SUBMISSION

The House of Representatives Standing Committee on Primary Industries and Regional Services Inquiry into Development of High Technology Industries in Regional Australia based on Bioprospecting

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INTRODUCTION

We believe Australia will become a world leader in how it facilitates, manages, and brings to commercial reality, discoveries made from bioprospecting. It already has a highly skilled science base and is profoundly rich in marine and terrestrial biodiversity, most of which remains unexplored. This is a highly unique combination in a developed nation with an active supporting administration provided at both State and Federal levels. Added to this are recent initiatives such as the National Biotechnology Strategy and the Biotechnology Innovation Fund which provide the scaffold and funding mechanisms to jump start realisation of wealth from biodiversity.

Australia is now highly active in creating precedent in evolving novel legislation and policy designed to facilitate bioprospecting, while ensuring that environmental bottom lines are not compromised. The process is transparent and aimed at maximising all the benefits that accrue from bioprospecting research and ventures. Recent agreements such as the AIMS - Queensland Government Biotechnology Benefit Sharing Agreement, are being used globally as examples of how all stakeholders can benefit from exploration of biodiversity for biotechnological leads.

The potential of natural compounds for commercial application has only just begun to be realised (Beese , 1998). Marine natural products in particular represent the most diverse and unexplored source of compounds (de Vries and Hall, 1994, Capon 1998, Cragg et al 1997). There are many and varied applications such as drug discovery, agrichemical discovery, nutriceuticals, adhesives, biomolecular tools, antifoulants, and many more (Colewell 1999). Value can be added at all stages of biodiscovery from collection and taxonomy progressively down the value chain of development. Some drugs generate over $1billion per year in sales, while the value of a 50g to 1kg sample of an organism can be $US100-200/sample. In between there are many opportunities for capture of IP and revenue.

Natural chemicals remain the best leads for development of novel drugs, agrichemicals and industrial biocides. Synthetic manipulations can substantially enhance these chemicals, but nothing can equal the 4 billion years of innovative chemistry undertaken by Nature. We can only add to that with our artificial technologies. If anything, bioprospecting needs to be substantially upgraded and the quality of the approach substantially improved. It needs to become a science not an activity.

Natural products will always be the best source of novel and use chemicals (Breese, 1998) because:

- natural products have unique features not present in synthetics
- unlimited structural diversity compared to human developed chemicals
- their patentability due to their distinct chemical identity
- Complex mixtures: biologically active metabolites often occur in complex mixtures, variations on a structural theme and frequently leads are identified from mixtures. Indeed a number of leads can be derived (with different bioactive functionalities) from one mixture.
- Many structurally diverse chemicals in any one sample increasing likelihood of success

GENERAL COMMENT

This submission provides comment on all four issues raised in the Terms of Reference Document and takes up the challenge to specifically identify opportunities in rural and regional Australia. A few key comments can be usefully made at this point on general issues and discussion made in the Terms of Reference document. The submission has a marine focus.

Potential barriers to Australia reaping the benefits of bioprospecting

LIMITED FUNDING AT THE COLLECTION AND IDENTIFICATION PHASES OF BIOPROSPECTING

Significant here is the lack of early phase funding in the bioprospecting process. This severely limits/compromises capture of all potential IP and wider environmental, community benefits. It also severely compromises the quality of the collections themselves particularly for future use. For example, in most instances of bioprospecting activity, a company will hire collectors to do the field work and may hire taxonomists to value add the collection with identifications (often only those samples which are found to be active in the companies particular screen). If unskilled contractors are used then there can be limitations imposed (due to cost) on quality of vouchers and how they may be accommodated in appropriate museums. Their value to taxonomists is reduced and the quality of identifications can be suspect. This clearly limits value to the company (hinders/misleads dereplication) and limits

additional benefits to the community (e.g. marine managers). Conversely, if the collecting activity is adequately resourced and professionally conducted, resulting species lists will add enormously to the store of biogeographic information for better resource management as species lists to add to the store of biogeographic information cannot be compiled (see below Appendix 1). If there is sufficient funding at early stage, additional information such as quality of the environment, microhabitat condition etc can be collected. These data are invaluable to all stakeholders, in particular the company. Information about why a particular species may be active is of crucial importance to establishing that the lead is a good one and indeed, to widening the opportunity as search for close relatives, or species in similar microhabitat etc can lead to better discoveries. The benefits to other stakeholders, i.e. public, marine managers, posterity, etc. cannot be lauded highly enough. Invaluable information is gained on species diversity, bioregion makeup, habitat quality, endangered habitat, biodiverse/bioactive hotspots etc (see below). Without accurate, rigorous data attendant to each sample collected, recollections for more detailed screening and analysis will be very difficult.

If funds are available to bioprospect diligently with wider long-term public good benefit in mind, the sample base can represent a long term resource for the nation, and the growing bioinformatics base an extremely valuable asset. Adoption of such an approach need not compromise exclusivity as such rights can be negotiated serially and for varying periods of time. A common scenario is for bioprospecting contracts to be arranged on an exclusive basis with a company where sample access by others is severely limited (samples are deemed to be exclusive property of the contracting company. This can prohibit the use of the biodiversity for many different research activities that would maximise the possibility of finding commercially promising chemicals.

An ideal situation is one of co-investment in the collection and taxonomic phase of bioprospecting to ensure that all collections are made with quantitative habitat information, identifications are made by the best people available and allow extended research/training opportunity, that samples have clear ownership detail with clear links to the region of origin, and that samples become available for other screening opportunity once the key collaborator/company has decided which ones are of no further interest (this will be most of them). Such a scenario maximises information, opportunity for science/ community benefit (particularly through a knowledge base for better resource management, via species lists, bioregion establishment etc) and maximises opportunity for any one sample to be screened many times thereby enhancing the likelihood of a commercial success. Quality data acquisition at collection and in identification of samples also represents commercially relevant IP, as it provides enormous benefit to any collaborating company. They are able to expand upon any lead by examining closely related species or investigating correlations with

microhabitat (an active chemical lead may be associated with evidence of recent pathogenic attach for instance). They can also negotiate access to an accumulating store of information to widen any lead. Such a nationally significant bioinformatics base exists at AIMS for marine samples and elsewhere for terrestrial biodiversity. At AIMS correlation among a wide range of parameters (species, habitat, chemistry, pharmacology etc) is readily achievable for a growing sample base of over 20,000 macro and micro-organisms. Samples are accessible for collaborative repetitive screening both nationally and internationally and the database is regularly used for generating species assemblage lists for many marine managers and research projects. Matching fund sources do not exist for this type of collaboration however, and it is difficult to maintain the collection without this support. The retention of ownership of samples and IP at the ground floor would be reason enough to suggest that funding or support at this level is significantly in the regional and national interest.

SIGNIFICANT VALUE ADDING TO NATURAL PRODUCTS DOES NOT ONLY OCCUR AT COMMERCIALISATION AND PRODUCTION PHASES

We consider that the statement made in the discussion document attendant to the Terms of Reference is erroneous:" The significant value adding to natural products occurs at the commercialisation and full scale production stages of the process, not at the collecting, sampling, analysing and screening stages".

Indeed we feel quite the opposite is the case as introduced above. It is at this very early stage that benefits for regional Australia can be set in motion. As will be discussed in detail below, the benefits of fully qualified data acquisition at sample collecting and in subsequent taxonomic work are substantial. They include lists of species (often the first and only records, particularly in remote or unsavoury locations), and are of paramount importance in setting biogeographic zones, identifying habitat under threat, for protection or providing baseline information for comparison when impacts occur (pollution/marine invasions etc). Invaluable data is thus also available for users of 'bioprospected' samples to permit reliable and sustainable recollection (generation of recollection effects assessments/permits etc), and allow structured appraisal of possibilities to amplify leads and in the chemical dereplication process. This may include examination of closely related species, looking at microbiological/other correlates with desirable activities, and examination of variability in target chemistry over space/time (there may be better molecules or related structure biosynthesised in another season). In short, quality, skilled value adding at the basic step of initial collection will be highly beneficial to all. The significant beneficiary is of course the region (then State/Nation) and the natural resource owner/collection team/institute/company who can maximise capture of highly valuable IP. If this effort is linked to local or national capability in screening and structural chemistry, then potential to create novel compounds of more desirable

activity for a particular target (or indeed other health/agrochemical/etc targets) is enormous.

In addition to this, it is possible to establish at the outset (for any 'leads' from natural sources), options for sustainable production. These can potentially include harvest, aquaculture, fermentation, and synthesis. The former three are ideal for regional development. If contracts are well structured, these options can be funded and entertained early in the process at scales appropriate to the current progress of particular leads, and at locations likely to effect best options for sustainable supply - in many instances this will include regional production sites. There must always be a commitment to identifying the most reliable and economic method to supply global demand for any successful compound/tool, but if IP on the production side is captured within Australia, then the benefits are clearly obvious. If fermentation/harvest/aquaculture modes of production currently being investigated are found to be economic (even with synthetic post harvest manipulations) the options for substantial regional development are enormous.

POTENTIAL VALUE OF COMPOUNDS AND SAMPLES

We strongly concur with the statement that potential value of compounds be recognised from the outset. This needs to be extended to the potential value of 'samples' as these can be made available for re-screening in different sectors at different times (sequential agreement/contract to exclusivity periods). Most samples screened by a company are rejected, yet these samples may contain compounds which are highly desirable in other sectors (anti-tumour/anti-viral active compounds have completely different biological activities/attributes to agrochemicals - a rejected antiviral candidate which simply has too much toxicity may be the next wonder pesticide). Additionally, there are new screens and new targets arising constantly. The long-term cumulative value of any one sample is very high indeed. Any significant collection or library of samples, particularly if curated for natural products discovery, should be considered a significant national resource and maintained as such for future generations/opportunity.

IN FIVE YEARS, ALL OF AUSTRALIA'S BIOTA SCREENED? NEVER

As above, there will always be new targets, new pathogenic threats, resistance, new screens, new ways of extracting compounds and new ways of synthetically/artificially modified natural leads be it manipulating physiologies or DNA. The range of metabolites produced by organisms in different biological and physical microhabitats of itself means that there are endless compounds available from the existing store of biodiversity. Added to this is natural evolutionary process, likely to be fast in micro-organisms, and the fact that only a fraction of biodiversity has been sampled to date. All biodiversity rarefaction curves (numbers of new species per cumulative sampling effort) are at maximum slope with no indication of reaching an asymptote, and

estimates of species number for most phyla have been increased 5 fold in the last seven years (Hooper et al, 1999). This is not counting the microbiota. Total global biodiversity is estimated to be over 500 x 10^6 species. A typical eukaryote has 50,000 genes and global marine macrofauna are the source of over 1.5 x 10^{12} primary products and more secondary metabolites (de Vries and Hall, 1994). Australia supports a significant proportion of these species. The options are limitless.

It is relevant to add here that it is this very diversity of interactions that promotes strong links between bioprospecting and conservation. One is dependant on the other. This is a benefit in itself, as new very real economic argument can be added to the plea for preservation of biodiversity and maintenance of habitat in its integrity.

Accessing natural resources and protecting the environment

REGULATION OF ACCESS TO AUSTRALIA'S BIOLOGICAL RESOURCES

Australia can do a great deal internally with respect to finding and developing to commercial reality natural compound leads to drugs and other products. At the same time there is urgent need to make the most of the opportunities offered internationally and we need to be pro-active in taking up the challenge and using the international collaborations on offer. There is an urgent need for a nationally consistent policy on how these interactions can progress (Baker et al, 1995). We wish to present the AIMS/Queensland Access and Biotechnology Benefit Sharing Agreement as a model to demonstrate how these issues may be accommodated to full advantage (see below). A fundamental need to progress the development of agreements is identification of ownership, and this still needs to be resolved in many instances, particularly traditional ownership. We hasten to add that there is an advantage to all in being able to identify an owner, since it provides a clear signatory to the agreements. Users of bioprospected samples (pharmaceutical companies for instance) want to have a legitimate owner identified since it secures agreements and greatly reduces the likelihood of surprise claims. The key to AIMS approach is to untangle access issues from benefit sharing ones. Thus these can be negotiated separately and with clarity. This two-step approach (separating access from benefit sharing) was also recommended by the Voumard inquiry into access to Australia's bioresources in Commonwealth areas, for application in regulations to support the EPBC Act.

CONSERVATION RETURNS

The fact that "returns to conservation have not been as great as anticipated" is due mainly to the fact that no drug/agrochemical company will pay large upfront fees for access (in developed countries) as they argue it is in the countries interest to provide opportunity for screening. Other benefits to conservation (documentation of natural

resources etc, as outlined above) have been largely overlooked or the opportunity not made use of.

Downstream costs of drug development for example are huge ($US300million plus per each drug) and hence there is resistance by companies to pay more upfront at an arguably risky phase. The debate about early investment in regional conservation effort has unfortunately confounded the endeavour of bioprospecting and hindered opportunity for realising potential wealth from natural resources (marine bioprospecting has stagnated in Australia for at least 7 years). The issue has also undermined realisation of the conservation benefits of this type of exploration and research. If a policy is adopted to facilitate access (with all environmental checks and balances in place together with appropriate audit), and investment is possible as outlined above, then there can be immediate and significant benefit to conservation. An example is the AIMS' approach to 'biodiscovery'. We use this term rather than 'bioprospecting', as it does not imply mining and suggests that long term multiple values can be attained from the first step in the process (collection). From the collected samples taxonomic data is made available to marine environmental managers/community to aid in setting biogeographic zones from species assemblage data and in support of argument for representative marine reserve location. In AIMS' collection effort, substantial effort is made to characterise habitat. For species of continued interest a substantial amount of work is carried out on it's distribution and abundance, variability in population size and in characterising habitat including associated species assemblages. On average for any species target, over $60,000/yr is invested in related ecological/taxonomic research. This is often the only data available for regional coastal Australia where assemblages are identified to species and ecological relationships are rigorously investigated. Additionally in any re-sampling exercise, there is immediate opportunity to secure external funds to permit extensive ecological survey. There are several examples from New Zealand that illustrate this point:

- re-collection of a deep water sponge was preceded with large scale survey and experimental work on effects caused by dredging the sponge. In all well over $1million was spent on this work (NCI/Public good science fund investment) including analysis of alternate modes of production and a great deal of information was generated for Ministries of Fisheries and Conservation Departments to aid in marine management.
- voluntary closure of fishing areas (to protect benthos from trawling),
- establishment of marine reserves to ensure natural ecosystem protection for biodiverse/bioactive hotspots,
- use of biodiscovery data in the decision making process for continuance/enlargement/establishment of marine reserves,
- data has also been used in review of setting environmental performance indicators for marine systems by the national management authorities.

In short conservation returns can be substantial, but rely heavily on quality data being available.

'COMBI CHEM', ARTIFICIAL EVOLUTION AND BIOPROSPECTED LEADS

There have been downturns in interest in natural products leads, particularly compounds from macro-organisms as they are expensive to collect/recollect and often the compounds of interest are difficult/uneconomic to synthesise. Indeed, over the last 10-20 years, there has been a highly variable investment of effort in this area. Australia's own experience in bioprospecting marine environments is a good example with the rise and fall of ROCHE, NCI and now AMRAD collection effort in the marine area. The reasons for the start/stop nature of company interest in bioprospecting are varied as aspects of economics, success, advent of combinatorial chemistry, and recently advent of artificial evolutionary techniques to manipulate DNA move in and out of vogue. Interestingly, bioprospecting for natural leads always has returned to the fore as arguably they provide the very best sources of novel compounds with highly specific biological activities. In Australia, much of the biodiversity (particularly in marine environments), has been locked up for over 5 years due to Access issues and represents an extremely attractive source of novel compounds. There have however been a number of lost opportunities (Salicylihalamides, Phorboxazoles, Eleutherobins - all anti-tumour active leads from Australian organisms). The information and indeed samples from this previous collection effort need not be wasted however as there can still be opportunity for screening and development.

Only a minute fraction of Australian biodiversity has been explored however and enormous potential exists for new discoveries from bioprospecting. Natural leads remain the best sources for development of novel drugs, agrochemicals and industrial biocides. Synthetic manipulations can substantially enhance this natural diversity, but nothing can equal the 4 billion years of natural combinatorial chemistry that is represented in the evolutionary process. We can only add to that with our artificial technologies. If anything bioprospecting needs to be substantially upgraded and the quality of the approach substantially improved. It needs to become a science not an activity.

Potential for regional benefits

DISCOVERY, DEVELOPMENT AND PRODUCTION ARE ALL OPPORTUNITIES FOR WEALTH CREATION IN BIOTECHNOLOGY

The approach of the Australian Institute of Marine Science to Marine Biotechnology is to optimise potential for wealth creation (in capture of IP, generation of new ventures) at all stages of the natural product lead and development process from discovery through to commercialisation. Thus we create new science in the

biodiscovery process and generate multiple outcomes as discussed above, we capture IP by elucidating the structure of leads and co-invest in development and we create new opportunity in assessing/developing methods for sustainable production of target compounds to meet projected global demand. There are two fundamental streams of research and development - discovery and production. The latter in particular has potential to lead to regional development and jobs both in raw material production, but also in value adding. For example, there are a number of marine derived compounds on the market today, used as biomedicinal tools (e.g. Bastadins, Okadaic acid, manoalide, source CalBiochem). These cost between $US9,000 to $US25,000/mg. These compounds come from Australian marine organisms (sponges, crabs etc) among other things and some could be sustainably produced by harvest, extraction and purification. Recent work at AIMS demonstrates that some of these compounds can be economically produced by aquaculture at orders of magnitude lower cost (inclusive of extraction and purification). This offers enormous potential for regionally based production industry (sustainable harvest, aquaculture, fermentation) and chemical industry (extraction, purification, synthetic value adding to the base chain molecule/warhead etc). These industries will be low volume, high quality and high profit enterprise and may be added to existing infrastructure (for example, polyculture integrated marine farms, expansion of existing dairy, animal by-product processing or chemical industry etc). The potential of bioproduct production industry is put into context when one considers that most of today's modern drugs are derived from natural product leads and since it is more economic, over 25% of these are still extracted from agricultural crops even though these terrestrially derived compounds are synthesiseable (Duke, 1993). The shortage of Kainic acid (derived from a marine alga) is now hindering neuroscience research is another very good case in point (Tremblay, 2000). There is an urgent need for alternate production protocols and natural biosynthesis from cultured organisms is an economic model.

It is this downstream long term production which is viewed as the most significant opportunity for Australia. Novel biotechnologies created in the discovery and production process are also of very high value as captured IP is patentable and therefore an asset. Thus, Australia not only has the potential to become an intellectually self-investing Nation, but also a discovery/production base for the globes new pharmacopoeia and agrochemical/industrial product arsenal.

DNA, GENES, GENE BIOTECHNOLOGIES AND BIOPROSPECTING

The recent advance of molecular technologies that artificially enhance evolution of DNA is certainly an area of cutting edge science and development. It still relies on bioprospected material for source organisms, micro-organisms and DNA. It does have the potential to remove the investment base distant from regions, but there are mechanisms where co-investment in this type of research and development can be based in country/state even region of prime biodiversity origin thereby maximising

scientific outcomes for the Nation. This research is in its infancy and will be reliant on maximising input of new genetic material (given the extreme high sample throughput capability). Proximity to pristine well-managed areas of high biodiversity is an enormous advantage as there is an exponential die off of micro-organisms in the time between capture and processing. Additionally over seasons and space there is endless complexity of biochemical interactions experienced in any habitat. In order to get close to realising even a small proportion of the possible proteomic outcomes from any organism, sampling will need to be intensive and frequent. We hasten to add that this sampling effort can be completely impact free as only very small amounts of tissue or cellular material need be taken in most cases without causing mortality. As above, we are suggesting an intensive scientific approach to bioprospecting, one that of necessity needs to be aligned with well equipped institutions which are in close proximity to biodiverse regions.

As above, there are significant opportunities to be experienced in the supply side of this biotechnology. With products based on expressed compounds from micro-organism culture, fermentation industry represents new venture for Australia. Once again this will need to be coupled with extraction, purification and value adding industrial capability.

REGIONAL INDUSTRIAL INFRASTRUCTURE OR CITY BASED?

The discussion point raised in the Terms of Reference preamble needs comment: i.e. that there is a 'tendency to invest in key city industry (even in other countries), and that Australian regional development is uneconomic or limited to a small royalty share due to a discovery in the locale'.

It is true that much of the chemical industry required for value adding new biotechnological products or in the extraction/purification process can be found in cities. It is also true however that these very companies exist in regional Australia close to the source of natural product supply (dairy, meat, sugar, minerals). It is also true that operating costs in transport, freight, rates, other resources for industry are lower in the regions, storage handling is cheaper and ports/freight out facilities are usually more assessable and strategically positioned. There are a number of key regional towns (admittedly now growing into reasonable cities) around Australia that are being identified as the best places for industrial investment because of their very regionality (access to natural resources, cheaply run industry, access to ports, etc). Examples include Townsville, Dampier etc. In biotechnological industry, there is advantage in being close to source of discovery and supply. There are many examples where biotechnological research and development of mega-clusters have simply been created *de novo* in regional areas (Maryland biotech villages sprang up on the outskirts of Bethesda, Biotech Valley was created in suburban/rural San Diego…). Land is affordable, there is investment and room to grow. Once established, these

ensembles of science institutions, companies, scale-up facilities and production industry create their own momentum and infrastructure.

THE FUNDAMENTAL REQUIREMENTS TO ALLOW AUSTRALIA TO MAKE THE MOST OF ITS BIODIVERSITY

- Early phase investment in bioprospecting by national and state government
- Transparent and fair policy on access to biological resources
- Diligence in environmental effects assessment of bioprospecting
- Independent management/audit of environmental performance, biosecurity and benefits to Australia (owner, region, state, nation)

Terms Of Reference

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

The vision we have for AIMS marine biotechnology development is as follows: We are concurrently exploring marine biodiversity for new leads across a wide range of health, agrochemical, industrial, environmental sectors; linking with premier research and development companies in each while establishing additional biotechnological initiative to produce the new products for global markets. Our philosophy is to use knowledge of Australia's Marine Biodiversity, underpinned by understanding of biochemical process in the marine environment, to generate new biotechnological products, amplify leads and provide the technologies by which they can be sustainably manufactured in Australia for global market. A structured quantitative 'biodiscovery' phase has been developed. This is defined as zero impact bioprospecting, sustainable fully controlled/audited recollection if necessary for secondary assay, and undertaking for zero extractive long term production of successful leads. This provides instant valuable output of biodiversity and marine conservation information in a form amenable to marine manager interpretation and use. It also provides the ground work for intelligent discovery of new leads. We envisage a growing 'stable' of key biotechnology industry partnerships, development of a variety of new products and establishment of economic production options in Australia with particular emphasis on rural Australia.

Burke (2000) lists seven traits for effective biotechnological developments/sites based on a continuum of technology development: foundation research, technology transfer, investment, company involvement, testing, trials and public acceptance. *These can all be best accommodated in regions where there is proximity to source of discovery, large-scale testing and manufacture ability and relevance:*

- Key components include researchers, universities, entrepreneurs and investors, ethicists and policymakers, companies and professional infrastructure, biomanufacturing capability*. Once again regional bases can offer all of these requisites and usually in very close proximity in regional centres such as agricultural or marine industry hubs*
- Any gaps in the continuum of development to commercialisation must be filled (created, funded or resolved through collaboration)*. Even the most centrally positioned (city) biotechnology cluster will have gaps. In the electronic age, long distance collaborations are easy. Key factors include those phases of operation where large scale manufacture and testing are involved…here regions have advantage.*

- The human factor is paramount. A cohesive interactive 'smart' community must be nurtured.
- Societal issues must be addressed: Foundation science, industry and other societal issues in biotechnology are more relevant/important than in any former technology. Public perception, policy and ethics are key issues.
- Cultural imperatives need to be understood. *Introduction of novel biotechnological concepts/tools/products in regional areas is likely to be accepted and or promoted first and with most ease, particularly in areas where environment, agriculture, health, welfare and economics are most critical…i.e. the benefits and issues are best appreciated in the regions where there is usually urgent demand.*
- The task is long term, 20years at least for any one product. It is apolitical and commitment must be grounded in State or Regional policy.
- An endeavour not just an industry must be built. *Development of interactive research platforms linking discovery to production to industry and creation of wealth is the goal.*

2. The impediments to growth of these new industries

The obvious and most immediate impediment to all biotechnology development based on bioprospecting is Access to resources in State and Commonwealth estate. Once again the AIMS-Queensland Agreement creates a precedent and useful model that has been adopted/commented on in the **Voumard Report**. This issue is critical. The solution has been to clarify the benefit sharing process, and isolate it from environmental scrutiny of applications to access resources. This has created legal certainty over the use of collections and provided protection of resource stakeholder interests, while ensuring environmental sustainability of resource use. These issues have been a significant impediment, and while they have been progressed substantially over recent years, adoption of workable procedure remains to be implemented in most jurisdictions. Important work on these issues must maintain a high level of priority to ensure timely resolution.

Another important impediment to gaining maximum benefit from new biotechnology based on Australian biodiversity is funding *bona fide* researchers in the bioprospecting process. Sample collections are often funded on a quota system for very little. The quality of the samples and the information attendant to them is therefore often very low. This reduces the usefulness of any information for other outputs (conservation, management, academic, social) and also greatly reduces the opportunity of making a useful discovery. As an example the compound Bryostatin I was almost dropped from clinical trial until it was found that chemists were collecting the wrong species variant in recollections. If the initial sampling had been done rigorously and included analysis

of distribution of the active metabolite within the populations, such a lead would have been progressed 10 years sooner.

In addition data/samples are frequently linked to just one company and then lost. IP is usually traded at this extremely early stage for extremely little. Rights of the public, both current and future generations, are frequently overlooked. The likelihood that viable genetic material is exported is also a significant concern if not correctly managed. It is true that the early stages are the most risky, but if done well where maximum benefit can be exploited for a range of stakeholders, the commercial beneficiaries of biodiversity will also benefit as the likelihood of making the discovery can be enhanced by orders of magnitude. For example, if a lead is found in Species X, and the information is available in properly managed databases, then closely related species or populations of the same species, can be readily identified and explored for similar compounds potentially with better activities or shifts in activity providing insight into how the natural product may be synthetically modified to effect desirable bioactivity. The AIMS approach adopts these concepts and at early phases we feel we have a model of collaborative operation (public good and commercial) that will benefit all interest groups for the long term. It is however very difficult to fund.

WHAT SORTS OF IMPEDIMENTS ARE UNIQUE TO REGIONAL AND RURAL AUSTRALIA?

Some suggestions (and it is acknowledged that some of them are generic to regional scientific research as a whole and not just bioprospecting, so their removal will benefit more than bioprospectors):

- Regional biotechnology institutions are viewed as being distant from large pools of investment dollars to support economic activity from the bioprospecting and biodiscovery process. Rural and regional economies are not large enough to invest in their own right and so other investment dollars must be attracted to support these activities and their transfer to the private sector. To garner such investment takes significant effort and lack of regular exposure reduces the likelihood of investors succumbing to the activities' appeal
- None of the "Group of 8" universities are located in rural and regional Australia, thereby limiting access to ARC and NHMRC funds because of their dominance of these granting schemes. These bodies (ARC & NHMRC) should be encouraged to favour bioprospecting activities in regional Australia without compromising standards
- There has been a lack of immediate contact with drug companies for whom bioprospecting is essential, to provide them with lead chemicals for development. International drug companies with a presence in Australia are located in capital cities and rarely venture beyond the Brisbane, Sydney, Melbourne triangle. Homegrown drug companies are also based in these major cities (except for Fauldings which is in Adelaide) and again they rarely venture away from the capital cities. By contrast agrochemical companies, by their nature, have a rural

and regional outlook. Some their development science is best done in regional and rural Australia (eg field trials) with obvious success. This issue is being proactively addressed and companies should now be further encouraged to look to the advantage in investment in regional Australia.

- Lack of regular personal contact with patenting lawyers who are based in the capital cities and having to rely upon phone and e-mail communication. Regular contact allows the researcher to become more IP skilled and the IP attorney to proactively identify IP. Of a more generic nature, it needs to be made clear that the initial and continuing costs of patenting are often not recognised and accommodated in grants. For example, the NHMRC is encouraging greater commercialisation of biomedical discoveries yet what provisions are made within NHMRC grants to pay for patenting costs during and beyond the term of the grant.
- Few of the scientific support industries have major efforts in regional Australia. For example *Lab Supply* is the only scientific supply company in Townsville that has facilities beyond a sales and technical rep*. Crown Scientific* are investigating expanding their Townsville operations. Instrument service and repair as well as supply of reagents and consumables is therefore much slower.

WHAT ARE SOME OF THE ADVANTAGES OF MAINTAINING THESE ACTIVITIES IN RURAL AND REGIONAL AUSTRALIA?

- There is existing expertise in some regional centres e.g. Townsville, Rockhampton.
- Proximity to biodiversity which is the lifeblood of bioprospecting eg GBR, Wet Tropics, deserts, dry savannahs, cold habitats (eg the current work at AIMS, U. Tasmania and the CRC for Antarctic Research)
- Lower overheads, like real estate, and cost of living and/or quality of life that can be used to attract quality researchers, support staff and business staff (it is these qualities linked to the presence of internationally recognised biotechnological science capability, that have recently attracted high profile Japanese investors to Townsville).

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

Please Refer to AIMS submission to the Voumard Inquiry attached.

Biotechnological discoveries can lead to new production industry and jobs, particularly in regional areas. Bulk production of many natural products in farms (terrestrial and marine) can be envisaged with extraction, purification and value adding based in more centrally located chemical industry. New fermentation and bioprocessor plant will develop and new products are likely to be a marriage between natural production

of unsynthesiseable or uneconomic to synthesise natural product chemical base chain/warheads and synthetic reconfiguration for the final product.

If funding is available at early phases of the bioprospecting/biodiscovery process, then IP is also captured early. As experience, infrastructure and wealth grows, so does the likelihood that all aspects of biotechnological industry development can be based in Australia. Regional development is likely to be the significant beneficiary in this as explained above.

Support and local investment is needed to start this process. In this context, it is worth mentioning Biotrade (www.biotrade.org), which is a United Nations effort to coordinate and encourage biodiversity-based industry in developing nations in this context. While Australia is not a developing nation, northern Australia is part of the region under consideration. This type of support is appropriate and designed with full recognition of the principles of the Convention of Biological Diversity. Participation in Biotrade by regional bioprospecting centres may prove worthwhile but will require logistic and financial support and policies aligned with this concept need to be developed in Australia urgently.

4. The impacts on and benefits to the environment

IMPACTS

Bioprospecting has been an extractive process. In the past some bioprospecting exercises have been ecologically devastating leading to terms like biopiracy (particularly when material has been taken offshore without access and benefit sharing policy being signed off on and without appropriate environmental audit).

In most instances nowadays only very small pieces of tissue need initially be taken (grams). The process usually does not kill the source organism (for modular/colonial, branching species) and recent work at AIMS has shown that any excised tissue is rapidly regrown. Where recollections are required, species data recorded with the original collection can be used to assist environmental impact assessment. The Voumard inquiry recommends a tiered approach to impact assessment, with larger scale recollections or the presence of vulnerable species attributes triggering more stringent appraisal. Micro-organism samples can of course be cultured. Additionally, there is now enough bioprospecting data around to show that some species are not worth collecting for some screens/targets. Species of macro-organism that are rare should also not be sampled as any recollection has unacceptable impact and the quantity of material needed to identify lead compounds and follow-up testing in functional bioassay cannot be guaranteed (i.e. the drug company will not sanction recollection of rare species let alone the environmental agency). Bioprospecting for chemical extracts can therefore be almost based on a 'zero impact'.

Bioprospecting for genetic material is however another story. Not so much from the point of view of impacting the environment by extraction, but more by the fact that export of genetic material can impact on future options for that genotype within the source country/region. It is our view that genetic material should stay in the country (state/region?) of origin.

In short, impacts on the environment from traditional bioprospecting by well trained research groups is negligible. Even recollections of kilograms to tonnes can be accommodated with appropriate preliminary environmental effects investigations, and adoption of alternate means of production (aquaculture/fermentation eg, production of Halichondrin B from the deep water sponge Lissodendoryx in New Zealand, and recent work on producing the Bastadins at AIMS from sponge; Bryostatin I is now produced by aquaculture).

BENEFITS

The benefits to the environment are many. These range from both a "use" perspective: discovery of new environmentally friendly compounds for application to agriculture, to ameliorate impacts of pollution etc., to related outcomes from the bioprospecting activity itself. The latter include:

- Species identifications leading to biogeographic maps
- Identification of rarity, endangered habitats, biodiverse hotspots, bioactive hot spots
- Recognition and argument for reservation/protection of habitat/species
- Documentation/potential (owner approved) application of traditional use/applications
- Development of bioinformatic tools/databases for smart search of specific bioactivities
- Taxonomic/chemoecological amplification of leads

In addition there are new initiatives being explored at AIMS to invoke novel marine biotechnology in the Carbon Trade and Clean Development Mechanism opportunities. In recent work by AIMS in Western Australia focussing on development of two anti-tumour active leads, the basic ecological work that is currently being done (now underway for 6 months) to advance the discovery is worth to date $60,000. The taxonomic/biogeographic data that has been generated from earlier work in Western Australia in a bioprospecting exercise is worth over $100,000 due to expertise of the team that did the original work and already CD ROMS, advice on biodiversity and other conservation related initiatives have been progressed and grown. In other countries continuance and expansion of all marine reserves have utilised bioprospecting data, indeed several new marine reserves are being considered

because of bioactivity hotspots and species distributions (North Taranaki, Pouawa, Department of Conservation, New Zealand, Battershill and Evans-Illidge, 2000). Equivalent comparisons have not been made for terrestrial habitats, but Ruitenbeek 1989, cited in Breese 1998, has gone as far as putting a minimum dollar value on rainforest as a value for protection in its own right - this is $US7/ha. They hasten to add that if indirect use is factored in (watertable function etc) the value rises to $US360/ha/yr and add that the minimum estimate worth of discoveries from Rainforest is in the order of $US147billion, (not counting fungi - worth $US9billion/yr, see Breese 1998). Given the much higher biodiversity in the sea, conservation and natural product value can therefore be assumed to be much higher.

Today the environmental benefits of bioprospecting can far outweigh any impacts. This is only the case however, if this phase of biotechnological development is well funded, well controlled by transparent policy and well linked with all stakeholders.

Table 1
New Zealand Marine Protected Areas and the Relationship with Biodiscovery Programmes

Marine Protected Area	Role of Biodiscovery Data	Status
Leigh Marine Reserve	Evidence for the need to preserve uncommon invertebrate species	Field natural products research supported within the reserve
Poor Knights Is Reserve	High biodiversity. Rare and new MNP lead species need full protection	Reserve enlarged to full protection 1997, significant influence from MNP data
North Taranaki	DoC invitation/support to sample benthos and create species inventory	Rare and new MNP lead species prompt reserve application
Gisborne Marine Reserve	DoC invitation/support to sample benthos and create species inventory	Rare and new MNP lead species support reserve application, successful
Kapiti Island Reserve	DoC invitation/support to sample benthos and create species inventory	Potential extension of the reserve under consideration
Pukerua Bay	Maori/reserve committee invitation to sample benthos/inventory	Reserve application in progress
Wellington South Coast	Reserve committee support for sampling benthos, inventory	Rare and new MNP lead species support reserve application, in progress
Kaikoura Canyon	Location of rare sponge, 300 tonnes global biomass, MNP to clinical trial	Collaboration with Fisheries Ministry to protect the habitat and sponge
Akaroa/Flea Bay Reserve	DoC invitation/support to sample benthos and create species inventory	Reserve application successful 1998.
Nuggets Marine Reserve	DoC invitation/support to sample benthos and create species inventory	Rare and new MNP lead species prompt reserve application, successful.
Fiordland Marine Reserve	DoC invitation/support to sample benthos and create species inventory	Data used in ongoing reserve management.

DoC Department of Conservation

Recommendations

(Mindful that the Bailey inquiry is focussing on high tech industry development, not just research support and technology transfer issues)

- Promote and facilitate early bioprospecting phase investment opportunity within Australia
- Development of clear and transparent policy and procedure for access to biological resources and benefit sharing in all Australian jurisdictions.
- Investment in nationally significant collections and extract libraries
- Additional tax incentives for investing in these activities in regional and rural Australia so that investors seek out opportunities with the prospect of higher investment return
- Tax incentives to make the costs of doing these activities cheaper such as:
  1. All activities in the private sector related to bioprospecting and biodiscovery are GST-free
  2. Federal taxes to be waived for a set period to make employment of staff cheaper at the outset
  3. Incentives given to State governments to waive stamp duties, and all payroll related taxes for a set period for private sector activities
  4. Incentive given to local government to waive council rates and fees for a set period for private sector activities
  5. Similar incentives be given to science support industries
- Encourage the establishment of an investment fund to support these opportunities through tax incentives and the like - maybe even a targeted pooled development fund (like the "green" PDF Sage Investments). For example, one can look to the Amazon Biodiversity Permanent Fund (US$150 million), coordinated by the Brazilian NGO Bioamazonia and Banco Axial, a private bank. The Fund is intended to finance biotechnology R&D activities of the Brazilian Programme of Molecular Ecology which aims to develop bio-industries and promote the sustainable use of biodiversity, while improving the well-being of local populations
- Additional encouragement beyond the Pharmaceutical Industry Investment Program given to drug companies that undertake R&D in rural and regional bioprospecting (or biotechnology in general) OR incentive schemes put in place to encourage participation by the drug companies in an investment fund mentioned above
- Establish an incentive program for patent firms to establish regional offices, either fulltime or part time (eg 1-2 days/week) OR Special IP training fellowships for regional lawyers

- Introduce a Pharmaceutical Industry Investment Program-like scheme for agrochemical directed bioprospecting research to encourage further investment in regional and rural based R&D activities. (NB. With drug companies, the government has leverage in the PIIP, which compensates drug companies for the lower prices paid under the Pharmaceutical Benefits Scheme. This can be done because significant purchasing power can be exchanged for commitments to Australian R&D and value-added production).
- Encourage cooperation between regional development initiatives. For example, there is a significant increase in the activities and location of Australian Defence Forces in regional centres. While it is true that proximity to biodiversity is advantageous (and AIMS shipboard laboratory access to the GBR is an example we can cite), many of Australia's most interesting biodiversity is in very difficult to access areas (especially in the terrestrial environment). Cooperation between bioprospecting activities and sectors of the Australian Defence Forces would greatly increase our field access with high quality equipment and well trained personnel to assist in these unusual environments (and provide the ADF with interesting training possibilities)

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APPENDIX 1

National Inquiry into Access to Australia's Biological Resources

A Submission from the Australian Institute of Marine Science

March 2000

Introduction

The Australian Institute of Marine Science (AIMS) is a marine research and technology organisation that relies on access to Australia's marine resources for the conduct of its research. It was established as a Commonwealth Statutory Authority to provide the research capacity to facilitate management of Australia's marine environment and resources. Its functions, powers and administrative framework are described in the *Australian Institute of Marine Science Act* 1972 (Cth).

The research effort at AIMS is based on projects, each of which addresses marine issues of national importance. This effort involves extensive collaborations both within Australia and around the world and provides a major international resource for marine science partnerships, with other scientific institutions and with industry. The research is a mix of pure basic-strategic inquiry (ie towards a fundamental understanding of oceans), and research applied to the needs of resource managers and industry. More comprehensive information about AIMS and its research can be found at the website www.aims.gov.au.

This submission focuses on one area of AIMS research activities – that which relates to biodiscovery (or bioprospecting) with Australia's marine biodiversity. Resources within Australia's ocean territory, one of the largest and most diverse in the world, are widely recognised to have enormous potential as a source of raw materials for the discovery and sustainable development of new biotechnology products. Australia is in the unique position of possessing not only megabiodiversity but also the scientific facilities and capability to discover its potential. However, the path to realising this 'best of both worlds' position has not been clear, not least because access to these raw materials has been problematic.

The submission begins with an overview of biodiscovery research undertaken at AIMS. The current access situation will then be described, including limitations and impediments, and solutions proposed by AIMS and planned to be implemented in the first instance with the Queensland government. Next, aspects of the new *Environment Protection and Biodiversity Conservation Act* 1999 (EPBC Act) with respect to other legislation governing access to Commonwealth marine areas will be discussed. The

importance of exporting samples in order to take advantage of collaborative opportunities overseas, particularly with respect to microbial diversity (the overlooked megabiodiversity), with then be outlined. Finally, a suggested framework for access regulations covering Commonwealth marine areas will be presented.

1. AIMS biodiscovery research

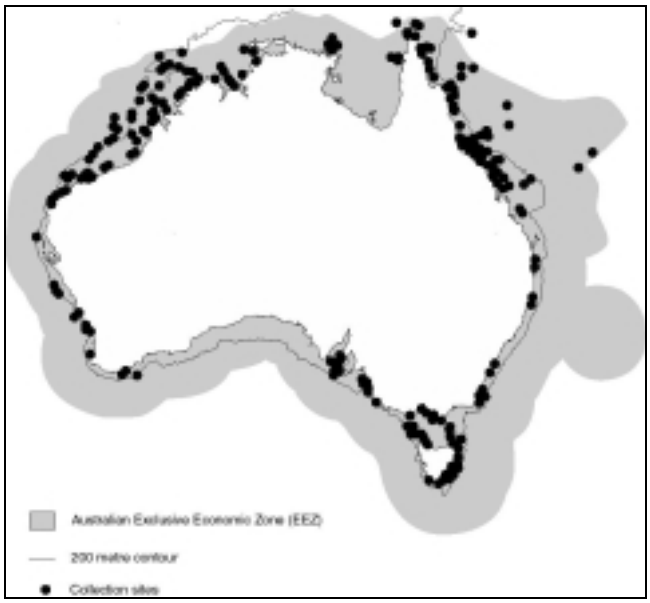
For over a decade, AIMS marine research activities have included biodiscovery (or bioprospecting) research. The goals of this research are:

- To discover biologically active molecules that can be developed as drugs, industrial biocides or other products by an industrial partner;
- To understand the ecological roles that biologically active molecules play in their source organisms; and
- To support sustainable development of new product leads.

This research involves the systematic search through biodiversity present in nature, for novel molecules (chemical entities) that cause a desired action in a molecular process associated with some commercial product. The 'Deriving Benefits from Marine Biotechnology' project is a multidisciplinary project which interfaces expertise among disciplines associated with research on the source organisms (marine biology, taxonomy and ecology, marine microbiology), with those associated with lead identification (bioassay development, screening and pharmacology), and those related to elucidation of the molecules themselves (natural products chemistry, structure elucidation). The project also focuses on developing sustainable production technologies to create new enterprise in Australia to supply global markets with fine chemicals.

In order to gain access to appropriate world class expertise and facilities to achieve its goals, the project needs to access facilities, funding, logistical support and expertise beyond that available in-house at AIMS. This is achieved through strategic links to various collaborators, particularly within industry. Product areas in which AIMS has a research interest include pharmaceuticals, agrichemicals, sunscreens and cosmetics, seafood toxin testing, antifoulants, bioremediation, environmental monitoring, and industrial enzymes.

FIGURE 1: AIMS AUSTRALIAN BIODISCOVERY COLLECTION SITES



Within this multidisciplinary framework, the centrepiece of the project is the Marine Biodiversity Collection. The collection includes material from around 10000 marine macroorganisms and 7500 marine microorganisms, collected and isolated from over 1500 sites from around Australia (see Figure 1). The collection includes all major marine phyla, and represents a wide biodiversity in terms of taxonomy, ecology, and geography. The collection was designed for natural products research, but also includes material and data for ongoing expert systematic and taxonomic study of the samples. It is associated with a comprehensive relational database, and material includes viable cultures, frozen bulk material, taxonomic vouchers and a library of extracts for screening. This collection is a major national asset for which AIMS is the custodian. Resources for the maintenance of the collection are provided by AIMS. In the process of acquiring permits to undertake the collection, AIMS has had extensive dealings with a wide range of access controlling/permitting agencies right around Australia.

2. The current access status quo and benefit sharing – the missing link

Access to biological resources in Australian marine areas, including Commonwealth waters, is controlled by a maze of legislation principally designed for either fisheries management or conservation. Many publications simplistically describe the jurisdictional marine boundary between the Commonwealth and the States/Northern Territory as a line drawn 3 nautical miles offshore from the territorial baseline (usually the low water mark). This is deceptive, and a single activity in one location frequently requires permits from multiple agencies representing more than one tier of government and administering a range of access legislation. However, as the legislation concerned is usually designed for resource management (generally,

environmental conservation or fisheries management), this complex system does achieve checks and balances, albeit in a cumbersome way, to allow for any access to be sustainable.

In addition to obstacles associated with jurisdictional complexity, AIMS can document a trend of increased reluctance on the part of some marine access controlling agencies within Australia (including Commonwealth agencies) to grant permits for biodiscovery research at AIMS. This reluctance has not been due to any environmental grounds, but has rather been over concerns that adequate benefit sharing will not take place, should commercialisation of a discovery occur. In other words, agencies (particularly natural resource management agencies) sense that they have some ownership that should in the long run lead to a financial return to them directly.

Legislation for access often allows for the imposition of conditions to govern the type of access and use of material collected, including transfers to third parties, and some agencies have attempted to use these conditions to require some downstream benefit negotiations in the event of a commercial discovery. In other cases, access has been delayed, restricted or denied.

This situation has created impediments to biodiscovery research at AIMS and elsewhere, and resulted in lost opportunities through stalled projects, sometimes after leads have been identified. The long term and insidious cumulative effect of a lack of legal certainty over existing and future collections is a more widespread loss of international industrial confidence in the field of natural products research and investment.

Benefit sharing through resource managers is problematic. One aspect of the problem is that, with the exception of the new EPBC Act in s 301, the resource management legislation administered by access controlling agencies does not provide a legal basis for benefit sharing. Consequently, the associated regulations fail to provide a process. A further practical hurdle to applying the current marine access regime to benefit sharing is that of dealing with multiple access controlling agencies for a single activity, each with a different interest in, and expectation of, benefit sharing. Another aspect is that within agencies there is a focus on the prospect of royalties and other monetary benefits, and an unrealistic over-expectation of their probability, timing and quantum.

The misunderstanding over potential monetary benefits is impossible to definitively resolve at the point of initial access, because the product leads, their proposed commercial application and potential value are unknown. Nevertheless, AIMS has received a strong indication from industry that provision of a ‘trigger’ clause that required further benefit negotiations after identification of a lead, would not be

acceptable. This is because of the risk that mutually agreeable terms may not be reached at that point, ("agreeing to agree") causing the project to be discarded after significant R&D effort and cost to get it to lead status.

AIMS takes the view that the benefit sharing solution lies in being able to, at the outset, identify the beneficiaries and a coordinated single approach for benefit negotiations, and generically define the benefits (including monetary share) . Indication from international industry partners suggests that this approach is also desirable from their perspective.

Despite some important initiatives for a holistic national approach to access (eg the Commonwealth State Working Group), progress has been slow. In order to provide a solution at least in the short term and for AIMS' need for access to Australian marine areas, AIMS has developed and recently adopted a benefit sharing policy.

3. The AIMS benefit sharing policy and the draft Queensland agreement

The AIMS Biotechnology Benefit Sharing Policy states "When AIMS receives benefits from conducting research into the discovery and development of potential new products from Australia's marine biogenetic resources, it will equitably share those benefits with the owner of those resources".

'Owner' is defined for this purpose as either the legal owner of the seabed at the location from which a sample is collected, as determined in Australian Commonwealth or State legislation; or the holder of the sovereign right to use and exploit biological resources at the location from which a sample is collected, as determined either by Australian or international law. In Australia, marine resource ownership under this definition typically rests with the Crown, either in respect of the Commonwealth, a State or Territory, based on the 3 nautical mile line. Uncertainties remaining to be clarified include the full legal effect of seabed title on resource ownership (eg if title to the seabed extend to things attached to it, what about things that crawl on it? and swim over it?), and the application of Australia's Native Title legislation. In general, clarification of biological resource ownership will be an essential element of application of the AIMS approach.

AIMS proposes to implement its Biotechnology Benefit Sharing Policy through a series of legally binding benefit-sharing agreements between AIMS and individual resource owners. This would be achieved through negotiation with the appropriate statutory head (eg the Premier of a state), or their representative (eg Premiers Department), or nominated lead agency. AIMS' policy is to retrospectively apply this policy to its existing as well as future collections.

The AIMS approach singles out the 'owner' of resources for benefit sharing rather than parties that control access to resources. Access controllers manage resources on behalf of the owner, so it is perhaps appropriate that their stake in benefits be controlled and administered by the resource owner rather than AIMS. Also, negotiations with a single 'owner' are more practicable, as access is often controlled by multiple agencies. By removing benefit sharing from the agenda of access controllers, they are free to concentrate solely on the issues accommodated in their existing legislation (ie resource management).

By defining a broad array of benefits that are available for sharing, the AIMS approach formally acknowledges all benefits of biodiscovery research including some that, to date, seem to have been overlooked by many resource stakeholders. When seen in the context of the total benefits package, purely monetary returns such as potential royalties take on minor importance.

While each benefit sharing agreement would be negotiated on a case-by-case basis, AIMS has developed the following framework within which it would expect these agreements to sit.

Prior to the emergence of a lead, benefits will be non-monetary. They will comprise documentation of biodiversity including lodgment of taxonomic vouchers in relevant museums, description of new species, and provision of data to aid resource management (identification of rarity, threats etc); opportunities for scientists in the jurisdiction of origin to participate in collection expeditions, and other collaborations which provide opportunity for the development of intellectual property in commercial discoveries (eg taxonomy, chemical ecology, natural products chemistry, biology).

An example of this style of benefit is the effect of Australian bioprospecting collecting on global knowledge of biodiversity of the phylum Porifera (sponges). In 1974, it was thought that there were up to 1000 species within Australia and possibly 5000 species worldwide. By 1997, primarily as a result of work done on bioprospecting collections in Australia, it is now known that there are at least 5000 species in this country and at least 15000 species globally.[1] The AIMS collection formed a substantial component of the resource for this work. This 5 and 3 fold increase in knowledge (respectively) would never have been achieved through traditional sources of funding for this kind of taxonomic/systematic research. Never before has so much biodiversity information been generated in a consistent and rigorous manner.

Another perhaps more tangible example of the benefits of biodiversity documentation is demonstrated by the proactive relationship between resource management

[1] Hooper JNA, RJ Quinn & PT Murphy, 1998. 'Bioprospecting for Marine Invertebrates', in proceedings of Biodiversity, Biotechnology and Biobusiness – 2nd Asia Pacific Conference on Biotechnology.

agencies in New Zealand and the National Institute of Water and Atmospheric Research (NIWA). Attachment 1 lists marine reserves that have been instigated or supported through resource information produced through biodiscovery research collections. The opportunity for a productive synergy between marine bioprospecting and the current 'Representative Marine Protected Areas' program in Australia is obvious. Similarly, this kind of benefit could be utilised under the requirement in Chapter 5 (conservation of biodiversity), Part 12 of the EPBC Act, which requires identification and monitoring of biodiversity and preparation of bioregional plans.

Once a lead has emerged, the research focuses on individual species and the potential commercial target. Thus, the potential commercial benefits are more specific and definable, and include the possibility of monetary returns such as an agreed percentage of monetary benefits received by AIMS (eg milestone payments, license fees, royalties). The actual percentage due to the resource owner will reflect the resource owner's IP and other contributions to the discovery and development of the lead.

More significant benefits at this point relate to opportunities for participation of scientists in the jurisdiction of origin in recollections and the development of intellectual property in options for long-term large-scale supply of active compound and other 'value adding' initiatives. Such involvement can produce the technology base for potential new marine biotechnology industries in the jurisdiction of origin.

A significant impediment to the progression of leads from marine bioprospecting has in the past been lack of certainty over reliability of long term large scale supply. This is because some of the best marine leads have been very structurally complex molecules which are not amenable to synthetic approaches for production. This apparent deficit actually represents enormous opportunity to develop economical and sustainable supply options in the jurisdiction of origin, for example by developing an aquaculture or fermentation industry to deliver the needed material. Such industry will most effectively be located regionally close to the original site of discovery.

An example of such 'value adding' benefits can be drawn from the development of a New Zealand lead. The Halichondrins are a novel family of compounds produced by a deep water New Zealand sponge *Lissodendoryx sp*, about to enter anti-cancer clinical trials. While the species is extremely rare in nature (the entire existing biomass is estimated at only 300 tonnes in a single limited range – information gleaned from a large scale recollection and attendant environmental impact assessment), it is an ideal mariculture candidate. Research into the chemical ecology of these compounds in this species has resulted in optimum culture methods that can return a growth rate

of up to 5000% in one month[2]. A joint venture with local industry has been established to produce the 10 tonnes required to supply enough compound for the clinical trials. The cost of producing one kilogram (wet weight) of sponge, with a current value of up to US$400, is only 50 cents. Should the compounds survive clinical trials, this ratio will decrease as the production scales up to meet the projected annual global demand of up to 60 tonnes. Combined with other supporting commercial ventures established locally (eg plant for chemical extraction and refinement), the capture of value adding biotechnology industry is a potentially massive regional socio-economic benefit.

Incidentally, there is also a strong marine conservation link with the progression of this project, because the development of new products based on biodiversity is intimately linked to its protection. The above example identified the rareness and vulnerability of an important new economic resource. Consequently, the fishing community has placed a voluntary trawling ban on the species' home range, pending formal marine reserve status. There is also evidence that growing this sponge amongst existing bivalve aquaculture (eg mussels) benefits production of both species and ameliorates some existing environmental impacts of mussel farming.

AIMS' benefit sharing agreements are proposed to be broad in scope to capture benefits from all leads that use a sample as a source of innovation, regardless of whether or not lead development involves derivation/synthetic approaches. They will provide legal certainty over AIMS' right to use the samples for biodiscovery research, including to transfer the samples to third parties. They will define all benefits to be delivered by AIMS, without any 'triggers' for further negotiation with the 'owner'. However, there should be provisions for review of the operation and success of the agreement as a whole, and procedure for amendments.

A key aspect of the proposed benefit sharing agreements is that they will not replace the need to seek a permit to access any resource. Such acts should still be subject to appropriate resource management legislation, to ensure such access is sustainable. Conversely, given the existence of a benefit sharing agreement, permit negotiations should focus solely on the environmental aspects of the access proposed, and not include benefit sharing discussions (although a permit condition should be that sample use is subject to the benefit sharing agreement).

[2] Battershill CN, MJ Page, AR Duckworth, KA Miller, PR Bergquist, JW Blunt, MHG Munro, PT Northcote, DJ Newman and SA Pomponi, 1999. Discovery and sustainable supply of marine natural products as drugs, industrial compounds and agrochemicals: chemical ecology, genetics, aquaculture and cell culture. Memoirs of the Queensland Museum, Vol 44:76. Also, Battershill *pers comm.*

Thus, the AIMS approach seeks to separate the issue of access (with resource managers) from benefit sharing (with owners), while allowing for a linkage between the two**.** The model holds great promise as a practical solution. AIMS has begun to implement this approach, and has negotiated a draft agreement with the Queensland government which is expected to be finalised soon. The concepts described above have been codified in this agreement which will be provided to the inquiry once finalised. This agreement is being negotiated with the Queensland Department of Premier and Cabinet, who coordinated a whole of government approach for the State of Queensland. Discussions have also commenced with Western Australia, where the Ministry of the Premier and Cabinet has undertaken to perform a similar role. Pending compatibility of this approach with the conclusions of the present national inquiry, AIMS proposes to begin negotiations towards an agreement with the Commonwealth later this year.

4. The EPBC Act in the context of access to Commonwealth marine areas

The terms of reference to this inquiry request advice on a scheme which could be implemented under S 301 of the EPBC Act, to 'provide for the control of access to biological resources in Commonwealth areas'. However, s 301 is not the only section that refers to access to Commonwealth marine areas. It is unclear how these other access arrangements, which sometimes come about through permitting the effect of existing access legislation (including state and NT laws) with respect to Commonwealth marine areas, would sit alongside any new s 301 regulations.

Specifically, aspects of s 23 – s 25 allow for continuation of arrangements (described below) where access to substantial proportions of Commonwealth marine areas is managed according to the law of the states or the Northern Territory, because such access is deemed to be part of a fishery.

Under Part 5 of the *Fisheries Management Act 1991* (Commonwealth) and an inter-government agreement reached in 1979 known as the *Offshore Constitutional Settlement*, provisions were made for the Commonwealth to enter into arrangements with the states and the Northern Territory to apportion fisheries resource management roles according to the boundaries of individual fisheries rather than the 3 nautical mile offshore state/Commonwealth boundary. While actual title to the seabed and subsoil is not affected by these arrangements, they result in some activities (such as access) in Commonwealth waters being subject to State or Territory legislation and vice versa, and the situation within the one location can vary depending on the species targeted or equipment used. In the cases of Western Australia, the Northern Territory, and Queensland (and probably other states), a 'general' Part 5 arrangement exists with the Commonwealth, whereby any aquatic resources (defined very broadly) within the Australian Fishing Zone (ie out to the 200

nautical mile line) and adjacent to the relevant state/NT, which are not covered by specific arrangements, will be managed according to the law of the state or NT (as appropriate). Attachment 2 contains the general arrangement relating to waters adjacent to WA as an example.

The present result of these general arrangements is that access to aquatic biological resources in Commonwealth areas is managed according to the fisheries legislation of the adjacent state or the Northern Territory. The EPBC Act appears to directly uphold these arrangements. The arrangements can be periodically reviewed. Given the recent emergence of the EPBC Act to cover access to Commonwealth marine areas, there may be grounds to review the effect of the general fisheries arrangements on control over Commonwealth marine areas. If the current general arrangements persist, there is complete overlap and potential conflict with any regulations over Commonwealth marine areas that may be attempted under the EPBC Act.

It appears that there are further sections of the EPBC Act, in addition to s 301, which could be applied to access regulation. For example, s 25 allows for actions to be 'prescribed', s 28 allows for Commonwealth agencies (ie AIMS) to obtain approvals by declaration if a proposed action is controlled by the law of a state or territory. s29+ deals with certain actions covered by bilateral agreements not needing approvals. s 32+ allows for 'declaration' of actions for which there is an accredited management plan – could this be applied to approved bioprospecting collecting programs? Sections 44-65 allows for the making of bilateral agreements with states/territories - could this be a provision for a multi-jurisdictional 'one stop shop' permit for collecting? Or the application of the EPBC Act to collecting in State/Territory waters? Then there are provisions for 'controlled actions', and 'strategic assessments'. Further, there is allowance for continuance of certain existing Commonwealth access legislation for marine areas, eg the *Great Barrier Reef Marine Park Act*, the *Fisheries Management Act*, and the *Torres Strait Fisheries Act.* Presumably, any EPBC regulations would not affect the requirement to obtain permits under these acts.

While the above discussion is by no means a comprehensive review of the EPBC Act (and other access legislation), it does appear that it presents a range of mechanisms that could be utilised for access regulation, in all Australian marine areas. This poses a danger that new EPBC regulations could precipitate an even more complicated access regulatory framework. Any new regulations must be considered alongside the existing regulatory framework, which is often inter-jurisdictional, to avoid and/or clarify potential conflicts.

5. Exporting samples – the issue of 'indirect' access

While regulations for exporting samples are outside the scope of the EPBC Act, some discussion of them is appropriate in the context of the current inquiry. This is because they present a convenient regulatory milestone in the use of samples of some types of biological resources. Such a milestone is currently utilised by export regulatory authorities. It is AIMS experience and understanding of common practice, that officers responsible for processing export permit applications consult with agencies responsible for granting the original collection permit, to determine whether or not the collection was made legally.

At present, movement of some classes of biological material overseas is controlled by the Commonwealth's *Wildlife Protection (Regulation of Exports and Imports) Act* 1982 (WP Act), which requires that 'harvesting' of material for 'export' is sustainable. Samples defined by the WP Act as 'wildlife' or their products (the definition excludes some important components of wildlife – a serious omission as discussed later) cannot be sent overseas without an export permit. If the purpose of the export is for screening or anything to do with biodiscovery research, then commercial export provisions apply. Of the commercial regulatory provisions, the most appropriate for exports for biodiscovery research are under s 10 of the WP Act, requiring the minister to declare samples as 'controlled specimens'. Commercial export permits can then be granted for 'controlled specimens'.

AIMS obtained a 'controlled specimens' declaration for the entire AIMS biodiversity collection in 1999. The process took six months, and involved a public consultation period. The resulting declaration (attachment 3) includes a condition that samples will not be exported unless a benefit sharing agreement is in place with the owner of the resources, and requires the lodgement of any benefit sharing agreements. If the access regulations under the EPBC Act include the negotiation of benefit sharing agreements on behalf of the Commonwealth as the 'owner' of resources in Commonwealth areas, then the export process provides a check and balance for that agreement before samples go offshore, at least in the case of classes of resources covered by the WP Act. Perhaps such a benefit sharing agreement should stipulate the conditions under which samples exports would be allowed (as is the case in the draft Queensland agreement).

EXPORTING SAMPLES IN CONTEXT

Biodiscovery research is a high cost, high risk, and long term process. The chances of identifying a lead that is then developed into a vendible product have been likened to those of winning the lottery. Given these odds, the key to maximising the probability of success is to expose as wide a biodiversity of samples as possible, against as wide a range of screening targets as possible. By being able to send samples overseas for screening in bioassays not available in Australia, the opportunities for discovering

useful sample/bioassay combinations are optimised. Regarding opportunities and benefits to Australia, there may be a pitfall in this approach unless the samples themselves and resulting intellectual property are managed carefully.

One scenario with respect to sample control is to convince overseas collaborators to transfer all technology to Australia. There are examples of this type of collaboration, which have resulted in large investment in R&D in Australia. However, not all potential partners are willing nor able to do this (eg duplication of facilities may not be cost effective). Also, the Australian partner may have some objections. Mega scale industrial investment (such as that required in some technology transfers) usually comes at a price, including a requirement for exclusivity and possibly a compromised intellectual property position. The Australian partner may end up resembling the Australian branch of the sponsoring company.

It is AIMS intention to avoid single large exclusive deals, and instead develop collaborative arrangements with a wide range of partners both within and outside Australia, in addition to niche screening available in house at AIMS. The single driving goal is maximising IP capture and sustainable industrial opportunity for Australia. These arrangements may require management of periods of limited exclusivity for the purpose of primary screening by the partner, for which minimal amounts of extract will be made available (and possibly need to be exported). These activities will probably involve a proprietary bioassay, and so the partner will be entitled to an IP stake. However, these deals will aim to capture the structure elucidation chemistry and technology transfer for secondary screening to be done either at AIMS or elsewhere in Australia. The IP associated with discovering the structure of compounds active in the partner's bioassay, plus the likelihood of additional value adding research for example into large scale supply options, is Australia's opportunity for an IP stake. AIMS has commenced discussions with several international companies that are interested in this approach.

An undesirable sample export situation is one in which samples are 'sold' to an overseas party to do with as they wish, with the possibility that some Australian party may receive a passive share in profits if a commercial product should result. This scenario presents complete loss of control over the material, and negligible opportunity to share in intellectual property, capacity building, or value adding industry.

Benefit sharing arrangements provided for in s 301 of the EPBC Act should be utilised to ensure that export of biological material for biodiscovery research results in creation of opportunity for Australia.

MICROORGANISMS – OPPORTUNITY AND IRONY

Microorganisms have long been recognised as holding enormous potential for the production of natural products. Many antibiotics on the market today have their origins in bacteria, and microbes from extreme environments have yielded enzymes and other industrial products that are stable in extreme conditions (eg enzymes in cold water laundry detergent). The microbial collection at AIMS has huge potential in this regard. It is unique due to the efforts spent in culturing previously unculturable strains from a wide range of microhabitats including extreme environments. Thus, it contains strains that have never been screened against most commercial targets.

There is an important bonus advantage in the discovery of commercial products in culturable microorganisms – if you can culture them, you also have the means of economic, sustainable, large scale production.

In light of these facts, there is great irony in the current restrictive export regulations with respect to finite amounts of raw sample or extract (which is unreproducible) of macroorganisms. This is that Australia's unique and endemic microorganisms, some of which are only now able to be culture due to large Australian R&D efforts, are not classed as 'wildlife' by the WP Act, and can therefore be exported unregulated and at will in live viable culture format. See attached letter from Environment Australia (attachment 4), which acknowledges that at least 8 kingdoms of life, described since the drafting of the WP Act in the early eighties, are unprotected. It is AIMS view that urgent legislative repair should be undertaken to enable the WP Act to comprehensively cover all Australian wildlife. However, such a step must be taken alongside the development of regulations to allow appropriate export of samples to collaborators and for the benefit of Australia, so as not to impede the efforts of responsible researchers who are currently engaged in international biodiscovery research using Australian microorganisms.

6. A model for access and benefit sharing regulations

A. THE NUTS AND BOLTS

Based on AIMS' experience, the following three elements are proposed as fundamental for effective 'biodiscovery' access to Australia's marine resources.

(i) Sustainable Access – a stepwise approach

All access, either for primary collection or subsequent re-collection, must be undertaken on a sustainable basis, and AIMS would welcome appropriate access conditions to ensure this. This would most ideally be provided by a single piece of legislation and administering agency (eg through regulations under the EPBC Act). However, this could also (less efficiently) be achieved by combined regulations under

this or other Commonwealth and state legislation appropriate to a particular area, or some combination of the above.

For primary collections, a small amount (10g-1kg) of material is collected from each of a wide range of organisms. As these collection activities involve remote places and poorly described organism groups, effective species-specific resource management approaches are not possible (and indeed, given the small quantities, probably not applicable). Instead, it is desirable to set out allowable collection methods and procedures that will ensure minimal environmental impact and avoidance of rare species. AIMS has established collection protocols to ensure this is the case. Following primary collections it is usually a requirement to report details of collection activities to the access-controlling agency. AIMS would welcome a requirement to provide this information in a format that was useful for direct input into resource management systems.

Where a medium scale secondary collection (10's kg) is required to progress a lead and determine its potential, AIMS would support the requirement for a separate permit. As the recollection would be targeted on a particular organism, species-specific environmental impact scrutiny becomes an option. With a view to the potential importance of the species and possible future requests for larger scale collections, AIMS would also support the requirement for concurrent detailed biological and ecological investigations into the organism (eg distribution and abundance studies).

Requests for large scale collections (100's kg) should be subject to full environmental impact assessment based on sound and extensive knowledge of the species, and mandatory concurrent investigation of alternatives (eg synthesis, culture) for long term large scale supply. Such a large-scale collection should only be considered as an option for progression of a lead to a point where justification for development of alternative production methods can be achieved. Continual wild harvest of large quantities should not typically be considered as an option for long-term supply.

In order to secure a level of confidence and certainty to attract industrial research support, generic conditions of secondary access should be set out at the time of permission for primary collection.

(ii) Ability to transfer samples to third parties

In order to utilise facilities and funding opportunities outside AIMS through collaborations and joint ventures, it is typically necessary to transfer samples to third parties. Where the third party is not located within Australia, export permission will be required and applicants should be required or at least encouraged to maximise the opportunity for development of intellectual property within Australia. The need to transfer samples to third parties is inevitable because the full gamut of expertise and

facilities to do everything from primary collection, through lead identification, and onto product development, will never occur within the one single organisation. In order to provide certainty to investors in biodiscovery research, it is essential that the terms and conditions of third party transfers are set up front, at the time of permission for primary access to *in situ* resources.

(iii) Benefit Sharing

A framework for sharing benefits arising from access to resources should be established at the outset, in order to provide legal certainty over the use of samples and clear ground rules for (and engender the confidence of) investors in the research. Benefit sharing frameworks potentially involving overseas partners should require the provision of opportunities for Australian capacity building and Australian development of intellectual property in discoveries and their commercialisation. They should also recognise all benefits including those that do not directly relate to commercialisation or monetary reward, such as documentation of biodiversity to support its effective management and conservation. Even though the details of monetary benefits cannot be estimated at the point of initial access, they should be generically defined (eg a % of defined net profit) in the agreement.

Benefit sharing negotiations should be conducted separately to access negotiations. The latter should be left to officers specialised and skilled in the management of sustainable access. The former should be conducted by parties representative of the resource or sovereignty 'owner', under a process nominated or coordinated by the appropriate statutory head.

B. THE FRAMEWORK FOR LINKAGE BETWEEN ACCESS AND BENEFIT SHARING

In reality, for a single collection it may be necessary for more than one access permit to be negotiated from a range of resource management agencies. While not ideal, this may be workable as long as information about who to deal with is well known, and the agencies focus on environmental management issues. The situation would be unworkable if each agency required benefit sharing.

The most workable single representative for negotiation of benefits is one who represents the owner of resources. The situation for multiple benefit sharing agreements should never arise, as long as there is only one recognised 'owner'. This agreement could then oversee the various access permits, stipulating the benefit sharing terms covering the use of samples collected under those permits, like an umbrella.

This model therefore includes a healthy linkage between access and benefit sharing. The owner would be responsible to 'on-share' any benefits appropriately with those responsible for managing the resource (eg inventories of resources, a share of

monetary reward), and the resource managers would require that the use of any samples collected under a permit be subject to the benefit sharing agreement.

It would probably be common for the 'owner' and some access controllers to be from different jurisdictions. For example, in the case of a collection from Queensland waters within the Great Barrier Reef Marine Park, the benefit sharing agreement will be with Queensland, while the permit will be from a Commonwealth authority (GBRMPA). Similarly, if the general fisheries arrangements outlined earlier persist such that access to Commonwealth areas are controlled by the fisheries legislation of the adjacent state, then the benefit sharing agreement will be with the Commonwealth, while at least one of the access permits will be from the state. Thus the success of this model will rely on good inter-jurisdictional relations.

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