absorb the current excess capacity, and by the time any proposed Australian facility comes on line, capacity will again be close to full utilisation. Note that aggregate biopharma capacity figures can be misleading due to the large proportion of fermenter volume which is dedicated to in-house use, and therefore unavailable to service the contract demand sector.

3.2.2 Mammalian Cell-Based Biomanufacturing

a. Mammalian Cell-Based Biomanufacturing - Demand Side Overview

- Potential customers for a new mammalian cell scale-up facility fall into two groups. One group is represented by drug developers who already possess in-house mammalian capability. The other group comprises companies whose business model does not contemplate any in-house production. This latter group typically includes start-up drug developers whose primary asset is IP and molecules at the proof-of-concept stage (lead compound).
- Of the Bio Plan 2005[4] survey group, 41% of biotherapeutic manufacturers (all types of expression) were already outsourcing some mammalian production. Further, the study reported that 62% of all biotherapeutic manufacturers expect to be outsourcing some production within 5 years (up from 47% in their 2003 survey). Of companies currently producing in mammalian culture, 54% indicated an expectation to be outsourcing some mammalian work by 2010.

b. Driving Forces-Demand for Mammalian Cell-Based Biomanufacturing

- Mammalian cells are increasingly being chosen as the preferred host/vector vehicle for expression.
- Monoclonal antibodies must be made using mammalian cells, and such antibody-based strategies are being used for cell therapies for cancer and other diseases. Antibodies are also the mainstay of the diagnostic kit.
- For human health applications, mammalian cells are preferred in many cases because of the need for appropriate glycosylation (post-translational carbohydrate substitutions) for efficacy and to minimise likelihood of immunological (allergic) reactions.

c. Mammalian Cell-Based Biomanufacturing - Supply Side Overview

- Leading CMOs such as Lonza, DSM and Diosynth typically offer both microbial and mammalian cell capacity.
- Those CMOs which have evolved with predominantly microbial capacity, [redacted], are unable to participate in the more lucrative end of the biomedical therapeutic market which is the fastest growing sector.

d. ***Driving Forces - Supply of Mammalian Cell-Based Biomanufacturing***

- Mammalian cells are a costly way to generate recombinant proteins compared with use of bacterial cells as the host/vector system. Eukaryotic cells are not as robust and cannot be grown to high cell densities under the conditions of high shear agitation and high aeration which are necessary in high productivity bacterial systems. Furthermore, the media for mammalian cell cultivation are often complex, with many expensive and labile constituents. This means that the price quotations from CMOs to prospective mammalian cell based clients are high.
- Mammalian cells require more technical know-how and are more susceptible to failure than microbial fermentation. The internal know-how developed within the CMO is therefore more difficult to replicate in the hands of new starters into the biotherapeutic arena, and therefore represents a driving force to outsource production.

3.3 Canadian Capability Review

3.3.1 Industry overview

A recent report has shown that Canada's biotechnology industry has remained stable throughout 2004[2], with the number of private and public Canadian biotechnology firms steady at 472 (390 private and 82 public), compared with 470 in 2003. Canada is second only to the USA in absolute biotechnology company numbers. Public company revenues increased 21% and net losses dropped 30%. However, Canadian biotechnology market caps dropped from C$13.8 billion in 2003 to C$13.7 billion in 2004, despite an 8% increase in the Canadian exchange rate during 2004. Canada has a robust and growing product pipeline. In 2004, 15 products entered phase 3 trials, 25 compounds entered phase 2 trials and several others were approved for sale[2].

Canada's research continued to be completed at a significant cost advantage in comparison to the rest of the world over 2004, with two reports showing significant cost advantages for completing research and clinical trials in Canada. One report, commissioned by Industry Canada showed that Canada had a cost advantage compared to the USA of between 30 and 45% over two trials for cancer therapeutics and one trial for an implanted orthopaedic device[27]. In addition, the recent 2004 KPMG study of comparative business costs ranked Canada as the leading cost competitive industrial country for the fourth consecutive year. The report ranked Canada as the most cost competitive country for pharmaceutical manufacturing and biomedical research and development, just ahead of Australia in second place [28] .

3.3.2 Bio-processing

Late in 2004, the national Canadian bio-processing initiative was announced after two years of planning. Under the initiative, the Canadian Centre for Bio-processing recommended a C$450 million investment be made in bio-processing over seven years to build capacity and skills and cement Canada's leading position in the biopharmaceutical industry. It is hoped that this will allow Canada to further capitalise on the C$15billion they have already spent on developing their biopharmaceutical product pipeline. It is estimated that in excess of 80% of the Canadian biopharmaceutical pipeline will require small-scale capacity production by 2010[29]. Prior to this announcement, a feasibility study was conducted to assess the need in Canada for a pilot plant manufacturing facility. Findings from the study indicated that a pilot plant capable of scaling up to phase 1/2 clinical trials requiring less than 5kg of protein, utilising mammalian and/or bacterial fermentation, would be utilised by approximately 65% of respondents[30].

3.4 German Capability Review

3.4.1 Industry Overview

The German biotechnology industry is beginning to mature and companies are starting to bring their first products to market and report their first sales revenues(31). Germany leads Europe in the number of biotechnology companies with 330 private and 11 public companies in 2004 and follows only the USA and Canada worldwide(32). Including all biotechnology related companies, this number jumps to 615 companies(33). More than 90% of the identified biotechnology companies are active in drug development, diagnostics or drug delivery. Germany is a leading producer and exporter of pharmaceutical and chemical products. In 2001 for example, it was reported that Germany exported pharmaceuticals worth 14.8 billion pounds, more than Switzerland, the US and the UK(34). Despite the high levels of pharmaceutical manufacturing, Germany has only been ranked 10th in terms of cost advantage for pharmaceutical production and biomedical R&D as compared to the rest of the world (35).

At the conclusion of 2003, there were approximately 177 products in development by German biotechnology companies, of which 60 were in clinical development(36). Approximately 25% of all therapeutics being developed are targeting cancer. The number of products going into development is continuing to increase(31) . German biotechnology offers a unique opportunity for partnership formation due to the immaturity of the sales and marketing departments in young biotechnology companies. More than half of the 30 products being launched into the market for 2004 had biotechnology origins (31).

3.4.2 Bio-processing

The German government is keen to attract bio-pharmaceutical manufacturing capability to the country by recruiting biomedical research firms and manufacturing plants from other countries. The German government is currently offering firms incentives to build or expand bio-manufacturing facilities in Germany. Some recent firm recruitments and expansions include:

- Roche Diagnostics announced in June 2004 that it was investing 300 million pounds in new production facilities for recombinant antibodies, in Penzberg, south of Munich, which is Europe's largest biotechnology production facility. Roche also announced plans for the construction of a similar facility in Basel (37).
- Boehringer Ingelheim Biopharmaceuticals expanded their new plant in Biberach with a US$316 million investment. The plant expansion involved installation of 12 15,000L mammalian cell reactors in September 2003 (38).
- EMD pharmaceuticals have committed to build a US$300 million dollar plant in Jena Germany after Germany made a bid including the offer to pay 30% of the building costs (39).

3.5 New Zealand capability review

New Zealand's Biotechnology industry is one of the fastest growing biotechnology industries in the world(44). Its biotechnology sector currently consists of 76 core biotechnology companies of which six are public(13). The profile of New Zealand biotechnology is gradually shifting more strongly towards human therapeutics. The share of human therapeutics companies continued to increase over 2004-2005, to 29% of the biotechnology industry. A further 5% of the biotech industry is developing diagnostics. For 2004, the biotechnology income in New Zealand was valued at NZ$675 million and expenditure was valued at NZ$430 million(45).

In 2002, a biotechnology taskforce was established by the New Zealand government to assist in boosting New Zealand's biotechnology development and international competitiveness. The taskforce issued a series of recommendations for the industry in 2003 to be carried out over a ten year period. Key recommendations for the industry included tripling the number of organizations involved in biotech to more than 1000, increasing biotechnology employment four fold to 18,000 and increasing the number of core biotechnology companies to more than 200(40). The New Zealand government subsequently released its "New Zealand Biotechnology Strategy" supporting the vision of the task-force for developing biotechnology.

New Zealand government support for biotechnology has continued to grow with an increase in funding over the past 3 years to NZ$170 million(47). In addition, through the Australia New Zealand Biotechnology Partnership Fund, $12 million dollars has been allocated to facilitate and accelerate trans-Tasman collaborations. The fund is to be distributed by 30 June 2007. In March 2005, an announcement was made that $6.76 million dollars had been allocated to four New Zealand companies to assist them with developing their biotechnology products. Recipients include Neuren Pharmaceuticals Proacta Pharmaceuticals, Industrial Research Limited, and Wrightson (47).

3.6 Australian Capability Review

In this section of the report, the Australian situation is positioned within the global context described in the preceding chapter.

The broader biotherapeutics issues are canvassed first, before looking in more detail at the Australian scene insofar as mammalian cell-based supply and demand is concerned. Again the reader is referred to Appendix 1 for a more detailed review of the driving forces affecting not only the local scene but also the global environment.

3.6.1 Australian Biomanufacturing – General

The bullish sector outlook reported for the global biotech industry is also reflected in the Australian industry figures for 2004, although major distortions were introduced by one-off events, principally associated with the absorption of ZLB Bioplasma into CSL. Revenues rose from US$980.6M in 2003 to US $1,472.5M in 2004. Similarly inflated growth was seen in the rises in R&D spend (increasing 25% to US$177.2M*) and employee count from 6,390 to 10,260. After adjustment for extraordinaries, the industry revenue growth was a more subdued 10%(2).

Australian governments, State and Federal, have invested heavily in growing the R&D base and intellectual capital required to sustain a world-class drug discovery "engine". Governments have also recognised the need to support the transition from R&D into commercial development, with many grant schemes, science parks, institutes and biomedical incubators.

In the case of therapeutic drug development, governments have also recognised the need to link fundamental and applied research with clinical research, pharmacokinetic capability (eg. Tetra-Q, Victorian Pharmacy College) as well as to clinical trial capability (eg. Clinical Trials Victoria, Queensland Clinical Trials Network, Q-Pharm, Cmax(a division of IDT Ltd)). This linkage strategy seeks to create and support an integrated chain of capabilities offering the full range of services necessary for accelerating drug development from discovery right through to commercialisation.

For the Australian drug development pipeline to deliver the best outcomes for the country, the clinical development process must be linked to facilities for scaling-up production of new biological drugs to the exacting standards required by codes of Good Manufacturing Practice (GMP). Ideally such specialist facilities should be available on a contract basis to service the needs of early stage companies whose business model does not contemplate manufacturing.

* The estimate from Ernst and Young (2) appears to be low but has been accurately quoted above. Anecdotal industry estimates suggest the figure should be much larger. The absolute value is not pivotal to the discussion; rather that the trend is rising and supporting the overall position.

There have been at least four recent Australian studies, which have addressed the supply and demand for biopharmaceutical manufacturing scale up and production, including mammalian cell-based manufacturing, in Australia [9][10][11][12]. These studies have since been updated and are reviewed in this report to provide a current picture of biomanufacturing and mammalian cell expression systems in Australia.

Several of the earlier studies identified a rising demand for pre-clinical and clinical quantities of drug candidates; demand fuelled in part by a larger number of active companies, a more vigorous research environment, and an increasing trend for Australian firms to perform development further down the clinical trials pathway in order to increase company value.

These surveys also concluded, however, that the market demand in Australia at that time would not wholly support an entirely domestic CMO operation, and any that prospective manufacturers wishing to produce GMP-certified molecules on a contract basis would need to market internationally in order to be profitable.

3.6.2 Australian Biomanufacturing - Demand Side

Table 3 - Products in Development in Australia Requiring Mammalian Cell Culture

Drug Category Number	Discovery	Develop-ment	Preclin	Phase 1	Phase 2	Phase 3	Clinical Trials*	Grand Total
Recombinant Protein	2		13	1	1			17
Recombinant Vaccine	0		1	1	2	1		5
Therapeutic Antibody	13		5					18
Diagnostic Antibody	2	13					4	19
Grand Total	17	13	19	2	3	1	4	59

Source : Innovation Dynamics Pty Ltd proprietary database

** Diagnostics in clinical trials are not required to undertake the 3 Phase drug approval process*

From Innovation Dynamic's surveys of Australian companies, of approximately 410 therapeutic or related products currently in formal development (from identified lead compounds to late stage clinical trials) in Australia, there are currently 59 compounds (14%) that are understood to be produced by mammalian cell culture. Table 3 is a summary of this demand and Appendix 4 provides a list of companies with products in development.

This data is consistent with earlier surveys indicating a strong potential demand for biopharma production capability in general, and for future mammalian cell capacity. The latest figures show a large increase in compounds in development over the previous survey in 2004 (305 compounds). The table includes diagnostic antibodies,

and most of the newly listed compounds are early in development. Innovation Dynamics concluded that this represents both an increase in compounds identified as lead compounds (companies are bringing more compounds forward) as well as additional compounds that were missed in the earlier survey. Since all of these compounds are associated with companies (rather than with research institutions (see below)) this figure of products in discovery are conservative.

This survey indicates 6 mammalian derived therapeutics are in clinical trials in Australia. Of these, two are in Phase 1, three are in Phase 2 and one, by CSL, is in Phase 3. Given their stage of development with the manufacturing decisions already made, these compounds would not contribute to the demand for a new facility.

Companies have a choice of expression system for the manufacture of compounds and it is not possible to identify very early in development which products will be produced in mammalian, bacterial or other production systems. This is especially so for products in discovery, since, prior to formal preclinical studies, the decision on route to manufacturing may not have been finalised. However, it is likely that the majority of protein products and possibly some large peptides requiring activity in humans will need mammalian expression systems in order to ensure correct protein folding etc.

It has been assumed that all monoclonal antibodies will be produced in mammalian systems and that therapeutic antibodies, numbering 18 in development now, represent a major product class for which any proposed facility will be used. Single chain or domain antibodies may be produced in either bacterial or mammalian culture system. Australia has a large number of research groups using and developing monoclonal antibodies. Most of these are reagents and tools for research and will not become products but some may find application in diagnostic kits and in some cases therapeutics.

Monoclonal antibodies used for *in vitro* diagnostics are manufactured using mammalian cell culture and, in the Australian market, in licensed facilities that comply with GMP. However the amounts produced are generally small (tens of grams) and do not require the same regulatory compliance as therapeutic products. Therefore, although this represents a relatively large number of products in development, the amount of product is small and may not contribute significantly to the manufacturing throughput in a new facility aimed at larger GMP compliant therapeutic products. Production is currently catered for through existing facilities and contractors (see below).

Peptides are not included in this analysis since they are typically manufactured by solid or liquid phase synthetic chemistry procedures. Longer peptides (composed of more than 40-50 naturally occurring amino acids), such as some hormones, may be produced by recombinant expression and fermentation either in bacterial or mammalian systems. Other products from mammalian cells may conceivably require fermentation such as whole cells, lipids and carbohydrates. In particular stem cell expansion for whole cell therapies is expected to become a major user of mammalian cell culture, but the scale will be relatively small.

Mammalian cell research in not-for-profit organisations

Work in non-profit and academic institutions is difficult to identify and quantify, and clearly will fall in the discovery, or "lead seeking" category. However, it is of interest to gain a broad understanding of the extent of effort focused on mammalian cells, since this represents the next generation of commercial prospects. If the demand

which is forecast from the survey of companies is to be sustained, there needs to be evidence of substantial momentum emanating from research institutions.

An effort was made as part of this report to identify institutes known to have active research programs involving mammalian cell culture. Contact was made with UniQuest (P.Divine), CSIRO (G.Lovrecz), AusBiotech, BioInnovation SA, Bio21 and others to assemble an idea of overall activity.

In Victoria, Melbourne University (Department of Microbiology and Immunology) is reported to have several projects involving monoclonal antibodies, and 1-2 using mammalian cells for protein production. At Monash University, up to 5 monoclonal-based projects are understood to be active. Once laboratory refurbishments are complete, the Austin Research Institute is thought to have mammalian projects of interest. The Ludwig Institute has significant experience in development and scale-up of mammalian cell-based products and commissions overseas CMO work on a regular basis (refer also 3.6.3, 4.2 below).

In South Australia there appears to be considerable activity, [redacted]

Current mammalian cell activity at Queensland University appears limited to the group headed by Professor David James, which operates as a Contract Research Organisation (CRO). Professor James has an international reputation in mammalian cell line development, and currently has Lonza amongst his clients. Once the AIBN is completed in 2006, it is expected that there will be an increased number of projects involving mammalian cell expression.

Future pipeline

It has been estimated that 60-90% of early-stage products (leads) will proceed to preclinical studies[23] [24], and about 70-80% of these move into Phase 1 clinical trials[6] [25] with 50-90% of these proceeding to Phase 2 [24] [25]. The rate of success in moving from Phase 2 to Phase 3 is 90-93% [24] [25]. The success rate out of Phase 3 is 50%[6]. By applying the relevant drug candidate survival rates to the actual numbers from the survey (Table 3), then multiplying by the assumed "CMO project value" for each step in the clinical process (Table 4), some rough projections as to potential value can be derived (refer section 5.2.1 "Confirmation of Australian Demand").

Since all of the compounds listed above are associated with companies (rather than with research institutions) this figure of products in discovery is an underestimate. If, for instance, there is double this number of compounds in discovery, there could be about 15-30 compounds between preclinical and Phase 3 clinical studies requiring mammalian cell culture manufacturing in future.

On the other hand, many factors can work to potentially reduce the number of compounds that would be captured for manufacture in a new Australian facility. These include alliances that client companies may have with overseas partners which predetermine manufacturing rights, lack of confidence in ability to meet particular regulatory compliances, and the need to carry out processes or at scales not offered by the facility. Other Australian or regional facilities will also compete for projects.

From this analysis of the products in development, and from an earlier survey(11) many researchers and companies require only milligram to low gram amounts of biological product in their early studies, and have generally manufactured their product in-house. Their mammalian culture systems were considered unable to generate the amounts required , nor under required standards of GMP, and 88% of survey respondents said that they would have to consider out-sourcing their scale-up requirements by means of contract manufacture, licensing or partnership. Nearly half of the survey group of 34 research institutes and development companies identified lack of suitable local CMO scale-up facilities as a major hurdle facing their organisation.

For the continued supply of products necessary to support a manufacturing facility it is clear that attracting drug developers when at the lead compound stage is vital, and would be needed to underpin the long-term survival of the facility.

Availability of funding has been identified as a significant limiting factor on local firms moving to later stages of development, hence reducing potential CMO demand. This theme was picked up at the industry level via the Pharmaceuticals Industry Action Agenda, who reported to government that lack of local biopharmaceutical manufacturing facilities represented an impediment to industry development. The recommendations of the industry group included that government should support the establishment of a scale-up mammalian cell facility which would provide a CMO service to drug developers

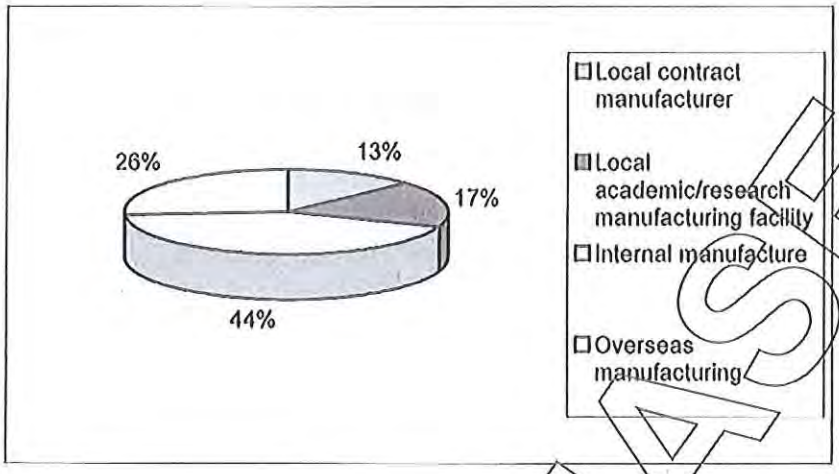
The growth in demand for local mammalian cell culture biomanufacturing arising from current Australian research will depend on the rate of new product discovery and the transfer of the technology to drug development companies here (as distinct from licensing to oversees companies who will manufacture elsewhere). This transfer is also affected by many factors, including the success rate with proof of concept and preliminary animal studies, and access to sufficient funds to conduct the clinical trials in man. Other factors include the ability to find suitable providers of the necessary skills in formulation, toxicology, and other specialist services.

3.6.3 Australian Biomanufacturing - Supply Side

Sources of current manufacturing

From the survey of respondents developing biopharmaceutical products using mammalian cell expression (Table 3) the location of current manufacturing services was identified for seventeen companies (out of 25). These are summarised in Figure 1 below. Some of respondents use a mixture of in-house, local and overseas suppliers.

Figure 1. Mammalian cell manufacturing by facility location. (n=17)



Source : Innovation Dynamics Pty Ltd survey.

The biotherapeutic capabilities of some prominent Australian contract manufacturing organisations are briefly reviewed below.

Bresagen

South Australian company Bresagen offers prokaryotic (bacterial) fermentation and downstream purification services, as well as making its own products (equine growth hormone and new biogenerics). It is probably the best regarded company in Australia for bacterial host/vector construction and protein purification know-how. This expertise has been developed in association with its in-house growth hormone products from *E.coli*.

Bresagen has recently signalled intent to install 10 litre mammalian capacity, with aseptic liquid fill also in the planning stages. The 10 litre fermenter will be fully dedicated to a single project (Psiron Ltd); hence there will be no surplus capacity for other potential clients. However, Bresagen also has conceptual plans for extensions to the building which could include additional GMP suites.

The facility is new and state-of-the art, and was designed with FDA-level GMP compliance in mind. It has been producing API and clinical batches, but can be readily upgraded to produce aseptically-filled liquids in finished dosage form. The facility was also designed for future installation of mammalian fermentation capability (now proceeding, as mentioned above).

[redacted] Bresagen is ≈ 40% owned by Cbio, who acquired its interest in order to facilitate the clinical development of its therapeutic protein Cpn10.

[redacted]

CSL

The R&D group at Parkville has two containment facilities which perform small-scale bacterial fermentation and downstream purification for in-house projects. [redacted]

Recently CSL has announced its intention to install 5 litre, 50 litre and 500 litre mammalian cell fermenters to service in-house clinical development projects to Phase 2 stage. The equipment will be installed in the newest of the contained R&D buildings. This decision was made following a review of 8 overseas CMO options, with quotations received in the range [redacted] for a nominal 400gm antibody. Target for completion of the new facility is by end 2006.

Another recent development is approval of a new bioformulation facility, a project worth some A$6.6M. [redacted]
The targeted completion date is end 2007 and comprises an extension wing to the existing R&D building. The facility will have two aseptic fill lines, one dedicated to CSL's use; the other will be available for industry on a contract basis.

AGENIX

Agenix is a Brisbane-based, listed company with revenues of nearly $40million in 2004. It has considerable in-house expertise in mammalian cell culture, both in roller bottles and fermenters. Agenix core business is centred around diagnostic applications of its D-dimer antibody technology. D-dimer is associated with blood clot formation, and Agenix claims 13% of the global medical diagnostic applications based on D-dimer detection. The manufacturing of its lateral flow diagnostic kits will be transferred to China, freeing-up production facilities for other purposes. [redacted]

Agenix has also applied its antibody technology to medical imaging of blood clots (a US$3-6B market). This *in vivo* application requires clinical trials, and Agenix upgraded its facilities to enable production of its Phase 1 and 2 material in-house. [redacted]

[redacted] Agenix will work with Diosynth (USA plant) to generate its ThromboView product for the market. Setting up in Australia was not considered to be viable proposition, particularly given that the main market is in the USA.

ACYTE Biotechnology Pty Ltd

ACYTE is a spin-off company of UNSW which specialises in protein expression and production by mammalian cell hosts. The company has developed and patented three platform technologies in the fields of stable and transient protein expression in

CHO cells, and in the rapid selection of clones expressing protein at high rates. The company has bioprocess development capability, and has produced preclinical grade monoclonal antibodies and recombinant proteins at up to the 130litre scale.

CSIRO

The Clayton group headed by Professor Michael Zachariou operates prokaryotic fermentation development on a contract basis (up to about 100 litres). Mammalian cell process development work is performed by the Parkville group headed by George Lovrecz (small bench vessels of a few litres capacity). The Lovrecz group is well known in the biotech industry, and provided useful information regarding activity in research institutes in Victoria in particular.

Ludwig Institute

The Ludwig Institute, a non-profit international organisation based in the USA, has a GMP-compliant mammalian cell facility in Melbourne to support its local R&D projects. The Ludwig also has an association with US CMO Cardinal Health for outsourcing of certain of its scale-up projects. The local operation has seriously considered developing a larger facility, including mammalian cell culture at 100 litre scale.

Gro Pep

This Adelaide-based firm has recombinant bacterial fermentation and downstream processing production experience. The products are growth factors such as IGF. The facilities and operations are high calibre, but GroPep is not a CMO.

Q-Gen

Brisbane-based Q-Gen was established in 2002 as the production arm of the Queensland Institute of Medical Research (QIMR). Q-Gen has some 1,000 square metres of manufacturing and process development area, with two floors above housing HVAC and services support plant. There are 6 cleanrooms all with independent environmental control. The facility is TGA approved for some activities, including sterile liquid fill. The single fermentation suite has 10 fermenters ranging from 3 litres to 70 litres (total) capacity which can be configured for mammalian, microbial or viral applications. There is a cytotoxic room, and 2 rooms certified to PC2.

Very recently Q-Gen has been spun off from QIMR as a separate corporate entity and is already operating as a CMO. Because of its origins within QIMR, Q-Gen has not yet been seriously marketed and promoted as an independent CMO in its own right. Q-Gen has a certain number of clinical trials projects arising from QIMR, currently handled on a cost-plus basis. There is potentially room for expansion into the adjacent building.

Q-Gen has fermenters suited to mammalian cell culture, but these are not yet validated for clinical trial applications. However, in the near future, Q-Gen will be able to offer both mammalian and prokaryotic culturing for production of liquid drug products to GMP. Processing of a number of autologous cell therapy products, stem

cell expansion, and formulation and aseptic dispensing of small molecule actives are already being performed.

3.6.4 Australian Biomanufacturing - Mammalian Cell-Based

a. Australian Biomanufacturing - Mammalian Cell-Based Demand Side

The latest survey data relating to mammalian cell-based clinical activity was incorporated in the Table 3 above and discussed in section 3.3.2 in order to position the mammalian route to expression within the broader framework of biopharmaceutical development.

b. Australian Biomanufacturing - Mammalian Cell-Based Supply Side

It is noteworthy that there is *today* not a single Australian CMO able to offer mammalian cell stirred-tank fermentation on a contract basis on the open market for manufacture of therapeutic grade materials.

Q-Gen, Progen, Bresagen, Acyte, CSIRO and Agenix have claim to certain mammalian cell capabilities, but lack a critical element such as installed and qualified equipment, validated clean rooms or some other item preventing the *immediate* performance of such work. The recent decision by CSL to develop in-house mammalian cell facilities up to 500 litres capacity for generation of material for phase 1 and 2 clinical batches is a reflection of this gap (amongst other considerations). As previously mentioned, Bresagen has recently announced that it will extend its activities to include mammalian cell fermentation, albeit at small scale (10 litres) and for a single client.

3.7 Analysis of Australian Capability Situation

3.7.1 Gaps in capability

The products in development (see Table3) in Australia fall loosely into 3 groups in terms of need for manufacturing capability. These are, (1) products with diagnostic applications, mostly for analytical applications rather than "in man", (2) products needing further optimisation and development before becoming "production ready", and (3) products in the clinical trial system, where gram to hundreds-of-gram quantities may be required. Each product group is discussed below to establish whether a gap in capability exists in Australia to accommodate the needs of biotherapeutic developers.

Group 1 - Production of Molecules for Diagnostic Applications

Typically, diagnostics use antibody reactions and are made using mammalian cell technology. However, the standards of GMP required are not as exacting as for active drugs, especially sterile injectables. There are several local suppliers who can supply the early development needs of discovery companies, for example G.Lovrecz's CSIRO group, and Adelaide's MABSA. The AIBN will also be able to service this segment once the facilities are on line in late 2006.

Once GMP conditions are required, the options are reduced. Q-Gen and Agenix can potentially cater to this market although capability is limited currently.

For applications using microbial expression, Bresagen, Progen and others certainly have the wherewithal to take on local contracts.

Group 2 - Products needing further Optimisation and Development before becoming "production ready"

Australia's biomedical institutes have some good bioprocessing and applied research capability. Such groups can perform optimisation, yield and recovery work for discovery companies with compounds needing lead compound development.

Alternatively, the optimisation and development may be done as part of a CMO contract. As work progresses into the preclinical and phase 1 stages, the need for GLP and GMP will preclude academic institutions from further direct involvement in manufacturing. However, partnering arrangements may continue between CMOs and universities for specific investigations and analytical development as part of a broader clinical plan.

The current provider situation for Group 2 is essentially the same as for Group 1.

Group 3 - Mammalian Cell Derived Products for Clinical Trials and Commercial Applications

It is in this category that the lack of contract facilities to service local demand is clearly evident. The technical capability exists, but this capability is not available on a contract manufacturing basis to firms wishing to enter the clinical trials process. Rather, biomanufacturing capabilities have typically been developed to suit the in-house needs of individual companies (eg CSL, Ludwig Institute, Agenix). This capacity is unavailable to new entrants to the industry. Further, the in-house development route is not feasible for many small to medium sized companies because of the very significant barriers to entry presented by high capital costs, lack of established cash flows, long construction timelines, limited product portfolios to spread risk of failure during clinical trials, and long hiatus periods between generation of clinical trials batches and regulatory approval for commercial sale.

There is apparently no Australian company currently operating that was established with contract manufacturing of biopharmaceuticals as its primary mission. Certainly there are a number of firms offering CMO services to the biopharmaceutical industry, but typically such firms have been driven into contracting by the need to cover facility overheads because of under-utilisation of capacity (capacity which was originally installed for reasons other than contract manufacturing). Such under-utilisation can arise during periods of extended downtime associated with lengthy drug approvals processes [redacted] changed locally-made product mix [redacted] poor market uptake of a core product [redacted] or inadequate internal project flow [redacted].

It is also important to realise that companies which offer CMO services as a sideline to their primary mission cannot, by definition, maintain the same strategic business focus and support to the CMO side of the business. To be a successful CMO catering to the global market, a company requires a very specialised skill set, a good track record, and a focused management approach.

Beyond mammalian cell fermentation itself, related technical gaps or deficiencies have also been identified. These include the lack of CMO capability to perform reasonable scale (1,000 – 10,000 vial) aseptic "fill and finish" (including aseptic liquid dispensing and lyophilisation) in conformance with regulatory standards governing sterile biologicals. CSL has recently announced construction of a bioformulation centre which will partially address this gap by making aseptic filling available on an economical basis to Australian clients*. However, the lack of commercially available pilot-scale sterile lyophilisation will remain.

Contract lyophilisation is currently offered by Mayne Pharma (Mulgrave facility, Victoria) and Radpharm (ACT). The Mayne facility is geared to large scale applications (many thousands of vials), and is very expensive, as pricing has been based upon the opportunity cost of internal production foregone. Radpharm's facility, whilst GMP certified, is not validated for the dispensing and drying of sterile

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* [redacted]

biologicals. Its own products (injectable tracer compounds) are terminally sterilised. However, Radpharm has very recently indicated (Ausbiotech Perth Nov 20-23 2005) that it is planning a completely new facility which will cater to the aseptic fill and drying of biotherapeutics. [redacted]

3.7.2 Reasons for Gaps in Capability

The current situation in Australia, in which there are no CMOs offering "full service" pilot or large-scale capability is a reflection of a number of influences, many of which have been touched-upon in the preceding discussion. These influences are summarised below.

Geography

The biotech industry is heavily concentrated in the USA and Europe. Around 75% of biotech firms are located in the US. In this context, there have to be reasonably compelling arguments to NOT locate near "the action". Industry of any type tends to gain leverage by clustering around kindred operations, as this promotes the development of a whole web of training and support services.

Biotech is a young industry

The first CMO's with mammalian cell fermentation appeared in the early 1980's, and in the countries which are today the biotech powerhouses of the world. It is only during the last two decades that Australia has developed the capability to support a CMO operation in terms of the drug development pipeline activities upstream (critical mass of research and applied research institutes offering bioprocessing skills) and downstream (clinical trials, pharmacology) of the CMO.

Market size

Australia's small population and remote geographical location predisposed the country to a slower takeoff in overall biotech capability. In fact, the entire Asia Pacific region, with the possible exception of Japan, remained undeveloped for the same reasons. This meant that locally-generated demand was not sufficient to justify the investment in a company operating on a purely contract basis. There were forays into biopharma manufacturing, but these tended to be motivated by a desire for in-house use, and were specific to a particular application. An efficient CMO plant, on the other hand, is ideally designed and built with multi-use operation in mind from the outset.

Barriers to entry

The high capital costs associated with construction of GMP biopharmaceutical plants has already been highlighted. This stems not only from the sophistication of the equipment and the environmental controls required in the building design, but also from the high costs associated with the initial and ongoing validation. Validation costs typically add of the order of 15-20% of the capital cost. Once up and running,

the costs of maintaining GMP compliance are a heavy impost on the operation. The costs of clean services, maintaining environmental controls, and the investment in staff training are very high in comparison with many industries.

Limited strategic sector development

When one considers the constraints to CMO development outlined above, it is understandable that an individual enterprise would not have "the stomach" for taking on such an investment in Australia. In countries such as Ireland and Singapore, where similar constraints existed, pharmaceutical industry development has been fostered by substantial publicly-funded support. This support took the form of integrated strategic plans stretching over many years and included funding of scale-up facility construction, bonded post-graduate training schemes, long-term tax holidays and other incentives of a very substantial nature being offered to industry.

Even in countries such as UK and USA with well established biopharma sectors, new CMO facilities have often involved major government backing. Examples include the National Biomanufacturing Centre (NBC) [17] in UK and the Maryland Bioprocessing Centre (Mbio) in USA[28]. In both cases, government funding was used to design and build the facilities, which were then leased out to specialist operating companies (Eden Bioscience and Cambrex respectively). The recently completed NBC provides a particularly relevant point of comparison to the options developed later in this report; further detail is provided in Appendix 6.

3.8 Summary and Conclusions

The key issues in the Australian context emerging from this analysis of global and local biotherapeutic manufacturing and CMO activity are:

- The barriers to entry are high for large-volume CMO product markets, where large companies have established reputations as reliable commercial partners, and have facilities which are very costly, often several hundred million dollars. Therefore any local proposal aiming to compete in this sector is highly unlikely to be successful.
- There are relatively few CMOs worldwide (about 20) who identify themselves as being primarily dedicated to scale-up production of biotherapeutics. This indicates a possible niche marketing opportunity for an Australian initiative.
- Whilst there is currently a global surplus of CMO mammalian cell and microbial capacity, this is of doubtful significance for any small-scale Australian proposal. This is because growth predictions indicate that any surplus capacity will be required for continued industry expansion. Further, the relevance of mainstream, large capacity operators is questionable if Australia perceives its competitive advantage to lie in the specialist scale-up segment of the CMO market.
- The importance of "industry credibility" cannot be over-emphasised in terms of gaining commitment from potential clients. One way of achieving this is to "slipstream" on the reputation of an established player, either a big pharma company or established CMO. A number of options can be considered:
  - CMO interest could be as a facility operator (following the model of Cambrex and Mbio in Maryland, USA),
  - the imprimatur of a leading CMO could be gained via a joint venture development (following the model of Lonza and Bio*1, Singapore[14]),
  - a leading CMO could be attracted to a proposal based upon Australia as a developmental "feeder" of new production-ready compounds to the CMO's existing large-scale facilities,
  - a big pharma company could underwrite the start-up of a new operation by virtue of supply contracts, or by effectively out-sourcing scale-up capability to the new facility,
  - [redacted] a new facility designed in collaboration-with and controlled-by the big pharma interest, but with a production area set aside for contract work. CSL have followed this model in setting up their proposed bioformulation centre at the Parkville site. CSL will operate the CMO production train, with [redacted] access to [redacted] customers [redacted].

These issues will be further developed in subsequent sections of this report.

4. Impact of the Capability Gap on Australia's Competitiveness

4.1 Evidence of Offshore Procurement

There is, apparently, no published data available which quantifies the number of, and value of, clinical manufacturing contracts made by Australian drug developers with foreign CMO's. Firms are often bound by confidentiality regarding the terms of quotations from CMOs, and are also unwilling to disclose the scope of services requested, since that may reveal to the market the type of product and status of the product's development. Beyond the disclosure limitations, developing "typical" pricing for clinical development services from CMOs is fraught with difficulty for other reasons.

Each product has its own technical peculiarities in terms of expression system, yield, stage of process development, and status of optimisation of that process. The physical mass of product required is dependent upon the potency of the compound, the nature of the disease target, and the extent of clinical trials planned. For example, the needs for multi-country phase 3 studies are obviously vastly different from early phase safety determinations. These differences will all affect the prices quoted by CMOs.

Drug developers also seek different combinations of services; for instance some may require straight-forward production of phase 1 or phase 2 batches only, others may require cell banking and extensive process development (optimisation of expression and downstream recovery for example). Usually there is a need for a trial or "engineering" batch to test all systems including paperwork and controls before the CMO undertakes the GMP batches. Assistance with regulatory affairs and liaison with authorities may also be offered by the CMO.

Superimposed upon the customer's needs are different CMO approaches. For example price may be discounted against trailing commissions or licensing fees associated with use of a CMO's proprietary cell lines. Alternatively potential customers may have to pay a higher fee to secure a production slot which "bumps" an existing commitment.

Notwithstanding the issues mentioned above, some approximations can be made to roughly estimate the volume of business currently lost to overseas CMOs, and to generate a context for consideration of what this loss will likely grow to in the future. These estimates (refer table below) have been gleaned from anecdotal reports provided by Australian firms who have recently sought quotations from CMOs.

Companies which are known to have signed deals with overseas CMOs include [redacted]

[redacted]

4.2 Cost to the Economy

Hopper et al [10] imputed a total value of $15-60M to the value of CMO biologics projects exported. This covered all types of expression, not only those using mammalian cells (which constitute a minor fraction overall).

The theoretical value of the "lost" projects identified in 4.1 above [redacted] represent some $18M or more.' It is unclear how much of this value would have been captured by a local scale-up facility, even had it been available. This is because of the early stage that partnering occurred with [redacted] and heavy emphasis on co-development rather than a contracted service [redacted], on the other hand was interested in commercial manufacture and, being conscious of the USA as its consumer market, would have leaned to manufacturing locally in any event. In the case of the [redacted] decisions regarding suitability of locations are influenced by the head office [redacted]. Typical costs for work which is currently flowing overseas are listed in Table 4.

Table 4 Typical CMO costs for clinical development services

Project Type	$M/Project
small preclinical/clinical	0.3
major process development	1.5
preclinical/phase 1 batch	2.0
phase 2 batch	1.5+
Tech transfer/phase 3	5.0+

[redacted]

There is a broader cost to the economy of doing nothing (i.e. maintaining the status quo). Australian drug developers have, until recently, worked on a licensing model which has meant that they form relationships with multinational companies who then take over clinical trials, manufacture and marketing. Once a relationship is established it is difficult to change, as the Food and Drug Administration prefers manufacturing methods to remain stable. Even though drug developers are now moving further downstream and are more likely to conduct their own clinical trials, any manufacturing relationships developed early in trials will need to be maintained. In the longer term this will hamper export growth and local employment, as trials and manufacturing will continue to take place overseas

The challenge for any new facility will therefore be to effectively promote its capability to early stage developers as the facility of choice. This approach will be needed to break the pattern of international out-licensing for preclinical and phases 1 and 2. There is not an objective basis for the estimation of the proportion of forecast demand which could be captured by a new facility. In the financial projections developed in this report, it is assumed that a majority of future projects will be secured (see also 5.2.1, 6.2.2).

4.3 Benefits that could accrue

4.3.1 Direct Benefits Arising from the Facility

A stand-alone facility can develop economies of scale which means that it should be cost-competitive and hence profitable. This produces taxes payable by the business.

In terms of direct positive impacts, it is probable that a significant proportion of the potential realisable value (Table 4) could have been captured by an appropriately equipped and well-marketed facility in Australia. This estimate is rather subjective, but could be even greater if there were a well-known and well-credentialed alternative at the time of the decision-making by the drug developer. Given the lack of a local opportunity, the companies interviewed perceived that the commercial options did not include an Australian solution, nor a local option to leverage in negotiations.

4.3.2 Indirect benefits from facility operations

Indirect benefits (spillovers) from facility operations are those components of economic activity that cannot be directly measured as part of the economic transaction between parties. Indirect benefits include those that accrue to organisations external to the facility, including customers suppliers, R&D institutions and the wider economy. These benefits are difficult to quantify in advance but can be observed in principle and by reference to the impacts of similar facilities in other locations.

Customers

An indirect positive impact arising from the establishment of an Australian mammalian cell culture manufacturing facility would include an increased capacity for Australian drug developers to bring their products to market quickly, and for a lower cost. A local Australian facility would enable drug developers to work closely with manufacturing facility staff without the expense and time costs incurred by traveling overseas.

The ability of drug developers to benefit from these factors will depend, *inter alia,* on cost-competitiveness of the facility, its ability to meet their needs in a timely fashion, and the standard of service (including regulatory compliance) provided.

Suppliers

There are also immediate benefits within the region in which this facility is located. These include enhanced size and capacity of local service providers, including those providing facility management, and technical training; and an enhanced capacity of local drug developers to conduct local clinical trials. Further, the developers benefit from increased speed to market for their products. The facility itself, and local service providers, could provide services to drug developers in New Zealand, Asia and elsewhere.

Value chain

Development of a mammalian cell culture manufacturing facility will enable a greater proportion of the value chain of pharmaceutical manufacturer to remain in Australia. In particular, the existence of a manufacturing facility may increase the potential market for other complementary service providers in areas such as facility management, testing services and technical training. These, in turn, will create further knowledge spillovers regionally and nationally.

Direct and indirect employment.

For example a study of the pharmaceutical sector in Quebec reported direct creation of 16,000 direct jobs amongst 170 biotech firms (including R&D centres) (42) This study used a multiplier of 2.02 to estimate the direct and indirect employment impacts, concluding that the total number of direct and indirect jobs was more than 30,000. A study of US pharmaceutical manufacturing (43) used an employment multiplier of 2.9, however this relates to commercial manufacture across a range of industry sectors additional to pharmaceutical manufacturing and may be an overestimate.[*]

This effect can already be seen in the medical devices manufacturing sector, where existence of a number of major manufacturers (for example, Cochlear, Resmed), has led to development of an industry sub sector with activity along the full value chain.

[*] The study used input output tables for 5 SIC codes: 2833, medicinal chemicals and botanical products; 2834, pharmaceutical preparations; 2835, in vitro and in vivo diagnostic substances; 2836, biological products, except diagnostic substances; and 8731, commercial physiological and biological research.

As a result, there is a number of major engineering-based designers and product developers in this sector (e.g. Invetech), a second tier of contract manufacturers (e.g. Corbett Research) and links through into other suppliers in sectors which supply both medical devices and other industries (for example, plastic injection moulding, electronic components and the like).

Local Knowledge Spillovers

Interaction between, and movement of people is one of the most common ways in which knowledge spills over from one organisation to another. Such knowledge spillovers are important in the building of capacity at regional and national levels, as staff move between firms, taking their firm-specific knowledge with them. The ability of recipient firms to use this knowledge depends on their own knowledge base. Much of the literature on the benefits of foreign direct investment centres on these types of spillovers. However, there are also potential benefits of spillover from domestic firms, where skills developed in one firm are transferred to others through the transfer of staff.

An important aspect of this knowledge transfer is that it is often geographically concentrated. For example, Australian firms' use of overseas manufacturers will not generate the same level of knowledge spillover as Australian firms' use of an Australian-based manufacturer for the same service.

Overseas studies have found that local knowledge spillovers from manufacturing plants are more significant in those which are "high-tech", possibly because local interaction is more likely to be required in such facilities (18). In the highly regulated pharmaceutical sector, it might be expected that skills developed within a pharmaceutical manufacturing facility in relation to scale up, GMP and other steps of the manufacturing process will be valuable to third parties. In time, this knowledge will diffuse more broadly in the manufacturing sector in Australia. This is likely to lead to an overall change in the innovativeness of the sector (19).

Such knowledge spillovers are also a risk. A central manufacturing facility will need to obtain confidential information from each of its clients. Those clients may be concerned about potential for leakage of intellectual property and local skills embodied in staff from the central facility. In order to minimise such risks, a central manufacturing facility will need to establish procedures covering management of intellectual property and confidential client information. Such procedures are common elsewhere*.

Spillovers also accrue to suppliers, who gain experience from working with a major manufacturer and can use this experience in acquiring and performing future work. The most obvious and early stage spillover here is for the company building and/or designing the facility. Similar examples of this type of spillover have been quoted in studies by the Productivity Commission (40).

* For example, the National Biomanufacturing Facility in the UK runs three GMP labs for viral, bacterial and mammalian production and has developed a range of procedures to ensure confidentiality of client material and processes.

Spillovers from Foreign Direct Investment

The location of a mammalian cell culture facility in Australia could provide additional benefits from spillovers from foreign direct investment. These benefits may accrue whether or not the operator of the facility is an overseas- headquartered firm.

If an overseas-owned firm is contracted to establish the facility, additional knowledge spillovers may be obtained through transfer of know-how from the overseas firm to local staff, and then on to other companies within Australia as staff move from company to company. The ability of Australian organisations to capture this knowledge may depend on the foreign firm's ability to keep its IP close (for example, if it appoints staff from its overseas head office and limits local recruitment then capacity for knowledge spillovers may be minimal), and the degree to which it engages local suppliers (41) . While such spillovers may also occur between firms which are Australian owned, the involvement of an overseas firm in a central role provides an opportunity for Australian organisations to tap into the international knowledge networks which would be unavailable with solely domestic linkages.

For such spillovers to occur it is vital for local firms to be able to interact closely with the foreign-owned firm. In India, for example, local spillovers were limited by restrictive policies implemented by the Indian government regarding the degree to which domestic firms could become closely involved with these organisations (20).

Expanded skill base

Although biopharmaceutical manufacturing employs few people compared to other industries it requires highly skilled labour and there is a current world shortage of workers at all levels. The skills required involve an understanding of working in a regulated environment, Good Manufacturing Practice, strict adherence to production protocols, cleanroom and aseptic work, process control, safe handling of potentially toxic products, etc.

It is expected that most personnel/staff would have tertiary qualifications and it is possible to some extent to recruit upper level workers from overseas. The larger pharmaceutical companies such as CSL and large local facilities of pharma companies have internal staff training programs and on-the-job guidance. Courses in the whole pharmaceutical manufacturing process are limited however, although some courses are offered by universities (eg Swinburne University of Technology offer a Diploma, Certificate and Masters qualifications in Good Manufacturing Practice) and TAFE (for example a Certificate III in Pharmaceutical Manufacturing in Queensland).

The spillover from increased activity in Australia is the increased skill base in the broader advanced technology industries as well as the pharmaceutical process industry involving the major international companies and small biotech companies. It will increase the manufacturing capability of companies in early stages of development and raise awareness in research based organisations of the ramifications of proper manufacturing principles and regulations that must be recognised earlier than they are now. It also feeds into the IT, electronics and food industries where clean-room processing and higher level manufacturing occurs. Educational service organisations feeding into the sector will benefit by demand for courses relevant to industry.

4.4 Measurement of potential benefits

Direct benefits can be measured easily from standard company metrics. We have calculated the following based on assumptions elsewhere in the report:

- Company turnover, $30m p.a.;[1]
- company taxes paid[2], around $2.3M p.a. after year 6;
- Additional direct jobs in the facility – est. 50;
- additional export income, included in above; and
- employee taxes paid[3] – est. $1.3M p.a.

Indirect benefits, as noted above, are difficult to measure but are likely to include the items in the Table below.

Table 5 Potential areas where indirect impacts will be identifiable

Benefit	Quantified by
Expanded skill base	• personnel employed in biotech companies (e.g. facility customers) at lower levels – graduate opportunities and training • courses established to provide training in biotech manufacturing • More graduates and TAFE skilled people available • Personnel returning from overseas • Secondment of personnel between Australian facility and overseas client companies
Infrastructure established	• Greater cluster formation resulting from facility location • Expanded service companies available for facility – based on multiplier of 2, expect further 50 positions to be available in all service areas nationally
Increased sale of products	• Stronger, higher-valued biotech companies

[1] Using assumptions from 6.2.2

[2] Based on company tax rate of 30% on EBIT from above operations in 2005 dollars and neglecting effect of tax losses carried forward.

[3] Assuming employee salaries average $75,000 per person and assuming the facility requires 50 staff. Personal income tax on a salary of $75,000 is about approx $26,000

manufactured in Australia	• Greater ability to raise investment funding • More local products that are advanced in clinical trials and in market • Export revenue from biotech sector • Major pharma companies in contracts with facility • Major CMO involvement in facility
Licensed products taken further along development	• Number of products in clinical trials and preclinical • Time and value of pharma licensing deals - Deals with pharma done later in development
Contract manufacturing earning revenue	• Time to facility break even – likely to be 3-4 yrs post construction • Dollar turnover as above
Cost effective support for R&D – earlier manufacturing	• Greater early adoption of GMP in the manufacturing of R&D products – this will have flow through benefits in terms of licence fees earned by Australian biotech companies • Enforcement of regulations for GMP in preclinical stage & Phase I • Fewer failures due to manufacturing in later stages • Faster time to market - opportunity to earn revenues and extend patent life
Attraction of large pharma companies	• Contracts – number, value • Potential for additional R&D effort by these firms in Australia • Joint venture projects • R&D centres attracted • More alliances between pharma and biotech firms • Staff secondment between companies • Co-operation with local pharma companies for know-how & training

5 Biomanufacturing Facility Commercial Viability

5.1 Introduction

This section of the report seeks to integrate the issues identified from the earlier analysis and apply these findings to developing a recommended strategy which will best suit the needs of Australian therapeutic drug developers. Ideally, the strategy should also position Australia to participate in the wealth created by the rapidly-growing global biotherapeutic CMO industry.

In devising the strategy for an Australian facility, attention has been paid to the social, political, economic, and technological driving forces which are shaping the global drug industry, and the local scene. The business strategy and business model are framed around the key success factors identified by the driving forces analysis (see also section 3. Gap Analysis, and Appendix 1 which provides further detail).

The key success factor overriding all others is the ability to attract sufficient revenues to justify the capital investment and cover the operating costs of the facility. Therefore, salient issues relating to the demand-side discussion in sections 3 and 4 will be further explored to properly underpin the strategy, and to define the type of facility needed to fulfill the objectives of the strategy.

5.2 Key Demand-side Issues

5.2.1 Australian demand

There is clear evidence of sustained growth in research and development activity in Australia in the pharmaceutical sector. Innovation Dynamics surveys showed a rise in the number of developmental products from 315 in late 2004[10] to at least of 410 in quarter 3, 2005 (data gathered for this report). 59 mammalian cell-derived products were identified in the current survey of Australian companies. Whilst much of this activity remains concentrated in the lead-seeking area of development, there are encouraging signals regarding the number of compounds moving into clinical development, and a number of examples of Australian companies going offshore for clinical trial material have been noted.

Prominent players include [redacted], aiming to generate 1-2 molecules per year and [redacted] 3-5 per year. Firms such as [redacted] and [redacted] also have advanced programs developing monoclonal antibodies. [redacted] has at least 10 antibodies in preclinical development, translating to a need to push at least 2 compounds per year into trials. Significantly, [redacted] has expressed an in-principle interest in an alliance with any proposed scale-up development.