowering Australia's corporate tax rate or raising the level of tax credits available to companies conducting medical research in Australia.[43] However, in order for these to be effective in encouraging entrepreneurial pharmaceutical manufacture in Australia, they would need to be substantial. In CSL's view, there are other mechanisms that could be helpful in maximising the value of the innovation economy to Australia.

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[42] KPMG (2014) http://www.kpmg.com/global/en/services/tax/tax-tools-and-resources/pages/corporate-tax-rates-table.aspx (last viewed 17 July 2014).

[43] CSL (March 2012) *Submission to the McKeon Strategic Review of Health and Medical Research* at 4.

## 6.4. Patent boxes

The problem of attracting investment into R&D, and the concomitant footloose investment in development, manufacture and exploitation of IP from a host country, is not unique to Australia. This is particularly problematic in countries which appear to have a substantial investment in basic research and early stage R&D, but then fail to reap the full benefits from development, manufacture and exploitation.

One response to this problem has been the emergence of so-called 'patent boxes'[44] under which profits earned from the exploitation of patents and related IP are taxed at a concessional rate. The UK scheme came into effect in April 2013, phasing in a concessional corporate tax rate of 10% over a four year period. It appears to have had some early success; for example, GlaxoSmithKline alone has relocated GBP700 million worth of R&D to the UK and patent registrations by German companies in the UK have increased by 27%.[45]

Patent boxes have become widespread, including in a number of OECD countries which otherwise have tax systems that are comparable to Australia. Most of the larger countries who have implemented patent box policies (UK, Netherlands, Belgium and Spain) have relatively broad definitions of IP (not just IP defined through patents), but require IP to be self-developed (or at least further developed), excluding acquired IP. They typically apply the concessional rate to embedded licence income from internal use of IP. These features make the policies more likely to attract both real activities and IP related incomes. Conversely, countries with smaller innovation bases (Cyprus, Hungary, Malta and the Swiss Canton of Nidwalden) have implemented patent box policies designed to attract IP income without requiring any original R&D activity or the real activities associated with IP exploitation.

The sequential adoption of patent boxes across Europe suggests that countries are using these policies to compete for shares of the global pool of innovation-related activities and income[46] which is likely to see redistribution rather than an increase in the amount of R&D.[47] Increasing inter-country competition is likely to erode the benefits that early adopters have achieved. Nevertheless, the trend appears to be continuing; Portugal has

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[44] So named "because there is a box to tick on the tax form".

[45] Freshfields. (2013). UK patent box: EU decision deferred. http://www.freshfields.com/uploadedFiles/SiteWide/Knowledge/UK%20patent%20box%20-%20EU%20decision%20deferred.pdf (last accessed 7 July 2014).

[46] Evers, L., Miller, H. and Spengal, C. (2013). Intellectual Property Box Regimes: Effective Tax Rates and Tax Policy Considerations. http://ftp.zew.de/pub/zew-docs/dp/dp13070.pdf (last accessed 8 July 2014).

[47] *Op cit* Wilson (2005).

announced plans to introduce an IP box,[48] the approach has been proposed under the forthcoming Swiss tax reforms, and in the United States legislation to introduce a patent box has been introduced.[49]

It is beyond the scope of this submission to comprehensively review the various patent boxes that have emerged in recent years. However, it is clear that they are resulting in substantially reduced corporate tax rates on exploitation of patents and redistribution of where value added exploitation of IP takes place. In the face of this international trend, it seems clear that Australia is unlikely to reap the rewards of its innovation investment, to develop high skill, high wage jobs and industries in Australia, if it does not introduce a similar type of initiative. The challenge is to design a system that confines the concessional corporate tax rates to genuinely new investment that is based on intellectual property that has been substantially developed and remains owned in Australia.

### 6.5. Tax offsets for R&D conducted overseas

For the reasons presented in section 5.2 above, Commonwealth tax offsets are effective at increasing private sector R&D in the face of knowledge spillovers from which the private firms cannot benefit. Overseas expenditure is only eligible for this concession if, amongst other things, the expenditure on the overseas activities is less than the expenditure on the related R&D activities conducted in Australia.

The reality of biopharmaceutical development is that late stage clinical development (especially phase 3), which is the most costly stage of development, must largely take place in the target markets. There are two reasons for this: the experience gained by clinicians and centres involved in phase 3 clinical trials is enormously important in ensuring market acceptance of product should it succeed; and,it also assists with the regulatory processes in the target markets if clinical trials take place in that market. This means that clinical trials must take place in the US and EU, although not to the exclusion of Australia. The resultant expenditure is typically ineligible for the tax concession.

This R&D no doubt results in some knowledge spillovers, but some will inevitably accrue in the overseas market where the clinical trials are undertaken rather than in Australia. Foreign spillovers are not a sound basis for Australian government support. Nevertheless, Australia would benefit if more of this expenditure was eligible, provided the IP related to the product being trialled is held in Australia at the time. The benefits would derive from stronger incentives to maintain IP in Australia, and to take products closer to market from an Australian base, thereby enhancing the value of the IP to the Australian economy. In

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[48] KPMG. (2013). Tax News Flash September 2013, Portugal Tax Update, Corporate Income Tax 2014: https://www.kpmg.com/Global/en/IssuesAndInsights/ArticlesPublications/taxnewsflash/Documents/portugal-sept13-2013.pdf (last accessed 8 July 2014).

[49] *Op cit* Evers, L., Miller, H. and Spengal, C. (2013).

general, the longer the IP is held and developed in Australia, the greater the value it will deliver to Australia.

CSL would expect an extension of the overseas expenditure allowance to be tied to a clear demonstration that it will deliver value to Australia. The concession might, therefore, be confined to those firms that domicile their intellectual property in Australia at the time of development.[50] If the IP is owned in Australia, current Australian tax rules will ensure that Australia will receive appropriate compensation for any commercialisation of that IP.

[50] If, as may often occur, the IP is subsequently purchased by a foreign entity for development offshore, Australia can expect to benefit through the sale price and royalties that arise from that purchase.

## 7. Conclusions

The matter of Australia's innovation system was referred to the Economics References Committee for inquiry on 18 March 2014, framed in the context of 'the challenges to Australian industries and jobs posed by increasing global competition in innovation, science, engineering, research and education'. Based on the foregoing, CSL makes the following observations in respect of the terms of reference for the inquiry, from its perspective as an Australia based global biotechnology company.

***A. The need to attract new investment in innovation to secure high skill, high wage jobs and industries in Australia, as well as the role of public policy in nurturing a culture of innovation and a healthy innovation ecosystem.***

Australia is a relatively unattractive location for entrepreneurial manufacturing or as a base from which to commercialise locally developed intellectual property ('IP') into global markets. CSL is not saying that Australia is unsuitable as an entrepreneurial manufacturing location – indeed we have several significant operations in this country. The observation is a comparative one, based on CSL's direct experiences and observations as a global corporation. This is principally a function of Australia's uncompetitive corporate tax system, but is exacerbated by declining access to some important specialised skills, high overall labour costs, location, terms of trade (resulting in a sustained strong currency) and the complexities of dealing with Australia's system of government and regulation.

Australia will find it difficult to secure this economic growth unless it is willing to emulate some of the policies of other sovereign nations. Australia should learn from those who have been successful in attracting entrepreneurial investment, such as Ireland, Singapore, the UK and Switzerland. CSL observes that Australia's competitors are increasingly offering concessional tax treatment for the development and commercialisation of IP through so called 'patent boxes'. The patent box recently adopted in the UK is a notable example. CSL envisages that a similar scheme in Australia would offer the prospect of narrow and targeted support for genuine IP development and its follow-on, new entrepreneurial manufacturing, both of which would stay in Australia and drive economic growth.

Direct support can be helpful in attracting important R&D infrastructure to Australia that can strengthened Australia's innovation system, delivering benefits to the wider medical research and biotechnology communities. There are also opportunities to develop manufacturing which makes use of existing know how or IP, for example in extending existing global manufacturing at new sites. If these investments take place in Australia, they can help embed Australia more securely into global supply chains. While these investments might not add as much value as new entrepreneurial manufacturing, they can nevertheless deliver secure high skilled jobs and significant multiplier benefits

to the broader community. Government help can be instrumental in securing these types of projects.

## B. *The Australian Government's approach to innovation, especially with respect to the funding of education and research, the allocation of investment in industries, and the maintenance of capabilities across the economy.*

Australian governments' expenditure on basic science is likely to remain highly productive and should remain a priority. Although Australia is currently a relatively unattractive location for entrepreneurial manufacturing, it is at the world forefront in a number of areas of basic research in biological science and human health. This expertise has developed in part as a result of State and Commonwealth Government funding of basic science through the university system and research institutes over many years.

This type of basic science gives rise to substantial knowledge 'spillovers,' which can be inter-generational in nature. These spillovers mean that the benefits of the basic science extend far beyond those involved in the research itself, into many other spheres. Private companies would not normally be willing to invest in this type of basic research because they would not expect to make any immediate commercial returns from it. As a result, the private sector will (in aggregate) invest less in basic research than is socially optimal. Accordingly, basic science would be under-supplied if left to the private sector without government support. Australian governments' expenditure in this area should therefore remain a priority.

Australian universities and research institutes are central to Australia's biotechnology ecosystem. They are located at the heart of the developing Australian clusters such as the biotechnology hub in Melbourne. They provide an environment in which scientists are trained either for research or the workforce. They attract eminent scientists to the clusters, bring with them important skills and experience. And the researchers who develop through these institutions generate the early IP that larger firms can go on to commercialise.

CSL maintains its centre of excellence in early stage R&D in Australia in large part because of this ecosystem and the high quality of IP that it generates. This is not simply prospective new patentable targets and molecules, but also technologies independent of these such as new experimental processes and paradigms. CSL also relies upon the Australian universities and medical research institutes for its skilled Australian workforce.

CSL would welcome further government support for university science and technology and the research institutes in order to increase the supply of these essential cornerstones to the sector: knowledge spillovers; IP that can be developed into

commercial products; and a large pool of highly skilled scientists and researchers entering the workforce.

The Commonwealth tax concession is a valuable source of support for Australian R&D, particularly in the area of new product development. CSL understands that the 45% tax offset available to smaller firms is similarly valuable. CSL's view, which is widely echoed in the economic literature, is that private sector R&D also produces knowledge spillovers, if perhaps fewer than basic research. Accordingly, there is a strong rationale for government support of business R&D, and CSL believes this is best delivered through the tax concession.

The reality of biopharmaceutical development is that late stage clinical development, the most costly R&D stage, has to take place in overseas markets (particularly the US and EU), even if the products are developed in Australia. In CSL's view, Australia would benefit if more of this overseas R&D was eligible for the tax offset, provided that the IP related to the product being trialled is held in Australia at the time. This would tend to prolong the amount of development that takes place in Australia, thereby increasing the likely returns to the Australian economy.

CSL notes that Australia sits, broadly speaking, somewhere close to the average of OECD countries in respect of the proportion of its GDP spent on R&D. Although CSL does not suggest a particular economy-wide target for the level of R&D, if Australia is to attract new investment in innovation to secure high skill, high wage jobs and industries, the proportion of its GDP spent on R&D will need to increase. This will require increased contributions from government that, in turn, stimulate higher R&D expenditure from business.

### C. *The importance of translating research output into social and economic benefits for Australians, and mechanisms by which it can be promoted.*

Australia lacks resources and capabilities in translational research that would complement its high quality basic research base. The level of translational research in Australia is inadequate given the high quality of our scientific community and basic research.

There is a compelling rationale for further support in this area beyond CSL's private interests. Translational research occurs in the early stages of the R&D process and therefore delivers, in relative terms, larger knowledge spillovers than later stage developments. Furthermore, this component of the R&D process benefits from close collaboration between academia and business, further enhancing these benefits.

CSL recommends that the government, through the NHMRC, increase funding of this research through Translational Grants similar in form to the grants provided by the NIH in the US. CSL notes the announcement of the new MRFF in the May 2014

budget and that it will be used to fund medical research priorities, including through payments to the National Health and Medical Research Council. CSL considers that, should the legislation pass, this could provide an effective mechanism for increasing support for translational research.

Furthermore, there is a strong case for further government intervention to support small biotechnology firms, particularly when the support enables more of these firms to develop their IP to the proof of concept stage. Understanding the nature of the market failure that limits investment in small, early stage technology firms is important in designing the best form of support.

### *D. The relationship between advanced manufacturing and a dynamic innovation culture.*

CSL's operating paradigm, which has been in place now for many years, establishes manufacturing sites as entrepreneurial centres that hold the IP alongside the manufacturing and R&D resources necessary to maximise commercial value. In CSL's view, the model is commercially efficient, and is based on the premise that there is a strong relationship between advanced manufacturing and a dynamic innovation culture at the level of the firm.

At a broader level, technology clusters demonstrate the relationship between advanced manufacturing and a dynamic innovation culture. Technology clusters agglomerate a critical mass of know how across the range of activities needed for the development and commercialisation of innovative products. Hence typically, they arise around universities (which generate basic research and skills), they contain one or more large companies with manufacturing capabilities and commercial reach, capable of resourcing the most expensive elements of the development process, and a large number of smaller companies that both generate IP and support the activities of the other cluster members.

In the biotechnology sector, government support is often instrumental in securing infrastructure and strategic assets on which a cluster is based.

### *E. Current policies, funding and procedures of Australia's publicly-funded research agencies, universities, and other actors in the innovation system.*

CSL has made some specific recommendations concerning funding of translation research through the NHMRC. CSL is supportive of high levels of government investment in tertiary education, basic research and the research institutes, but makes no other observations on this issue.

### *F. Potential governance and funding models for Australia's research infrastructure and agencies, and policy options to diversify science and research financing.*

CSL makes no observations on this issue.

***G. The effectiveness of mechanisms within Australian universities and industry for developing research pathways, particularly in regards to early and mid-career researchers.***

CSL makes no observations on this issue.

***H. Policy actions to attract, train and retain a healthy research and innovation workforce.***

CSL makes no observations on this issue.

***I. Policy actions to ensure strategic international engagement in science, research and innovation.***

CSL makes no observations on this issue.

***J. Policy options to create a seamless innovation pipeline, including support for emerging industries, with a view to identifying key areas of future competitive advantage.***

Australia is at the world forefront in a number of areas of basic research in biological sciences and human health. Australia also has a sophisticated health system, quality universities and quality research institutes. For these reasons, CSL maintains its global centre of excellence in early stage R&D in Australia. In CSL's view, these elements are an important source of competitive advantage for Australia.

If Australia is to create a seamless innovation pipeline from this, it must first and foremost become an attractive site, by global standards, for entrepreneurial investment.

## Submission details


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