HOUSE OF REPRESENTATIVES

STANDING COMMITTEE ON PRIMARY INDUSTRIES AND REGIONAL SERVICES

INQUIRY INTO DEVELOPMENT OF HIGH TECHNOLOGY INDUSTRIES IN REGIONAL AUSTRALIA BASED ON BIOPROSPECTING

75 years of Australian Science

CSIRO

CSIRO Submission, February 2001

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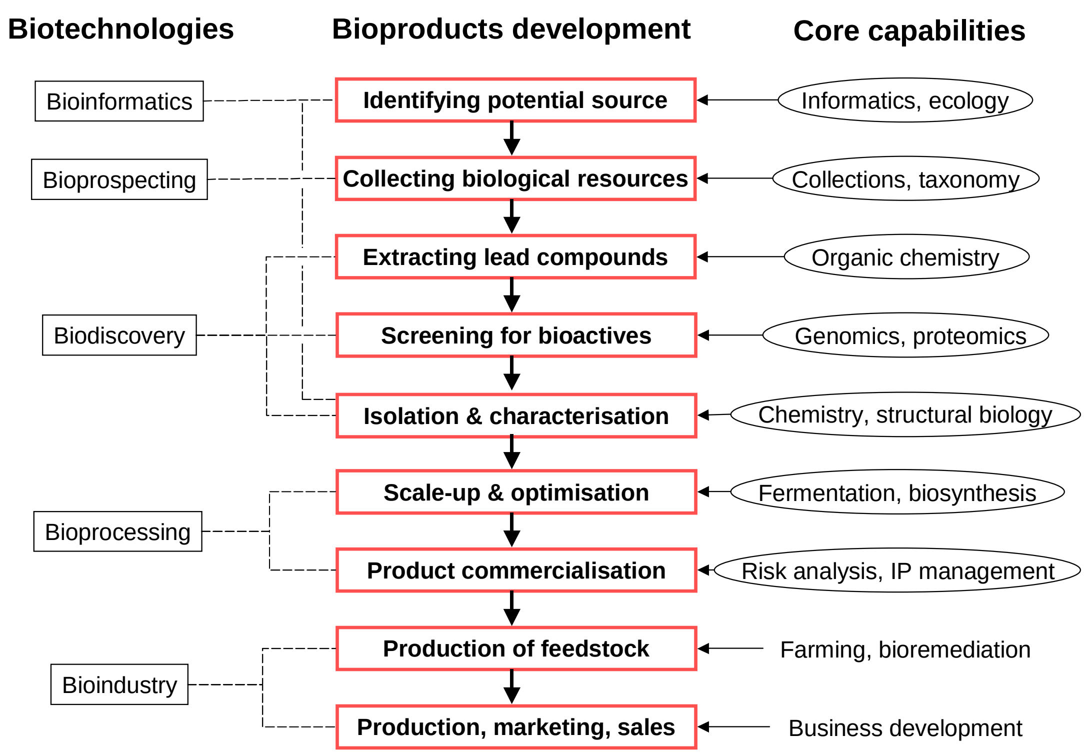
EXECUTIVE SUMMARY

CSIRO welcomes this Inquiry into measures that will assist the development of high technology industries in regional and rural areas based on the appropriate use of Australia's flora and fauna. In our submission, we suggest that the Committee takes a long-term focus on the potential for these kinds of industries and how the findings of the Committee may complement other policy developments elsewhere.

Australia cannot hope to be a world leader across all major biotechnology areas, but must carefully select the most appropriate niches and then be smart in the way that Australian intellectual property (IP) positions are used to exercise leverage over multinational companies.

It is therefore important that the Committee develop a whole-of-systems approach that takes into account the global nature of the business systems in which biologically active substances and genetic traits are sourced from our biodiversity, and where biological material can replace petrochemicals as "feedstock" in the manufacturing sector.

Moreover, there are a number of biotechnologies involved, for which core capabilities in Australia are essential to underpin the development of these industries. To this effect, CSIRO presents a framework (see below and on page 11) to illustrate how specific biotechnologies such as *bioinformatics*, *bioprospecting*, *biodiscovery* and *bioprocessing* are interdependent and collectively contribute to the development of biotechnology industries, or in short '*bioindustries*'. CSIRO suggests the Committee adopts this framework as a means to consider the various issues and biotechnologies of importance. CSIRO has also attached a glossary of the more technical terms used in our submission.



CSIRO believes there are tremendous opportunities for Australia to develop more companies operating within the bioindustries business system. Australia has three major advantages of significant importance compared to other nations:

1. Australia has a rich biodiversity and the knowledge to use it to our advantage.
2. Australia has an innovative and efficient primary industry sector with an infrastructure suited to the production of raw material or feedstock for manufacture of new products based on our biodiversity.
3. Australia has a highly developed research and development system that can support such bioindustry development.

Against that are three major impediments:

1. A perception of an "old economy" primary industries sector.
2. A need to encourage the development of visionary leadership within the industry.
3. Limitations in skills, infrastructure and links between potential collaborators.

Furthermore, there are specific issues for each of the following biotechnology areas:

- Ready access to quality data held globally and provision of highly skilled staff in Australia are key issues for *bioinformatics*. The establishment of the Global Biodiversity Information Facility (GBIF) will address these needs within *biodiversity informatics* whereas some of these issues remain for *molecular informatics.*
- The development of a nationally consistent approach to *bioprospecting* may have gained some momentum through the recent inquiry into Access to Biological Resources in Commonwealth Areas, but the need remains to progress the work on a national level and deliver solutions that will assist these biotechnology industries.
- Nationally, it is critical to clearly identify the market niches for *biodiscovery* projects that are of strategic importance to Australia. Furthermore, international collaborative ventures are important to support to ensure Australia retains a seat at the negotiating table when dealing with multinational companies that are active in this area.
- There are real limitations for pilot plant infrastructure necessary to undertake the research for scaling up *bioprocessing* prior to manufacturing new products.
- Finally, to develop successful *bioindustries*, continued attention to public perceptions of biotechnology would be necessary.

CSIRO believes that the current system of IP protection is adequate but there are shortages of strategic skills by some operators to secure the best deals for Australia.

Finally, CSIRO notes that the environmental impacts of bioindustries are overall positive. Biotechnologies offer significant scope for biological waste management, including *bioremediation* of chemical contaminants. The replacement of petrochemical feedstock with biological material produced by the primary industries sector will reduce the release of new carbon into the atmosphere and thereby assist in reducing the greenhouse effect. There are also opportunities for the use of genetically modified plants, animals and microorganisms to produce special substances that may originate from our biodiversity, but with greater efficiency and lesser risk. In these circumstances, issues of ecological risks are important and likely to become critical issues; CSIRO has established a research project to address this and develop appropriate risk assessment methodologies.

INTRODUCTION

CSIRO welcomes this Inquiry as a timely opportunity to enhance the synergies between a range of new policy developments such as the Government's recently launched Innovation Statement, the new Gene Technology Act, the National Biotechnology Strategy[1] released last year, the Inquiry John Voumard into Access to Biological Resources in Commonwealth areas[2] and a number of other, significant initiatives in the area of biotechnology policy. Collectively, these developments complement each other and are critical to support a number of emerging knowledge industries, in the traditional primary industries, mining and manufacturing sectors as well as a range of new and emerging high technology industries.

This particular Inquiry must look well ahead and consider how Australian biodiversity and various farming systems can contribute to the "new economy" paradigm as part of the modern biotechnology revolution. Only in this way can Australia achieve a sustained growth of new, high technology industries.

CSIRO encourages the Committee to advance some forward vision, especially in new areas where innovation in biotechnology can foster economic growth and job creation in regional Australia. Amongst other things CSIRO contributed to the recent Regional Summit with a brochure, "Creating Wealth in Australia's Regions"[3], outlining the contribution of our research for rural and regional Australia.

CSIRO notes from the Inquiry's Issues Paper that the emphasis of the Inquiry is on identifying new ways for industrial use of biologically active compounds, sourced from our unique flora and fauna, and how Australia can reap the benefits from these activities; in particular on a regional scale. CSIRO believes there is a tremendous potential at a regional level to develop of a range of new high technology bioindustries based on natural cultivation of feedstocks, such as starch, cellulose and other sugars, vegetable oils, and fibres from micro organisms, plants and animals, to make high-value bioproducts for the public health and primary industry sectors. In contrast to existing chemical and pharmaceutical industries, bioindustries have infrastructure requirements that are often more modest and can be met within rural areas, thereby stimulating regional growth.

The Issues Paper correctly observes that most existing manufacturing industries tend to be concentrated around capital cities with little benefit to rural areas. Secondly, the paper seems to suggest a concern that Australia can end up 'mining' the nations biodiversity for the large, multinational corporations to use naturally occurring compounds as leads for new products made overseas, but with little profit being returned to the benefit of regional Australia. Whilst CSIRO shares some of these perceptions, CSIRO believes this should be seen as a positive challenge to Australia; there are tangible opportunities for regional Australia.

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1 For further information see Biotechnology Australia's website: http://www.biotechnology.gov.au.

2 This Inquiry was commissioned in late 1999 by Senator Robert Hill, Minister for the Environment. The report of the Inquiry is available from: http://chm.environment.gov.au/documents/inquity.html. Further information can be found on: http://www.environment.gov.au/bg/chm/key.access.inquiry.html

3 Copies of the CSIRO brochure for the Regional Summit have been provided separately to the Inquiry Secretariat. Additional copies can be provided from Mr Geoff McAlpine, Office of the Deputy Chief Executive Environment & Natural Resources, CSIRO Black Mountain Laboratories, Clunies Ross Street, Acton Canberra ACT 2600. Email: geoff.mcalpine@exec.csiro.au.

THE SCOPE AND STRUCTURE OF THIS SUBMISSION

In this submission, CSIRO will focus on the broader, structural issues and challenges for the modern high technology or biotechnology industries with particular emphasis on the research processes and issues for new products based on industrial use of Australian flora and fauna, and agricultural produce. CSIRO notes, that considerable thoughts are being given at present to industrial production of ethanol from wheat starch, which is a useful illustration of the use of biotechnology, but this technology can be used for the biological manufacture of products that are of far greater value. Accordingly, CSIRO suggests that the Committee focuses on longer-term opportunities from high-value, refined products.

A key feature of this submission is to illustrate how core biotechnologies complement each other and collectively deliver the knowledgebase for these new industries. In order to achieve regional benefits from bioprospecting, this activity must benefit other research intensive biotechnologies in the entire business system and link new intellectual property (IP) into the commercial use of our biological resources. This is achieved through a whole-of-systems consideration of the "product value chain", i.e. the processes and technologies that flow from the intent to extract either useful compounds or gene sequences with desirable characteristics from living material to the establishment of new bioindustries and their products.

In addition to bioprospecting, core biotechnologies include bioinformatics, biodiscovery and bioprocessing, and we intend to address particular shortcomings of the innovation systems that are current barriers to develop new regional industries.

As primary producers' access to gene technology was explored recently by this Committee, CSIRO will not comment in any depth on the barriers to agricultural adoption of genetically modified crops and animals in the short term except noting that a new generation of genetically modified organisms (GMOs) under development are likely to have a key role in the primary industry sector. These GMOs will be engineered to produce high-value compounds or complex macromolecules intended for industrial processing, not the current use for the traditional food or fibre industries.

Secondly, there is another "family" of existing and more traditional biotechnology-based industries like breweries, pulp mills, food processing plants etc, which already have their place in regional Australia. Whilst these industries also offer significant opportunities for new ventures and products, we do not intend to comment in any depth on the potential of these industries to expand their traditional product range. Research providers will continue to meet the needs of these industries for the benefit of the whole Australian community.

Traditional biotechnology example: Rayon made from wood fibre
Baking and brewing are often used as examples to illustrate how the term 'biotechnology' also applies to industrial processes that have been used for many years. Another good example of traditional biotechnology is the making of Rayon, which essentially is made from dissolving wood fibres in organic solvent and then reconstituting cellulose into long fibres. It was invented in 1855 as the first manmade fibre, and the first commercial process to make artificial silk was demonstrated at the Paris World Exhibition in 1890. The process that has now been used for more than 100 years includes strong and toxic solvents. This led CSIRO to develop an alternative solvent system (Siron®) in the 1980'ies, which has not yet been adopted by the industry.

THE GLOBAL BIOTECHNOLOGY INDUSTRY CONTEXT

Today, biotechnologies are core constituents in a growing high technology industry sector that is both truly global and heavily dependent on scientific discovery. Significant market power is now concentrated within major multinationals that source specific technologies for their own research as well as trade their products globally. This represents a challenge for Australia, and as a nation we must think and operate globally to identify our own opportunities.

In the USA "biotechnology" has developed as an independent industry sector in its own right. A blend of academic and public sector research providers, government and business has established of critical mass. Core biotechnology companies are part of a wider innovation system that generates and controls key technologies as driving forces in both pharmaceutical and agribusiness sectors.

This contrasts with other economies such as in Japan, where biotechnology has been largely regarded as a set of tools to serve established industries. In these countries, biotechnology has provided a sound basis for capturing economic benefits but it has not provided the strong driving force that it has in the USA.

Many of the key biotechnology industry players began in the synthetic chemical industry, in particular the pharmaceutical and pesticide industries. In former times, chemists produced lead compounds from microbial or petrochemical feedstock, and then subjected these to various biological screens to test for active constituents. Following substantial industry restructuring and amalgamations over the last 10 – 15 years, the remaining companies have transformed themselves into vertically integrated life sciences enterprises.

Example of Industry vision
"The integration of biology with chemistry and materials science is the second profound technological revolution, along with the revolution in computation. All of life's processes are chemical processes, so our understanding of biology will improve because of the application of chemistry; and our practice of chemistry will begin to approach nature's elegance and efficiency through the application of biology".
Extract from DuPont's 25 year Vision.[4]

These new or renewed companies are building new business systems which incorporate seed companies as subsidiaries either to control the adoption of their products into agriculture or to ensure an independent supply-stream of biological feedstock to reduce their dependence on petrochemicals. Chemical synthesis is rapidly being replaced with microbial or enzyme fermentation methods, which can create the desired compounds with far more precision and structural specificity as well as generating less intractable waste.

Changing the feedstock from petrochemical to plant-based can dramatically change industry structure. The need for ready access to a refinery is replaced by the ability to access plant-based feedstocks wherever agricultural production is taking place. Moreover, with lower energy costs, higher production efficiency and lower waste production, high value product can be manufactured in smaller facilities that can be placed anywhere where it is most cost efficient to do so. Production of small volumes of high value products, such

[4] Reference: http://www.dupont.com/corp/science/25years.html

as drugs, biologically active substances, additives etc can be produced in small factories, which could be placed in rural areas if there are sound business reasons to do this.

Globally, the chemical industry is increasingly integrating technologies based on chemistry, polymer and materials science and engineering with biology, to produce a wide range of new chemistry and manufactured products.

Bioprocessing Example: Polyester from Starch
Propanediol is the key starting material for new kind of polyester fibre, polypropylene terephthalate. This polymer has properties unique for a polyester fibre such as stretch recovery, resiliency, toughness and easy dye capability without the use of chemical modifiers. DuPont, in association with Genencor International, has developed a process that uses a GMO to convert low-cost sugar from cornstarch into propanediol at high yield in a fermentor. DuPont believes this technology represents the world's lowest cost route to a future key intermediate and has backed this judgement with the construction of new processing factories based on this bioprocessing technology.[5]

[5] Reference: http://www.dupont.com/corp/products/dupontmag/97/polymer.html

AUSTRALIA'S OPPORTUNITIES IN THE GLOBAL BUSINESS SYSTEM

For its size, Australia is a strong player in global biotechnology and needs to build on that strength for future national economic, health and environmental benefit. Revenue amounted to $965 M in 1998/99[6]; on a per-capita basis it can be compared to the successful US and Canadian industries although characterised by proportionally fewer public listings, lower level of capitalisation and a less mature product pipeline. Hence our involvement must be strategic with strong, national leadership directed into areas and niches where our global contribution makes a significant difference, yet delivering benefits to local and regional communities.

Australia's science system plays a critical role to support the emerging biotechnology industry sector, but it does not have the critical mass to be a significant player in major international scientific endeavours such as the human genome program, or broadly across the research fields associated with pharmaceuticals, the biggest market for research and development (R&D). Neither can we compete with the large research budgets of multinational companies. We must carefully consider strategies for our research that will enable us to develop internationally competitive scientific strengths in selected niche areas. These need to be areas that are important for Australia (e.g. adding value to our strength in primary production) and which at the same time have potential to provide leverage on biotechnology advances made elsewhere by Australian research organisations trading on valuable IP that overseas companies need access to.

The challenges lie in bringing this global innovation on shore and developing local industries. There are particular opportunities for smaller bioprocessing industries specialising in product development and manufacturing based on fermentation and enzyme technologies, as well as in the broader, but related area of waste management technologies. Such industries may have different and more modest demand for processing plant and infrastructure making them ideal for placement in rural and regional settings adding value to the local economy.

Australia has three major advantages in the present context:

1. Our unique and rich biodiversity and our special knowledge thereof, which provides us with a tremendous biological resource of new biologically active compounds for use in novel products.
2. Our efficient, innovative and competitive primary industries, which are geared to produce important raw materials for the manufacturing industries, including plant materials that can replace our dependence of petrochemicals as the carbon source in the biochemical industry.
3. Our well developed R&D and innovation system, which can generate enabling platform technologies in genetics, molecular biology, analytical chemistry, fermentation and waste management to provide the springboard for new bioindustry opportunities.

Australia has already proven attractive to the global chemical industry inbioprospecting for the discovery of new drugs and agricultural chemicals, in new bioremediation technologies for environmental remediation, and in biomining (see examples later in the submission).

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6 Ernst & Young: Australian Biotechnology Report 1999, AusInfo, Canberra. The report is also available from: http://www.biotechnology.gov.au/Industry_Research/Reports/biotechreport.pdf

Moreover, Australian scientists are among world leaders in developing platform technologies in bioinformatics, bioprospecting, biodiscovery and bioprocessing.

The key to successful biotechnology linkages with the globalised life science companies lies in the generation of high-quality IP based on excellent science and linked to commercialisation mechanisms that provide down-stream control over applications of the technology. Benefits arise both from direct use in manufacturing, agriculture, health industries and the environment, and indirectly from the smart use of Australian-owned IP to gain maximum benefit to Australia when used as bargaining chips to negotiate access to core technologies developed by others.

In this way, tradeable IP provides a means not only to secure economic investment, but also to obtain valuable technology, generated overseas, for our own industries. However, the reverse is also true. Selective withholding of IP by overseas competitors may restrict the freedom to operate of Australian companies and research bodies wishing to access competitors' IP. It is therefore critical that Australia generate the IP to keep a seat at the international negotiating table, even when attempting to develop regional initiatives for high technology industries.

RESPONSE TO TERMS OF REFERENCE 1:

The contribution towards the development of high technology knowledge industries based on bioprospecting, bioprocessing and related biotechnologies

In considering the contribution of the specific bioprospecting, bioprocessing and other related biotechnologies towards the development of new high technology industries, we must understand the entire business system in which knowledge is generated and used.

Initial research mainly involves collection of biological material and identification of biologically active molecules. This happens before any industrial processes are developed. Further work using pilot plants and process engineering yields proof-of-concept, after which final product commercialisation is considered. Subsequent manufacturing processes may then be established, either through simple, but large scale extraction of desirable compounds from farmed feedstock or more often through innovation at the processing stage where fermentation and biological systems are involved in the synthesis of new compounds. With the advent of gene technology, the original source material from natural sources may not be used or even be relevant, as the genetic information could be inserted into other organisms to produce the desirable compound or at least intermediate products. These processes may be located anywhere but will usually be at overseas facilities because overseas companies are making the decisions.

The steps that are associated with the development of a new product are illustrated by the pipeline for bioproducts development. This is a value-adding chain from the initial research processes to the manufacture of final products. There are different biotechnologies – and at times separate business enterprises – at each step along this chain as well as requirements for core skills and capabilities, as illustrated in the following diagram:

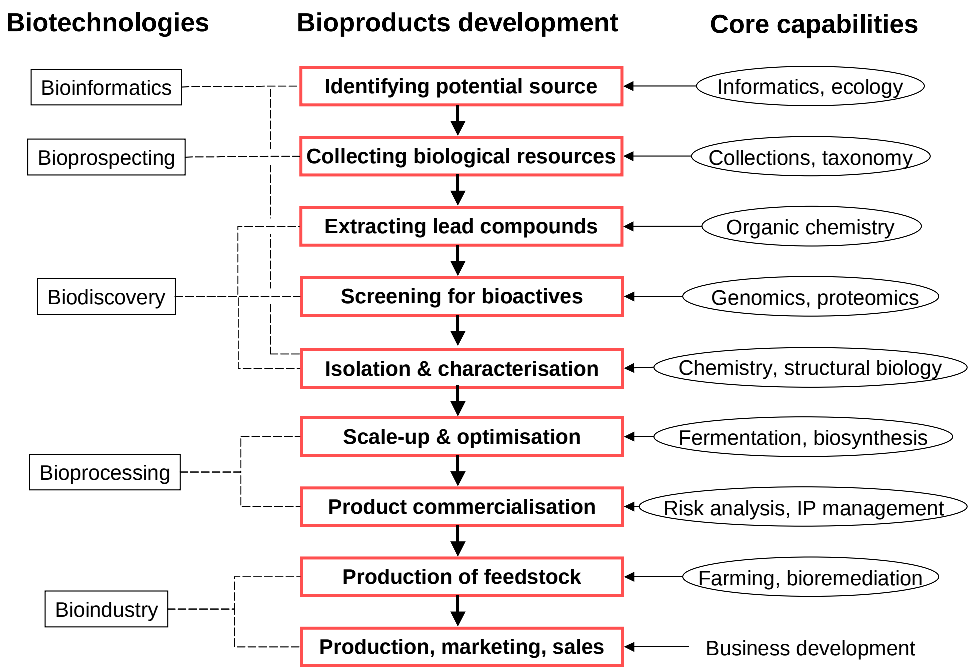

Figure 1: Product Value Chain for the development of new bioproducts based on extraction and bioprocessing of biological feedstock.

The terms used for the above processes have very specific meaning within the research and industry community. Each of the above technologies and their respective contributions can be described as follows:

Bioinformatics contribution

***Bioinformatics** is the use of powerful computational and statistical techniques to process a wealth of biological information for particular research purposes*. Bioinformatics is not an independent high technology industry in its own right at this stage but is an essential service industry that contributes the essential tools as a platform technology to provide knowledge input into the biotechnology business systems described in this submission.

Two separate fields of bioinformatics are relevant in the present context: At the first step of the value chain, *biodiversity informatics* will provide information about the organisms in which the desirable compounds occur, the natural systems where they occur, and information about their biology which will be critical for later confirmation of the origin and ownership of the IP, and in particular if the organisms are to be farmed for subsequent use. At a later point in the process, *molecular informatics* will provide information about the specific genes conferring the desired trait and how their expression is regulated. The latter is much bigger globally; however, both are critical for the development of new biotechnological industries based around bioprospecting for desirable compounds from our flora and fauna.

In the area of *biodiversity informatics*, Australian science is at the forefront and we are now a strong player in an current internationally effort to establish a Global Biodiversity Information Facility (GBIF) which evolved out of the OECD megascience forum. The key role of GBIF is to establish a global information network that will provide electronic access to the large amount of biodiversity information traditionally held separately within natural history museum collections (such as the national collections for insects, plants, wildlife, fish, micro algae, etc maintained by CSIRO). The ability to datamine biodiversity information across separate databases through GBIF for the first time will be a very powerful tool to source new information about where valuable traits can be found.

Molecular bioinformatics focuses on managing the vast data sets from the sequencing of genes and proteins, determining protein structures, and examining the interactions among proteins and metabolites. Raw sequence data are now being generated in huge volumes, especially stimulated by the Human Genome Project (see box below), but the real value lies in annotating the genome data by identifying the functions and regulation of desirable genes and then in studying the gene products (proteins) and their interactions.

Beyond the human genome, considerable effort is made to sequence valuable plant and animal species. However, large private companies overseas are in the forefront of these efforts and will in some cases control access to the data. Therefore, an important issue is gaining access to data from our native species and their interpretation on favourable terms and being able to process the information about the functions of desirable genes that can be used in subsequent industrial processes.

Although the type and origin of the information being processed in these two fields of bioinformatics are different, they are converging, as the underlying science of informatics and mining of large datasets are the same.

Genomics Example: The Human Genome Project
On 15 and 16 February 2001, respectively, *Nature* and *Science* published the entire sequence, or code, of the human genome. This was the culmination of 15 years work involving 20 sequencing centres in six countries, and represented a major breakthrough in scientific endeavour akin to the creation of the periodic table of the chemical elements, which is the foundation of modern science. At the time of the publication of the entire sequence, the Editorial in the Science Magazine[7] said: "Although we have made the point before, it is worth repeating that the sequencing of the human genome represents, not an ending, but the beginning of a new approach to biology. …The knowledge that all of the genetic components of any process can be identified will give extraordinary new power to scientists. Because of this breakthrough, research can evolve from analysing the effects of individual genes to a more integrated view that examines whole ensembles of genes as they interact to form a living human being". This applies equally well to the many current projects sequencing the genomes of valuable plants, animal and microorganisms.

Bioprospecting contribution

***Bioprospecting** is the process of collecting samples of biological resources that are used at the subsequent biodiscovery stage*. Like bioinformatics, bioprospecting is not an industry in its own right but provides the essential input into the business system by providing the organisms from which prospective chemicals are extracted. Invariably, target organisms are collected *de novo* rather than utilising existing collections to ensure clear title to any property or compound that may later be isolated and commercialised. This is nearly always done on a large scale, involving hundreds of small samples. The principal research activity at this stage is to identify the species or subspecies that have been collected including taxonomic studies of the material, and to secure ownership of the underlying IP.

Initially, bioprospecting was a supply-driven business with specimen samples being sold to pharmaceutical and agrochemical companies, typically $10 to $100 per sample. However, bioprospecting is now conducted in joint venture arrangements with either on-shore (eg. ExGenix, BioProspect Ltd) or offshore companies (eg. Astra-Zeneca, Aventis) that have the necessary resources to take interesting new biological or chemical entities through the long and expensive development phase. Amongst the Australian public sector research agencies, CSIRO, the Australian Institute for Marine Science (AIMS) and Griffith University are amongst the leading institutions collecting marine and terrestrial organisms across Australia.

Australia is one of the 12 megadiverse countries in the world reflecting its rich biological resources. Australian industry has the opportunity to develop new chemicals and new genetic material for biologically produced products ranging from drugs, new polymers, materials and fibres. Moreover, it has a well developed science infrastructure with an international leadership position in biodiversity research, and a stable political system attuned to the need of sustainability when considering economic development opportunities. The critical issue, however, lies in being able to access this biological resource in a consistent manner in all jurisdictions which would allow Australia to capture

[7] BR Jasny & D Kennedy (2001): The Human Genome, Science Magazine, Volume 291, Number 5507, Issue of 16 Feb 2001, p. 1153

the down-stream benefits rather than leaving it up to the multinational companies with little stake, if any, in Australia. We have elaborated on this under the next term of reference

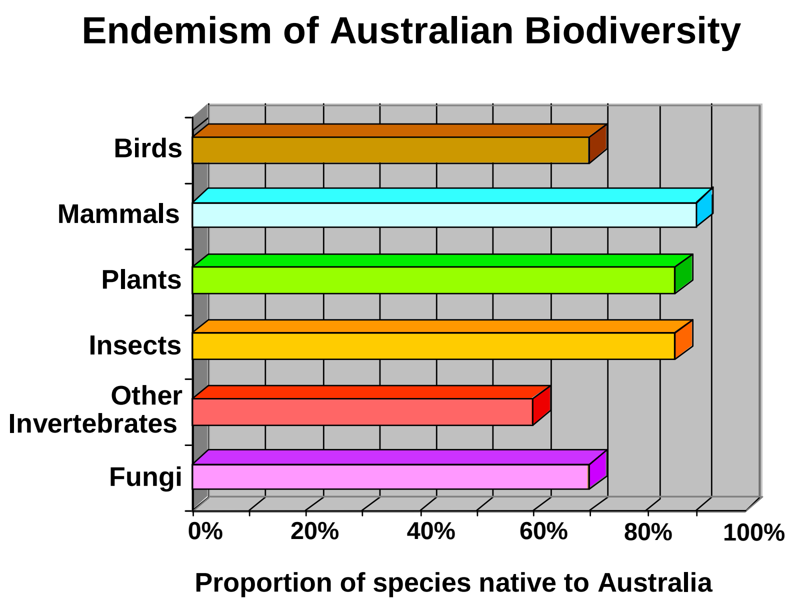

Figure 2: 80% of Australian species of plants and animals are endemic (i.e. they occur only in Australia)[8].

Biodiscovery contribution

***Biodiscovery** relates to the extraction of molecules and the subsequent identification of prospective compounds as "leads".* The extracted molecules are subjected to various biological screens to test for biologically active molecules. In these tests, often involving biological model systems, particular compounds from these extracts may be identified through molecular recognition by highly specific receptors in the biological screening system. Once biologically active molecules have been characterised as "leads", significant research is then undertaken to understand the molecular basis for the biological activity. Many of the original samples are discarded at this stage, either because of insufficient biological activity or lack of sufficient IP protection. As a result, the commercial value of remaining leads increases significantly, typically ten-fold.

Advances in gene technologies have provided scientists with new tools to identify the genetic basis for the biological activity observed from individual compounds in these screens. In many cases, the specific activity is caused by the interaction of small molecules or proteins with receptors on cell surfaces and intracellular membranes. *Structural biology* provides an understanding of the way proteins and receptors actually work in three dimensions. Through the sequencing of genes coding for such biological activity, new

8 Data from: Walker, B., Barlow, B., Caughley, G., Nielsen, E. et al. (1992): Australia's Biodiversity: What is it, its significance and what is happening to it. In: Scientific Aspects of Major Environmental Issues: Biodiversity, vi+19 pp. Office of the Chief Scientists. The paper was prepared and presented at the sixth meeting of the Prime Minister's Science Council, 18 May 1992

understanding of gene function and regulation *(functional genomics)* and the associated expression and regulation of the proteins *(proteomics)* can provide new knowledge about how to regulate either the expression of genes or the functions of the proteins in these interactions. As an outcome, the original gene function could be manipulated and then inserted into other organisms – even quite different organisms – to produce the compounds responsible for the particular biological activity.

Biodiscovery Example: Understanding protein structure leads to new drugs
Molecules interacting with proteins in biological systems has been a successful area of research in Australia as evidenced by to the development of *Relenza*, a new type of influenza vaccine that is far superior in stability to other influenza vaccines due to understanding the structural changes in the virus particles that render conventional vaccines ineffective over time. This represents a new and relatively rare direction for drug discovery, different from traditional chemical syntheses and screening approaches thus far used in the organic chemistry industries. The understanding and manipulation of protein-to-protein interactions such as in *Relenza* would be critical to obtain economic value from the wealth of information on proteins coming out of global efforts in genomics, proteomics and structural biology. It would be of significant commercial interest to industries active in pharmaceuticals, field crops and animals.

Bioprocessing contribution

***Bioprocessing** involves the development of the industrial processes to manufacture new biological products on a commercially viable scale*. This will typically lead to entirely new bioactive molecules such as used in pharmaceuticals, pesticides, food additives or other biological products. Advances in molecular biology and new fermentation systems involving either living cells or enzyme processes have enabled the production of many such compounds that could, until very recently, not be synthesised economically by conventional organic chemistry. The initial product development is conducted on a laboratory scale, but a considerable R&D effort is required to scale up while maintaining cost efficiency and process control, before a new product is commercialised. This is costly and time-consuming, often requiring some 10 years or more, and consuming up to 90% of the overall costs of developing a new product. As the subsequent manufacturing of products based on these compounds has high risk, the final decision to proceed is taken on purely commercial grounds.

Australia has a significant research effort and capabilities in the area of microbiological bioprocessing. CSIRO has been successful in attracting a number of collaborators from overseas industry into this area due to our capacity to undertake the necessary research for scale-up as well as devising methodologies for subsequent purification and waste treatment technologies. Examples of our work include:

- Producing proteins for research into human and animal vaccination.
- Producing plasmid DNA for vaccine use.
- Microbial anaerobic culture.
- Processing of foodstuffs.
- Aerobic and anaerobic fungal biomass production.
- Growth of rumen bacteria.
- Fatty acid production from micro algae
- Production of biopesticides
- Production of microorganisms and/or recombinant enzymes for bioremediation.
- Cultivation and adaptation of bacteria for mineral bio-leaching of mine heaps

Bioindustry contribution

Once the discovery and scaling up has been completed, a new ***bioindustry*** may be established *to manufacture these new products,* in many cases based around fermentation and enzyme processes. Often simple biological material can be used as feedstock and thereby replace the traditional use of petrochemicals, as discussed earlier. As the process can be very specific, waste production may be greatly reduced, and there would be an additional scope for the use of bioremediation technologies as biological waste is often less intractable than chemical waste. Another added benefit would be carbon sourcing from the atmosphere via plants, using “green carbon” rather than petrochemicals, and the consequent minimal contribution to greenhouse gas emission.

Australian agriculture is highly advanced and competes globally in terms of efficiency and productivity. Moreover, the regulatory environment is stable with a growing expertise in dealing with commercial production of crops with novel traits (both GMOs and non-GMOs). Primary producers are also well placed to manage change and diversity into the production of such novel crops or animals that can deliver precursor chemicals for subsequent processing, provided their profitability is maintained through ceaseless innovation. The disease-free status of Australia’s livestock may provide a competitive advantage in the development of production systems for high value proteins.

The logistics of using biological feedstock rather than petrochemicals means that some of these industries operating at a commodity-scale bioprocessing level would be better placed in rural areas where the infrastructure is already in place, such as around sugar mills and oil seed crushing plants. This is because biological feedstock tends to be more bulky than petrochemicals. However, an added advantage may be in the use of materials that may otherwise be regarded as waste products from conventional use, such as the use of straw from wheat production..

There is, however, a segment of this industry sector for which ready access to carbon-based feedstock is not the main business driver. Some bioindustries are geared to make quite specific products of very high value but in small quantities. These are typically highly active pharmaceuticals or chemicals for special purposes. These bioindustries have modest requirements for feedstock and are not dependent upon the primary industry infrastructure, but instead need access to a highly skilled workforce and a R&D based infrastructure, often found within a university or a CSIRO environment.

Assembling the business system

The bioindustry sector is characterised by a significant R&D component throughout the product value chain. It is a high-risk industry with typically 7 to 12 years lead-time from the concept of a new product to commercialisation, manufacturing and marketing and with a substantial investment at the scale-up level. Similar to the traditional pharmaceutical and agricultural chemical industry, the patent protection system provides for a lengthy period to recoup the cost outlays.

It is important to note that whilst the Australian biodiversity may provide traits, compounds or just gene sequences for new products with desirable characteristics or biological activity, the capacity to influence the distribution of commercial profits from the final stages of the process by exercising some ownership rights at the beginning might be limited (refer to the diagram in Figure 1). However, by ensuring that Australian research organisations and private companies are involved early in the process, there is scope to provide strategic leverage at the point where prospective leads are passed on to multinational operators. This can be very effective provided attention is given to ensure alignment and complementarity of strengths and capabilities by the various biotechnology operators in Australia, so that the economic and social benefits can be captured and channelled into rural and regional areas.

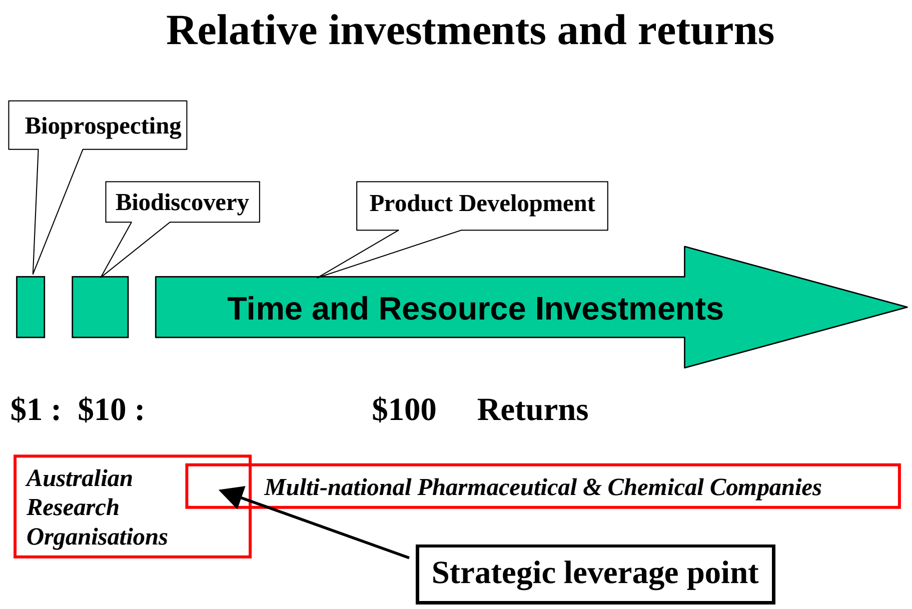

Figure 3: The relative investment in lead time and expenditures (size of the arrow) and the relative returns at each step. Whilst the down-stream operators are often multinational companies, Australian research organisations can exercise strategic leverage through the overlap in activities and our IP positions.

However, the market potential is significant, and it is critical to aim for high-value specialist products. This could be as active ingredients in the pharmaceutical industry, new generation pesticides, cosmetics, pigments, diagnostics, feed additives, fine chemical, reagents, industrial enzymes etc.

Bioindustry Example: The Market for Enzymes
The following extracts from the *1998 Biotechnology Annual Report of Burrill and Company*[9] are illustrative of some major opportunities for enzymes produced by fermentation:

- "The world- wide market for industrial enzymes was about US$1.8 billion in 1998 and is projected to reach US$3 billion in 2008. The projections include only growth in traditional enzyme markets and exclude new applications in the chemical industry or for bioremediation. Most enzymes are sold to the food industry (45 percent) followed by detergents (35 percent) and textiles (11 percent)...
- Prices for enzymes vary greatly from US$2 per kilogram for food enzymes to more than US$1,000 per kilogram for specialty enzymes...

[9] Burrill and Co is a private merchant bank based in San Francisco, see http://www.burrillandco.com/

- The discovery and commercialization of extremo-enzymes will create many new enzyme catalysts with new industrial applications, expanding the market to US$7 billion within five years...
- Recent progress with enzymes also has been made in the paper and pulp industry. Biocatalysts have been used for treating wastewater and new enzymes have been used successfully in removing ink from recycled paper and breaking down wood fibres (xylanases and cellulases)...
- Enzymes will also have a tremendous impact on chiral chemistry, important in the production of pharmaceutical and agricultural products. In 1997, sales for chiral drugs were US$90 billion or about 30 percent of total drug sales...
- One of the natural sources of plastic is bacteria, many species of which make plastics very similar to polyester. Biotechnology has given researchers the tools to take the process a step further. Companies such as Monsanto and DuPont have recently succeeded in transferring plastic-producing genes from bacteria into plants. Bioplastic could be made from barley, corn, oats, rice, soy, or wheat...
- As we engineer enzymes or microorganisms with new functions, we create opportunities to develop new biopolymers leading to biomaterial with unknown properties. These unknown materials could offer environmental and economic advantages over today's conventional fabrics, plastics, paper, rubber, or even construction materials...".

RESPONSE TO TERMS OF REFERENCE 2:

Impediments to growth of these new industries.

In a global industry, there is no necessary direct domestic link between identifying and isolating desirable substances from Australian flora and fauna and the subsequent manufacturing of new drugs or other biological products. Quite often, research and development are carried out by separate businesses trading in both intermediary products and the associated IP. The industrial R&D at the bioprocessing stage is likely to be conducted in overseas research establishments, operated by large multinational corporations. In fact, it might be advantageous for new manufacturing bioindustries to locate their plants overseas close to markets or other parts of the global company, unless Australia can offer other competitive business advantages. The link between Australian biodiversity and resultant high technology industries is not only through the chemical substances being extracted and produced, but more often than not with the actual knowledge embedded in the associated IP. The strategic role of that IP for industrial use of Australian biodiversity is further outlined later.

Further, as the entire process is based on mass screening with substantial downstream development costs, there is limited opportunity for, say, bioprospectors *per se* to have major influences on the business decisions at the commercialisation step.

There are three major impediments to the development of high technology industries based on bioprospecting and bioprocessing Australian flora and fauna:

1. The perception that the underpinning primary industry sector, which could provide the feedstock for the industrial bioprocessing, is largely an “old economy” sector. In the immediate term the bulk of biological feedstock may likely be sourced from conventional crops such as sugar cane, wheat, canola etc, but there are significant research efforts being undertaken for GMOs to produce highly refined chemical substances as biological factories or “bioreactors”.

2. Lack of visionary industry leadership to think globally but act locally, for which there is a role for Governments to support. Whilst some recent initiatives by the Commonwealth and State Governments have sought to address this such as the recent Innovation Statement and the significant infrastructure investments in some States, CSIRO believes there is still a way to go.

3. Limitations in the capacity to assemble critical mass, skills, and collaborative links between established operators across the various biotechnologies. There is a need to support this industry by key infrastructure and encouraging the development of a skilled trans-disciplinary workforce able to integrate chemistry, polymer and materials science, and engineering with biology.

There are also more specific issues and impediments for each of the biotechnologies covered in our submission:

Bioinformatics impediments

Bioinformatics is developing fast, partly driven by the escalating processing capacity of computers and partly by the urgent need to be able to process the vast amount of information being generated by gene sequencing as well as the need to capture and digitise the millions of paper records kept by various biodiversity collections.

Technologically, Australia is in a good position to keep up with advances in this area, but there is a critical shortage of people with the prerequisite skills and capabilities. Many universities are responding by developing various courses in this area, but there is a built-in lag and hence some scope to develop more linkages (and consistent curricula) among these educational institutions.

CSIRO was one of a consortium that bidded for a Cooperative Research Centre (CRC) for bioinformatics in the last round; one of the key drivers for the bid was to network the major universities to address this issue. While the bid failed, apparently due to lack of proposed industry involvement, the parties have continued their discussions, to pursue these objectives by other means.

In the area of biodiversity informatics, there is a significant international push to coordinate and network national databases. These will be in the public domain to provide scientists and other users free access to our natural heritage, which is an objective of the International Convention on Biological Diversity to which Australia is a signatory. The limiting factors in this area are two-fold: first the capacity to digitise and verify the information currently held in paper records, which are often incomplete; secondly, the many undescribed species in the Australian biodiversity, which are likely to contain traits of significant economic value. Progress in biodiversity informatics will enhance its predictive power and value of biodiversity knowledge to bioindustries.

Similarly, access to raw gene sequence data would also be free; but the real value lies in the annotations to the sequence data providing information of gene functions and biological activity and in the proteomics built on the genomics. This information is of proprietary value to the highly competitive drug development industry, and a few, large bioinformatics corporations overseas, such as Celera Genomics Inc., are assembling large sequence databases for plants and animals of economic value and may be able to dictate the conditions of access to these databases. Australian science organisations cannot compete with these endeavours but must be able to negotiate access to data on favourable terms relevant to our needs.

The bargaining chip that would be most effective would be collaborative arrangements in which we contribute to these databases with annotations relevant to our own biodiversity . Fortunately, we are in a good position to do so with these companies showing significant interest in our research capabilities, although they will source IP competitively from anywhere in the world.

Bioprospecting impediments

As described above, bioprospecting is basically a collection activity, which is largely demand driven by the subsequent biodiscovery processes and demands, and tends to be cyclical and vary over time. At present, there is a ready supply of “raw” samples in the system awaiting downstream screening processes, given the cost of screening relative to samples.

However, the real issues here are gaining access to material and securing clear title to any property or characteristics utilised in the subsequent industry processes. The latter is essential a matter of constructing the commercial arrangements using our biodiversity knowledge as a leverage point to gain control over how the IP is used down-stream.

As noted in the Issues Paper for the Inquiry, the policy issues surrounding access to biological resources are complex and have preoccupied all Australian jurisdictions for some years. These issues are much broader than just relevant to bioprospecting and have to meet a wide array of domestic and international policy objectives.

In more recent times, Minister Robert Hill commissioned an inquiry into access to resources in Commonwealth Areas under the chairmanship of Mr John Voumard[10]. In our submission to that inquiry, CSIRO pointed out that in many ways bioprospecting represents a special case as compared with access being sought for other purposes, such as research, plant breeding, and conservation needs, and that there would be merit in clearly differentiating between the different types of access. There is a real issue about ownership of material held in *ex situ* collections and we look towards the Voumard Inquiry for some clarification of this issue.

Furthermore, CSIRO made a strong point to the Voumard Inquiry that national consistency in the various State and Commonwealth permit schemes regulating access to biological resources must be achieved as a matter of urgency. This is particularly relevant to bioprospecting, as there are at present significant variations in both policy objectives and administrative systems between all jurisdictions. As a result, there is a real risk of international bioprospectors “shopping” between the various jurisdictions to suit their own needs.

It is relevant for the present House of Representatives Committee Inquiry to note that the policy development from the Voumard Inquiry is progressing, albeit somewhat slowly. The Voumard Inquiry has raised many significant issues, and, at the operational level, CSIRO is working with officers from Environment Australia towards addressing the issues that we raised in our submission. However, it might be helpful to get the specific issue of access to biological resources for the explicit purpose of bioprospecting back on the national policy agenda. CSIRO recognises that this means difficult issues like indigenous rights over traditional knowledge cannot remain unaddressed.

Biodiscovery impediments

More than any other area of the entire business system, biodiscovery is dominated by a global R&D system. Australian science is strong in many areas and can offer competitive advantages to attract and retain multinational industry interests in research work on our own biodiversity. However, we will not be able to service all needs, and the Australian science system needs to focus on our strengths.

[10] See footnote 1 for references.

As the whole area advances rapidly, there are classic signs of stress on infrastructure, skill development and retention, and competition between national centres. New areas of research show significant promise, such as genomics, proteomics and structural biology, and by and large funding and the capacity to attract venture capital to pre-commercial research limit growth. CSIRO notes that the recent Innovation Strategy aims at addressing these areas and looks forward to working with the Government in implementing some of these new initiatives. However, the particular problem of the lack of skills in core information technologies in support of bioinformatics requires special, urgent treatment.

It is essential for Australian science to maintain a seat at negotiating tables overseas; in particular researchers need access to IP controlled by multinational organisations. Similarly, participation in international collaboration provides us with strategic links to build strengths in critical but under-resourced areas.. We are at a natural disadvantage based on the size of our research system and the distance to overseas centres of excellence; in particular in the areas of biotechnology research where very significant investments are being made in the public sector. Continued support to showcase Australian science capabilities overseas and participation in international collaborations are important issues for Australian research organisations like CSIRO.

Domestically, despite the contribution the CRC program has made to build better links between industry and public sector research organisations, there is still some fragmentation of research effort. Encouragement of consortia of public R&D providers and the private sector to pool the necessary expertise and facilities to develop bioactive molecules further along the product development pipeline in Australia, e.g., to early stage clinical trials, would be a valuable contribution towards industry development.

Bioprocessing impediments

Industries involved in bioprocessing in Australia are mostly based on by small to medium enterprises. Whilst often very entrepreneurial, they lack access to sufficient capital to commit themselves to the high-risk commercial development of new products, hence focus on existing opportunities. This is unfortunate, as the infrastructure requirements normally are relatively modest, and therefore new industries can be established more or less anywhere, provided they have ready access to raw materials, skilled staff and good services. The case for the primary industry sector to provide “green” carbon sources rather than from petrochemical has been made above.

Technically, there is a shortage of pilot plants to undertake the necessary research for scaling up of fermentation processes. A lot of this work could happen in Australia, even in regional areas, but is often undertaken overseas. Whilst CSIRO has good capabilities and facilities in this area, we only have sufficient to support our own research needs, and we believe there is a need for some form of a national technology transfer centre or facility for bioprocessing R&D within the next few years to offer such services to industry to commercialise research in Australia prior to the commercial manufacturing stage.

Bioindustry impediments

To develop a prosperous bioindustry in regional areas would require solving all of the problems identified above. There will be infrastructure requirements, including the industrial scale-up capacity in fermentation, adjustments to primary industry sectors while maintaining production sustainability, as well as needs for a highly skilled workforce. Whether we attract companies to establish new production capacity in Australia or develop the technology onshore, this skills shortage must be addressed. This new industry sector will demand a new breed of production engineers, chemists and biologists capable of extracting value from a wide range of resources and data, and being able to operate in a cross-disciplinary manner.

Routes to market in these industry sectors are often very long with significant similarities to the old pharmaceutical and pesticide industries based on chemical synthesis of analogues to known active substances. As the majority of product development costs are incurred at the latter stages, a robust patent system is critical for success.

However, the majority of these issues should not be hard to overcome, and the barriers may have more to do with industry leadership and widespread perceptions than technological impediments.

Some of these perceptions are not just around industry issues but have more to do with public understanding and acceptance of the role of biotechnology in the Australian economy. CSIRO seeks to contribute to addressing the public information needs, for instance through public lectures, our science education activities etc. and follows the debate in the media. We suggest this area would continue to require some continued support over the next few years.

RESPONSE TO TERMS OF REFERENCE 3:

The capacity to maximise benefit through intellectual property rights and other mechanisms to support the development of these industries in Australia.

The development of these high technology industries would bring many benefits to regional Australia. Naturally, there would be direct benefits such as: the development of a highly skilled workforce; capital expenditures on infrastructure and manufacturing plants; the potential for primary industries to produce new industrial crops and commodities of very much higher value; and national prosperity from being part of a global business system which can then flow onto the regions. CSIRO asserts that there is a clear case for bioprocessing industries based on primary industry commodities as feedstock, and as capacity, infrastructure and strategic IP positions develop, there are increasing opportunities in the areas of pharmaceuticals and specialty chemicals.

However, these benefits accrue at the manufacturing end, whereas much of the IP is generated earlier in the product value chain. Joint venture arrangements in bioprospecting can provide the necessary mechanism to retain and manage these benefits in Australia through the existing patent system by licensing that enables inventors to reap the financial benefit of years of research. This system has proven itself over many years in the pharmaceutical and chemical industries, which share the problems of long lead times and high risks that characterise newer high-technology bioindustries as well. CSIRO believes, therefore, the current IP mechanisms do not appear to require major adjustment as such,

Nevertheless, CSIRO has observed that there is a significant lack of uniformity in skills in terms of negotiating deals with the multinational companies for maximum commercial benefit to Australia., It is important to avoid the situation in which some multinational companies play off local research providers against each other to secure the best deal for themselves. This includes structuring contractual arrangements at the bioprospecting end to ensure Australia retains the rights to renegotiate terms and to receive rewards from any subsequent commercialisation of products derived from Australian biodiversity. It is noted that a new Australian Centre for Intellectual Property in Agriculture (ACIPA)[11] to be based at the Faculty of Law at the Australian National University was launched in late February 2001, and CSIRO welcomes this initiative.

The Committee's Issues Paper correctly identifies the problem that there are often unrealistic expectations of the financial rewards for ownership of the initial biological resource or the associated knowledge. Whilst there are numerous examples where individual plants are known by Australian indigenous communities to have particular and desirable properties, it should be recalled that quite often the biodiscovery stage involves mass screening processes and the individual origin and characteristics of biological materials may be unknown to the company doing the screening and discovering biological activity. There is therefore a critical role for bioprospectors in identifying the original source and tracing it back to the biological specimen to secure a return flow of benefits. For these reasons, CSIRO is increasingly seeking joint venture arrangements with other agencies and companies.

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[11] For further information of ACIPA, refer http://law.anu.edu.au/centres/acipa/

Finally, it should be recalled that the rewards flowing back from the industrial use of anything originating from our biodiversity do not necessarily need to be monetary, in fact greater national benefit can sometimes be obtained from maintaining strong relationships that can give access to further and more involved collaborative ventures; access to core, enabling technologies; and to establishment of either research or manufacturing facilities in Australia.

RESPONSE TO TERMS OF REFERENCE 4:

The impacts on and benefits to the environment

The development of new industries based on the entire business system outlined in our submission may have some environmental effects that are positive. Naturally, there are environmental stewardship issues common to many similar industries, which can be managed through the conventional systems.

In terms of bioprospecting, there are concerns that unrestricted sampling may inadvertently threaten the conservation status of endangered species. However, the amount of material collected for samples for research and subsequent screening would in nearly all cases be so miniscule that any impact on biodiversity should be negligible. Harvesting large amounts of material for commercial extraction may be different, but at that stage it would be issues surrounding individual species for which there would be a lot more information available about conservation issues versus the logistics of sourcing sufficient feedstock. Furthermore, any cost-benefit analysis would quickly indicate the lack of commercial opportunity if wanting to exploit rare or endangered species., The various access regimes should be able to cope with any such conservation concerns, especially those relating to.

Particular issues arise when GMOs produce special commodities such as plants, milk or eggs for industrial extraction of certain chemicals. The adoption of gene technology into primary production is, of course, the subject of intense policy development and public discussion at the moment, but it can be assumed that solutions to issues of commodity segregation and identity preservation can be readily found and any security and biosecurity measures be established.

The broader issue of environmental impact of GMOs being introduced into the Australian environment and agricultural production system has been recognised by CSIRO as an issue requiring more research. Accordingly, CSIRO has developed a research strategy that provides for a systematic approach to ecological risk assessment involving basic, strategic and applied research aimed at meeting both immediate and longer-term goals. CSIRO envisages that the strategy will evolve within a broader, national framework and deliver against the visions of the National Biotechnology Strategy. In the first instance, a three-year study is proposed as a component of the CSIRO Biodiversity Sector Plan to build a centre of excellence that draws upon expertise across the breadth of the organisation and with collaborative links to other research providers, including universities and Cooperative Research Centres.[12]

Compared with traditional chemical plants, industries using fermentation technologies for biosynthesis of new products may have less of a waste problem. In many cases, traditional chemical synthesis will result in a reaction mixture where only some of the constituents are required and further purification is often necessary to remove reagents and catalysts. When using biological and enzyme systems, the actual reaction can be more efficient in terms of outputs. Furthermore, the waste, being of biological origin, will often be suitable for recycling or low-risk decomposition.

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[12] For further information see: http://www.biodiversity.csiro.au/2nd_level/3rd_level/plan_gmos.html

These industries have another environmental advantage. Because of the biological processes being employed, there are numerous opportunities to develop additional biodecomposition and bioremediation technologies, suitable to deal with specific waste problems and for them to become new industries in their own rights.

Finally, replacing non-renewable petrochemicals with renewable or “green” feedstock offers additional benefit in terms of the carbon cycle and impact on the greenhouse effect, especially when operating at a commodity scale. Manufacturing systems based on biological processes are inherently attractive because they use the basic renewable resources of sunlight, water and carbon dioxide in low energy processes to produce a wide range of simple to complex molecules. They use biological systems that have been fine tuned by millions of years of evolution to provide efficient synthesis of inherently high fidelity and low toxicity product, with minimal and often recyclable waste.

Environment Examples: Bioremediation

Microbes to clean-up toxic gold-mining effluent: CSIRO and BacTech Pty Ltd, a Perth-based mining biotechnology firm, have discovered species of microbes that can devour toxic effluent from gold extraction. This discovery opens the way for 'clean and green' processing of minerals such as gold, copper, nickel, and zinc. The newly found bacteria can break down the poisonous thiocyanate formed from the cyanide used to extract gold, leading to the development of a process for cleansing the waste streams from inland gold mines, where clean water is often a scarce and costly commodity.

Bioremediation - cleaning-up pesticide residues. Pesticide residues can be removed from the surface of fruit and vegetables, the soil, from industrial wastes, from water, or from human effluents, by adding pesticide-degrading enzymes derived from insects and microbes. The enzymes will be produced in industrial bioreactors containing transgenic microbes. CSIRO has an agreement with the Australian industrial chemicals manufacturer Orica to commercialise the technology. The beauty of the approach is that the biochemical reaction that breaks down the residues does not consume the enzymes, so only small quantities are required and as there is no need to release the transgenic microbes or cells that make the enzymes into the environment, the risks involved are inherently low.

CONCLUSIONS AND RECOMMENDATIONS

As outlined earlier in our submission, the evolution of these high technology industries based on bioprospecting, bioprocessing and related biotechnologies take place within a global business system in which a number of technologies and operators interact. The products that may arise must be able to compete with overseas markets and business opportunities, and it is therefore critical that Australia clearly defines some market niches in which we can develop and market our excellence. Trying to be a world leader in anything but selected niches will just not work.

At the same time there are tremendous opportunities to utilise our existing rural infrastructure to bring economic growth into regional Australia by encouraging the development of small to medium enterprises using fermentation and other microbiological systems to make product based on biological feedstock. CSIRO would like to reiterate that the only way to develop a prosperous bioindustry in regional areas based on bioprospecting Australian biodiversity would require solving all of the problems outlined earlier by taking a holistic, whole-of-business-system approach driven by visionary and skilled, entrepreneurial industry people.

Bioindustry example: Long-term vision for change with measurable targets
"DuPont will derive 25 percent of its revenues in 2010 from non-depletable raw materials, such as carbohydrates. This compares to less than five percent of revenues in 1998. Our goal is to create a "sustainable growth" company through the discovery and commercialization of new science, and through the ongoing reshaping our portfolio of products and services. We view modern biotechnology to be a critical enabling technology to help us shape our future".
Extract from DuPont's 25 year vision[13]

The field of industrial bioprocessing is rapidly evolving with almost limitless potential applications. Very large public and private sector investments are being made globally. In some areas we may wish to ensure access to the new technologies, in others we have an opportunity to develop the technologies *de novo*.

CSIRO notes the recommendation in the Draft Chemicals & Plastics Industry Steering Group Report to the Government[14] that "*A 'landmark' project that is at the forefront of science and innovation that integrates the chemical industry into other sectors, such as the emerging bioprocessing industry, should be supported.*" The challenge is to identify the niches where Australia can be competitive. This will require a close dialogue between the existing chemical industry, the emerging biotechnology industry and the R&D capacity within the public sector.

The key message is to adopt an operating paradigm of "think globally – act locally".

At the strategic and policy level, CSIRO recommends that a number of considerations should be made:

13 Refer http://www.dupont.com/biotech/difference/principles.html
14 The draft report was released for public consultation in December 2000 by the Steering Group but has not been placed on the Internet at the time of writing. The work of the Steering Group can be found on this web site: http://www.isr.gov.au/agendas/Sectors/chemicals/index.html

- These industries offer huge potentials but they are only in their infancy. Rapid technology growth and competing investments overseas mean that to develop these industries in regional Australia, some form of support or assistance may be necessary to facilitate this process. At the same time, such change may assist further structural adjustment in the primary industry sectors and allow farmers to diversify.
    - ***CSIRO recommends that these industries be afforded policy attention with consideration of financial support to enhance their development in regional Australia.***

- It will be essential that the process is driven by and owned by the industries themselves. Strong vision and leadership by industry will be essential although the Government can play a strong role by setting and monitoring some nominal targets to achieve change. These targets could be nominal but intended to lessening dependence on non-renewable petrochemical feedstock, replacing them with renewable raw materials
    - ***CSIRO recommends that the Government consider setting targets for industry development and encourages strong industry vision and leadership.***

- CSIRO believes a focussed and concerted effort need to be made through the National Biotechnology Strategy to enhance the capabilities in all core biotechnology R&D areas that underpin these industries. It will be important to identify national niches and to balance the efforts and interrelationships between these biotechnology areas; this will require a coordinated and holistic approach by the Government.
    - ***CSIRO recommends that the National Biotechnology Strategy be further developed to enhance overall national capabilities in core biotechnologies relevant to these industries.***

- CSIRO suggests that using the approach taken in this submission of focussing on the product value chain may assist in shaping an appropriate industry development framework.
    - ***CSIRO recommends that a bioindustry development strategy for these industries be developed around the product value chain as advocated in this submission.***

In addition, CSIRO recommends that there are a number of technological issues that can be addressed:

- In the area of *bioinformatics*, CSIRO notes that ready access to information kept in large databases and availability of trained staff are key issues. *For biodiversity informatics*, Australia's participation in the Global Biodiversity Information Facility (GBIF) is a major step forward and continued attention to maximise our involvement should be made; for *molecular bioinformatics* there is a need to maintain national involvement and access to large *genomics* and chemical databases held overseas.
    - ***CSIRO recommends the development of a national strategy for bioinformatics to deliver core skills and data access to Australian R&D organisations.***

- CSIRO notes that some momentum has been generated to address the issues relevant to *bioprospecting* in the context of the wider policy agenda on access to biological resources, principally at the Commonwealth level. Further work is necessary to develop a national approach that is consistent amongst jurisdictions; there are already mechanisms in place to achieve this outcome and the processes should continue.

- ***CSIRO recommends the Inquiry note progress being made in this area.***

- The quality of Australian research in *biodiscovery* must be at an internationally competitive level to ensure we continue having a seat at negotiating tables overseas to secure capabilities and holding IP positions necessary for our own needs. It would be beneficial if some effort were made nationally to identify attractive niches for our research and encourage further collaborative consortia between public and private sector research organisation to enhance the capacity to identify bioactive molecules.
  - ***CSIRO recommends further exploration of opportunities for collaborative research in areas of strategic importance to Australian science and industry development.***

- There is a shortage of pilot plant facilities in Australia to nurture and retain industrial *bioprocessing* research. The establishment of an industrial bioprocessing plant would showcase Australian capabilities and signal to the global market that Australia basic strengths in efficient agricultural production and biotechnology can be combined into innovative manufacturing capability.
  - ***CSIRO recommends infrastructure needs in this area be addressed through the National Biotechnology Strategy.***

- Development of *bioindustries* may still require attention to public concerns about biotechnology and gene technology in particular. This is a core role for Biotechnology Australia, which is supported by CSIRO. The establishment of a new regulatory framework may also help with addressing public concerns; possibly further aided by CSIRO’s research into the potential environmental impact of GMOs.
  - ***CSIRO recommends that the public awareness program of Biotechnology Australia be continued.***

These technological issues should be pursued collectively by the R&D performers (universities, CSIRO, private companies), R&D funders, and industry groups while being facilitated strategically by the Government agencies within Biotechnology Australia.

GLOSSARY

A wealth of terms is commonly used when describing specific areas of biotechnology. Many of these terms have quite specific, technical meaning whereas definitions of some of the broader terms differ between scientists, policy analysts, business people and the general community. Below is a list of terms and their meaning as used in this submission:

Biodiscovery

Biodiscovery of biological active molecules involves the extraction and screening of prospective compounds sourced from biological material. Often the processes involve a number of molecular technologies to identify and understand the genetic and functional basis for the biological activity in test systems.

Biodiversity

Biodiversity means the variability among living organisms from all sources, including terrestial, marine and other aquatic ecosystems, and the ecological complexes of which they are part.

Biodiversity Informatics

Biodiversity Informatics is a branch of *bioinformatics* using information technologies and mathematics to study complex biodiversity datasets principally based on observations, records and specimens of individual species held in collections, and to provide the tools to analyse such data on an ecosystem basis.

Bioindustries

Bioindustries generally refer to high technology industries using biotechnologies in their main manufacturing processes. In this submission the terms refers to manufacturing companies that produce products based on traits, compounds or gene sequences sourced by bioprospecting from Australian biological resources

Bioinformatics

Bioinformatics is the merger of the fields of biology and informatics to use powerful computational and statistical techniques to process a wealth of biological information for particular research purposes

Biological activity

In the biodiscovery process, biological activity refers to the suppression or enhancement of growth or other biological responses of a given test organism when treated with extracts from other organisms. Commonly used to identify therapeutic or pesticidal properties of particular compounds.

Biological Resource

Biological resources refer to living entities, populations, organisms, genetic resources or parts thereof, including genetic resources and biological collections, and any other part of ecosystems with actual or potential value for humanity.

Biomining

The use of micro-organisms in mining operations to extract metals from crushed ore.

Biopesticides

Application of micro-organisms that are pathogenic to specific groups of agricultural pests and diseases.

Bioprocessing

Bioprocessing include the development of industrial processes to manufacture new biological products on a commercially viable scale, often using fermentation or enzyme processes

Bioprospecting

Bioprospecting refers to the process of collecting samples of biological resources on a commercial scale for subsequent extraction and identification of substances with biological activity.

Bioremediation

Use of micro-organisms to remove toxins or chemicals from contaminated soil or produce, e.g. rehabilitation of mine sites and cattle insecticide dips.

Biotechnology

"The application of science and engineering principles to the processing of materials by biological agents to provide goods and services" (OECD, 1982). Sometimes the term 'modern biotechnology' is used to describe recent research activities as distinct from traditional fermentation and other industrial processes as well as plant and animal breeding.

Endemic species

Species that only occur in a given country and nowhere else.

Feedstock

Raw materials used for an industrial chemical or biological process, e.g. polymers used for plastic manufacturing or sugar cane being processed at sugar mills.

Functional genomics

The study of genomes to determine the biological function and regulation of all the genes and their products.

Gene Expression

In genetics, manifestation in a living organism of a characteristics specified by a gene. In industrial or agricultural biotechnology, production of a specific protein by inserting a gene into a new host organism.

Genetically Modified Organisms (GMOs)

A living micro-organism, plants or animal in which the expression of particular genes has been modified by the use of gene technology

Gene Technology

Gene technology is a specific subset of modern biotechnology involving the manipulation and modification of the genetic material ("recombination") of living organism. This can be in the form of switching off or "silencing" a particular gene within the same species or transferring gene sequences from other species.

Genome

The entire genetic material in the chromosomes of an organism.

Genomics

The study of whole sets of genes and their interactions rather than single genes.

Global Biodiversity Information Facility (GBIF)

GBIF is an international coordination mechanism for large and distributed networks of biodiversity databases, established to facilitate exchange at a global level of biodiversity information on electronic form. Australia is a participant in GBIF and is submitting a bid to host the International Secretariat for GBIF.

IP Commonly used abbreviation for 'intellectual property'.

Leads

Biologically active chemical substances extracted from plants, animals or micro organisms that exhibit a response in initial screening tests as part of the biodiscovery processes and progress further along the product value chain

Molecular Informatics

Molecular Informatics is a branch of bioinformatics using information technologies and mathematics to study complex datasets in molecular biology and genetics, and to provide the tools to analyse gene sequence data and related information.

Proteomics

The study of the full set of proteins encoded by a genome.

R&D

Commonly used abbreviation for 'research and development'.

Structural biology

The study of the three dimensional structure of large numbers of proteins using both experimental techniques and computer simulation.