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Funding of High Cost Biotechnology and Other Innovative Targeted Therapies under the Pharmaceutical Benefits Scheme

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Position Paper

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It should be noted that NATSEM does not hold a position as to whether or not new high cost biotechnological and other targeted drugs should be included on the PBS. However, we are assuming for the purposes of the position paper and as a starting point for discussion that difficulties are being encountered in getting these new drugs PBS listed. This assumption is not necessarily the view of NATSEM.

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List of Abbreviations

APMA	Australian Pharmaceutical Manufacturers' Association
ARA	Australian Rheumatology Association
ARTG	Australian Register of Therapeutic Goods
ASI	Adam Smith Institute (UK)
CTC	Clinical Trials Centre
CTN	Clinical Trial Notification Scheme
CTX	Clinical Trial Exemption Scheme
DHA	Department of Health and Ageing
DHAC	Department of Health and Aged Care
DMARD	Disease modifying antirheumatic drug
ESC	Economic Sub-Committee
FDA	Federal Drug Agency (US)
FISH	Fluorescence *in situ* hybridisation
GHAC	Growth Hormone Advisory Committee
GMS	General Medical Service (Ireland)
HER2	Human epidermal growth factor receptor 2 protein
hGH	Human Growth Hormone
HIC	Health Insurance Commission
HMO	Health Maintenance Organisation (US)
HREC	Human Research Ethics Committees
HSD	Highly specialised drug
HSDWP	Highly Specialised Drugs Working Party
LTI	Long Term Illness (Ireland)
MS	Multiple Sclerosis
NATSEM	National Centre for Social and Economic Modelling
NHMRC	National Health and Medical Research Council
NHS	National Health Service (NHS)
NICE	National Institute for Clinical Excellence (UK)
NPS	National Prescribing Service
OTC	Over the counter
PBAC	Pharmaceutical Benefits Advisory Committee
PBPA	Pharmaceutical Benefits Pricing Authority
PBS	Pharmaceutical Benefits Scheme
PES	Pharmaceutical Evaluation Section
PPR	Prescribing Practice Review
QALY	Quality Adjusted Life Year
QUOM-BARA	Quality Use and Outcomes Measurement for Biological Agents for Rheumatoid Arthritis
RPBS	Repatriation Pharmaceutical Benefits Scheme
TGA	Therapeutics Good Administration

Executive Summary

Brief

This position paper was prepared by the National Centre for Social and Economic Modelling (NATSEM) to aid discussions by stakeholders at the Collaborative Forum to be held at the University of NSW, Sydney, on 7 March 2002. The aim was to prepare a position paper that identifies and assesses possible mechanisms/models for funding new high cost biotechnology products and other innovative targeted therapies that are not achieving listing on the current Pharmaceutical Benefits Scheme (PBS). There is no intention for the position paper or the Collaborative Forum to undermine Medicare or the PBS, rather the objective is to build on their aims and positive achievements to date.

The position paper is based on two main sources of data: information extracted from the published literature, and structured interviews with key stakeholders.

Background – Key Issues

There was strong support amongst stakeholders interviewed for the position paper for the current Pharmaceutical Benefits Scheme. They noted that the scheme was seen internationally as one of the best in the world, that the 'cost effectiveness' criteria of the PBAC had generally delivered the desired health outcomes, and that the current arrangements had proved to be flexible enough to accommodate some new biotechnology and oncology drugs. However, the PBS is under pressure to fund new high cost biotechnology and other innovative targeted therapies. In most cases, these therapies represent major advances in the prevention and treatment of previously unmanageable diseases. The feature that differentiates these new interventions from the traditional small molecules currently being listed on the PBS is that these high cost biotechnology, oncology and macromolecule solutions are 'targeted' therapies i.e. they are designed for use in a well defined targeted group of patients who have specific biological markers. It is this target group of patients who will respond and benefit most from therapy. Clear criteria for patient eligibility therefore should be able to be established to both optimise health outcomes and accurately predict the budgetary implications to government and patients if the drug is listed on the PBS.

There are a number of key economic issues surrounding these new drugs. These include: investment in research and development: potential health benefits that may be gained from the use of these drugs; the possible effects of doctor prescribing patterns on the cost and potential health impacts; issues involved in drug pricing, consumer demand, willingness to pay and affordability; and long term sustainability.

Stakeholders expressed concern that, without changes to current practices, the PBS may not be sustainable in the long run. Ways of curbing the over 10 per cent per annum growth of

PBS expenditures since the early 1990s were discussed. Controlling 'leakage' was the most common theme, stakeholders noting that if expensive drugs could be better targeted to those gaining greatest benefit, then growth in expenditures would be lower. Greater patient awareness of the costs of PBS drugs that they use, greater patient responsibility for such costs (e.g. through copayments and expanded health insurance policies), and tighter controls of patient eligibility were also mentioned, as well as a greater focus on making best use of the cheaper existing drugs. There were also calls for considerably more research to demonstrate the 'worth' of such proposals before progressing to consideration of implementation.

Review of the PBS

The TGA assesses the efficacy and safety of new drug products. Products must be registered on the Australian Register of Therapeutic Goods (ARTG) before they can be marketed in Australia. A drug can only be listed on the PBS if the Pharmaceutical Benefits Advisory Committee (PBAC) has recommended it. The current legislation requires the PBAC to consider the effectiveness, cost and cost-effectiveness in its deliberations on listing of a drug. The Pharmaceutical Evaluation Section (PES) evaluates company submissions for comparative effectiveness, safety, cost-effectiveness and budgetary impact. The PES provides an evaluation report which goes to the Economic Sub-Committee (ESC) of the PBAC, the PBAC and the company. The ESC advises the PBAC on these issues. The PBAC may consider a drug or drug formulation for Restricted Benefit or Authority Required listing.

Current difficulties perceived by stakeholders, and/or reported in the recent literature in getting high cost biotech drugs listed on the PBS include: requirements for empirical and randomised trial data; issues of cost and price; high cost-effectiveness ratios; "leakage" in terms of problems with identification of the target populations or usage outside of defined populations and doctor prescribing behaviour; logistics and organisational problems with the approval process; and problems with the lack of transparency of decisions and consumer involvement. Some stakeholders expressed the view that the high development – and consequent market - costs of new biotech drugs resulted in products for which cost effectiveness was hard to prove. While some stakeholders felt that much tighter 'leakage' control was not only feasible, but necessary in future, others expressed doubt that 'leakage' control could be effective without a level of 'policing' that Australians may find difficult to accept.

Options for Funding

Six models are proposed. Three of the mechanisms attempt to precisely identify and specify patient and/or prescriber eligibility, and initiate treatment monitoring and evaluation of treatment outcomes (models 1-3). Option 4 examines possible structural and organisational changes to the current reimbursement process as a means of overcoming or at least diminishing existing problems. The last two options address the issue of greater cost sharing with patients or third party payers. There were calls by interviewed stakeholders for greater

efforts by government to educate both doctors with respect to appropriate prescribing behaviour and patients in terms of the full costs of drugs and their appropriate usage. While price is clearly an important factor, the models do not specifically focus on finding ways to contain costs through price control.

1. **'Quality Use and Outcomes Measurement for Biological Agents' Registry Model.** This model seeks to establish objective assessment and outcomes measurements by means of a Registry. The model is based on the proposal to establish the Quality Use and Outcomes Measurement for Biological Agents for Rheumatoid Arthritis (QUOM-BARA) Registry, developed in preparation for the introduction and proposed PBS subsidisation of novel biological agents for the treatment of rheumatoid arthritis. This model aims to ensure that only those patients who fulfil predetermined diagnostic and disease activity criteria will be granted subsidised access to the proposed biological agent, and that approval for continuation of the agent will only be granted to patients whose response meets predetermined continuation criteria. The system would monitor adherence to prescribing criteria, thus minimising opportunity for leakage, and be able to capture high quality data that can be used to analyse responses and outcomes.
2. **Staged 'Clinical (and Economic) Trial' Model**. This model represents a staged approach to the PBS approval process, in that proposed drugs enter a clinical trial as a provisional listing mechanism before full listing is granted. The model stems from current drug registration processes, where clinical trials play a fundamental role in establishing quality, safety and efficacy. The model also draws on the TGA's scheme that allows the supply of unapproved therapeutic goods through clinical trials, and has its derivations in an earlier proposal by Professor Paul Glasziou (1995) who argued for a new authority category for the PBS — namely an authority to prescribe within a controlled trial. This is a prudent strategy as it provides access to new drugs for patients in clinical need and a mechanism for collecting appropriate information for future decision-making. Assessment on a trial basis could allay the fears and concerns of those who believe there is insufficient clinical or economic evidence to warrant full PBS listing. To avoid any perceived conflicts of interest, rather than the PBAC, an autonomous organisation such as the NPS or NHMRC's CTC could act as the independent co-ordinator of the trials.
3. **Special Supply Scheme Model**. An argument put forward by stakeholders is that high cost biotechnology and other innovative targeted therapies are different to the small molecule drugs traditionally funded through the PBS and therefore different arrangements should be put in place for their funding. This model stems from the use of Section 100 of the *National Health Act 1953,* the special supply arrangements under the PBS for 'highly specialised drugs' (HSDs) and the special funding mechanism that has been recently put in place for the supply of the breast cancer drug Herceptin. As one stakeholder said *'we are not exploring the range of mechanisms currently available, we are not optimising criteria already there for inclusion'*. Many of the organisational mechanisms needed for a special supply arrangement mechanism designed to assess high cost biotech and other targeted therapies are already in place in existing programs or could be

relatively easily adapted. A model based on the special funding arrangement approach could provide a transparent and consistent process for assessing and funding these drugs.

4. **Incremental (Evolutionary) Organisational Reform Model**. It was generally agreed that the PBS was one of best schemes in the world. However, stakeholders believed that many of the problems currently being encountered could be overcome by change to the prevailing organisational culture of the PBAC (and associated committees), and evolutionary (incremental) administrative reform to the ways in which the PBAC operates and conducts the approval process. As one stakeholder said *'If the process worked properly, it would work well'*. Stakeholders want a rational, consistent and transparent process for determining what drugs should be PBS listing. This option identifies improvements that could be made to the approval process within the existing PBS organisational-administrative framework. Three main areas of change are identified. These are: 1) organisational issues including logistics and transparency**;** 2) assessing cost effectiveness; and 3) improvements to the quality of submissions. These changes are not specifically targeted to high cost biotech drugs, but rather address general problems with the PBS approval process.

5. **Differential Copayments and Public Subsidy Arrangements**. This option puts forward alternative copayment arrangements as a mechanism for government to share the cost of existing and new pharmaceutical medicines with prescribed drug users. With respect to the provision of price signals, the view was put forward by some stakeholders that if the patient was not prepared to pay for a drug (assuming they were able to afford to pay), then it was not appropriate to ask taxpayers to subsidise such drugs. The major differences in pharmaceutical subsidy arrangements are with respect to four key elements: 1) the eligibility criteria i.e. what section and proportion of the population is covered; 2) level of public subsidy i.e. the size of the drug list and level of patient copayment; 3) the type of subsidy list – positive, negative or both; and 4) the mix (balance) of coverage provided by public versus private schemes (Productivity Commission, 2001). There are two basic types of copayment systems (subsidisation schemes): fixed (flat) rates of patient copayment, as currently operating in Australia, and proportional copayments where patient contributions (and government subsidies) are proportional to final drug prices (or reimbursement). Proportional copayments usually operate as a sliding scale by drug category. The advantages of a fixed subsidy system – e.g. they are easy to understand and administer – tend to be outweighed by their failings. There are equity concerns with both fixed and proportional copayment schemes, but there are a number of subsidy arrangements that the Australian Government could explore with the view towards long term sustainability of the PBS. Although shifting to a proportional copayment system would add to the complexity of current PBS system, these types of subsidy arrangements have been used widely overseas.

6. **Cost Sharing with Third Party Payers – Expanding the Role of Health Insurance.** This option raises the possibility of shifting some of the cost of prescribed pharmaceuticals to

third party payers through increased use of either social insurance schemes or private health insurance funds. In Australia, private health funds play a very minor role in the funding of prescribed medicines – this role could be expanded in a collaborative manner. In the US, private insurers, HMOs and managed care plans use a variety of managerial techniques and incentives to regulate doctor prescribing practices and to encourage doctors to adhere to specific practice guidelines to help control prescription drug costs. Countries such as France, Germany and the UK also have used drug budget-holding with GPs as a means of controlling costs. Germany and the Netherlands also allow their high income earning citizens to opt out of their social insurance systems and take their taxes and wage contributions with them to purchase private health insurance. Increasing the involvement of health funds has the potential to bring additional resources into the reimbursement of pharmaceuticals which is unlikely to happen within the existing system. The economic argument for private sector involvement relates to cost-sharing and to increasing consumer choice, responsiveness and price regulation through market competition. For consumers to demand, participate in and pay for private health insurance then the coverage the schemes provide has to be 'good', reasonably priced and give value for money. However, an important issue with mixed public-private drug reimbursement arrangements, in which the role of the private sector is expanded, is the risk of developing an inequitable two-tiered system. The health funds would implement mechanisms similar to those used by the PBAC, or outlined in the other options, to assess cost effectiveness, patient eligibility, copayment arrangements etc.

Conclusions

Providing patients with access to effective drugs at affordable prices is a challenging task for any society. The need for effective review of submissions to the PBAC has to be balanced against the urgency for drug access. Each of the six funding options comes with advances and disadvantages. A cost-benefit analysis that would allow comparison of the expenditure required to implement each of these six options versus the benefits gained is a next step in the way ahead.

There are two basic sets of issues that need to be addressed in discussing the funding of pharmaceuticals. The first is ensuring equity of access to drugs at affordable prices to those in clinical need. The first four of the six proposed options are located within this debate. However, as a number of stakeholders voiced, these models and the entire debate about new pharmaceutical technologies need to be located within the wider public debate of *'How much is Australia prepared to pay for pharmaceuticals, who should pay, and what drugs do Australians want subsidised?'* These questions represent a second set of key issues, relating to taxpayer and consumer funding of drugs. The fifth and sixth options proposed relate to this wider debate. The PBAC has an unenviable task. In many ways, this Committee has become the custodians of part of the public health budget. Is this fair or reasonable? A broader debate raises funding options outside the current organisational framework, and perhaps beyond the mechanisms proposed in this position paper.

1 Introduction

This position paper was prepared by the National Centre for Social and Economic Modelling (NATSEM) at the University of Canberra to aid discussions by stakeholders at the Collaborative Forum to be held at the University of NSW, Sydney, on 7 March 2002.

1.1 Objective

> To prepare a position paper that identifies and assesses possible mechanisms/models for funding new high cost biotechnology products and other innovative targeted therapies that are not achieving listing on the current Pharmaceutical Benefits Scheme (PBS).

The aim is to outline possible options for the funding of these new drugs under either current PBS mechanisms or new or modified supply arrangements. Options may include specific patient assessment tools or guidelines prior to prescribing or possibly a limited prescribers' pool. Different prescribing protocols may be required for low and medium volume patients. This position paper is for discussion at a stakeholders' Collaborative Forum scheduled for 7 March 2002. The objective of the Forum is to propose preferred funding model options that can be incorporated into the PBS process for new, current and future high cost biotechnology and oncology therapies. These preferred models will then be taken to the Federal Health Minister for consideration.

There is no intention for the position paper or the Collaborative Forum to undermine Medicare or the Pharmaceutical Benefits Scheme, rather the objective is to build on their aims and positive achievements to date. Over its 50 plus years long existence, the PBS has served Australians well and its aim to provide timely, reliable and affordable access for the community to necessary and cost effective pharmaceuticals is still considered by most Australians to be a highly desirable goal. Stakeholders noted that Australia's Pharmaceutical Benefits Scheme was highly regarded internationally – including the cost-effectiveness criteria used as a key part of the reimbursement decision-making process.

1.2 Background

Many believe that, with the publishing of the full sequence of the Human Genome and the rapid advances in the related area of proteomics,[1] the world is entering a new era in medicine and in the development of pharmaceuticals.

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[1] Proteomics concerns the end products of genes, the proteins.

Knowing the genome gives us much greater insight not only into genetic abnormalities, but also into the disease-specific susceptibility of genes. We are now able to determine which genes are expressed or used in any particular situation and identify the "*DNA sequences that confer susceptibility to a range of conditions that afflicts us as we age*" (Doherty, 2001) – eg Alzheimers, cancer, arthritis (Doherty, 2001 and ABC, 2001).

Appendix A describes how this knowledge can lead to the development of drugs that are able to bypass a defective protein or protein pathway. Tracing the proteins involved in diseases is expected to lead to quicker and better diagnosis; more individualised and more effective drug treatment; considerably greater health benefits; and in the case of some now fatal diseases, the saving of lives. In some instances, the number of potential beneficiaries will be relatively small (eg leukaemia), and in others large (eg in the case of the degenerative diseases of ageing).

One example that has been widely reported in the media concerns the now PBS listed drug, Glivec. People with chronic myeloid leukaemia, who were expected to die because all traditional treatments had failed, had their blood virtually free of cancer, within months of going onto Glivec clinical trials. Although the longer term effects of that new drug are unknown, people previously bed-ridden reported being able to lead a normal life when taking Glivec. Successes have been reported in the media in a number of countries – for example by the Time Magazine (2001) in the US, and the ABC (2001) and The Age (2001) in Australia. ABC (2001) also reported that Glivec has also been found to be effective for patients suffering from until now an incurable very rare form of intestinal (connective tissue) cancer.

Professor Kirkwood (2001) considers that, recently, "*science has made hitherto undreamed-of advances in human biology*". As a result, he expects a quantum increase in life expectancies, together with considerable improvements in quality of life patterns as new drugs able to 'by-pass' some of the degenerative processes of ageing are developed. The unexpectedly fast approaching gains in life expectancies and in quality of life patterns, together with the prospect of being able to keep people with previously fatal diseases alive, raise the question of whether Australia's current, well tested and well regarded administrative systems will be equally effective in the new 'biotech' era.

The emerging innovative drugs and therapies have the potential to deliver very positive health outcomes. For example, 50 out of 100 patients using Glivec respond positively, compared with up to 2 out of 100 with the old therapies. While the hitherto undreamed-of benefits of such drugs are welcome by all, the associated very high costs – perhaps an order of magnitude higher than the costs of most existing therapies – are generally viewed with caution.

The current Pharmaceutical Benefits Scheme is under increasing pressure to fund new high cost biotechnology and other innovative targeted therapies for the prevention and treatment of previously unmanageable diseases. In most cases, these therapies represent major advances in prevention and treatment, and potentially have a great impact on health outcomes – but often at historically high costs. Internationally, the issue of who will have

access to such drugs, under what conditions and at what cost to patient/government, will need to be resolved in a way that is acceptable to the citizens of each particular country. In Australia, a recent survey suggested that people tend to place a very high priority on health issues and are willing to fund some of the costs of health services through their private savings (Irving Saulwick & Associates, 2001). However, regardless of the extent of private-funding, the new biotech-based therapies – if listed on the PBS – have the potential to increase considerably the already high growth rates of PBS expenditures. In 2000-01 government PBS expenditures increased by 20 per cent, and patient PBS expenditures by 14 per cent (DHAC, 2001). Stakeholders generally shared the view of the community and government that growth rates of that magnitude were unsustainable over the longer term. Writing in the Australian Journal of Hospital Pharmacy, Professor Lloyd Sansom (2001), Chair of the Pharmaceutical Benefits Advisory Committee (PBAC), suggests that '*the greatest challenge to the PBS is the availability of agents resulting from molecular design and the human genome project. We are already seeing the marketing of such drugs (e.g. Imatinib, Etanercept) at a cost which is generally much higher than we have previously seen for new agents. Further, the benefit of many of the newer anticancer drugs will be incremental resulting in extremely high and unfavourable cost effectiveness ratios, yet the community (and health professional) demand for these agents to be subsidised continues to grow*' (p257).

However, a key feature that differentiates these new interventions from the traditional small molecules currently being listed on the PBS is that these high cost biotechnology, oncology and macromolecule solutions are 'targeted' therapies i.e. they are designed for use in a well defined targeted group of patients who have specific biological markers. It is this target group of patients who will respond and benefit most from therapy. Furthermore, older traditional therapies used in the treatment of cancer and autoimmune diseases are toxic chemotherapaeutic agents because they are not well targeted, hence their risk:benefit ratio is high compared with that for the new targeted therapies. Clear criteria for patient eligibility for the new targeted therapies should thus be established to optimise health outcomes, accurately predict the budgetary implications to government if listed on the PBS as well as costs to patients and minimise opportunity for leakage.

Although surrounded by media hype, the public debate over the PBAC's recent recommendation to Government for PBS listing of Viagra[2] is very timely and apt, as it raises and draws attention to some of the very real issues also confronting the stakeholders in high cost biotechnology drugs and other targeted therapies. As reported in the Weekend Australian (Editorial, January 19-20, 2002, p16) "*… there is, [however], room for sensible discussion about the direction of a subsidised drug scheme that is imposing a sharply rising cost on*

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[2] The Minister for Health and Ageing, Senator Kay Patterson, announced on 13th Februrary 2002 (DHA, Media Release) that the Federal Government would not approve the listing of Viagra on the PBS. The Government, and the PBAC, were concerned about the potential cost of listing Viagra. Senator Patterson said "*The Government has decided, given the increasing demands on the PBS, that funding for erectile dysfunction should not be a priority*".

society. In fact, the Viagra debate should be used as a stepping stone to a rational analysis of the PBS's purpose, the criteria used to determine eligibility, the way the PBAC functions, and the cost Australian taxpayers can and should wear". As reported by Steve Dow in the Sydney Morning Herald (Jan 26-27, 2002, p 11) "*each acceptance or rejection is accompanied by questions: why this drug? Why not ours? Did the drug industry influence the decision? Did politics override good health policy?*" Lloyd Sansom has stated that "*the quality of the public debate about the PBS system and its future is appalling and must improve*" (2001, p 257). Sansom also states that "*we should not be afraid to think of new ways and ideas to improve the system and to make it more able to meet the challenges which are ahead*" (2001, p 257). This position paper aims to contribute to this improved and rational discussion of the future of the PBS.

The drugs and therapies that are the focus of the position paper are for commercial supply in Australia, with the companies wanting to supply through the market. These products therefore have been required to undergo pre-market assessment and have been approved (evaluated) by the TGA (Therapeutics Good Administration) for their safety and efficacy and are included on the Australian Register of Therapeutic Goods (ARTG). Approval by the TGA is clearly an important part of the overall process of introducing new drugs into the Australian marketplace but this is not the focus of the position paper. Rather, it is concerned with the issue of government subsidisation of therapies, in particular, the processes related to PBS-listing.

1.3 Structure of the Position Paper

The two main methods used in the data collection – an extensive literature search and structured interviews with 23 stakeholders from a range of consumer, industry, medical and government organisations and agencies – are briefly outlined next in Section 2. The position paper then has three main sections. Section 3 reviews the key economic issues surrounding high cost biotechnology and other innovative targeted therapies. This section briefly highlights the magnitude of the development effort by pharmaceutical companies and the potential health impact – including disease coverage of new drugs and the size and characteristics of the patient base that is most likely to benefit, the importance of general community expectations with regard to patient access to new drugs, and possible effects of doctor prescribing patterns on size of the above 'potential' health impact.

Section 4 then provides a brief review of the current PBS, including aims and functions, administrative structure, and submission and approval processes for listing of new drugs and therapeutic products on the PBS. It also reviews current difficulties in obtaining reimbursement under the current PBS mechanism for high cost new therapies *viz* leakage, controlling doctor prescribing behaviour, targeting patient recipient groups, interpretation of economic analyses and modelling.

Section 5 details six alternative models and mechanisms for funding. These options take into account prescribing monitoring and restrictions (closed vs open loop systems), assessment of patient outcomes and address the issues of accountability and transparency. Wherever possible the models have been illustrated using case studies of drugs, some having been rejected and others accepted for PBS listing in one form or another. The paper concludes with a brief summary and overview.

2 Methodology – Data Collection

The position paper is based on two main sources of data: information extracted from the published literature, and the views and opinions of key stakeholders.

2.1 Literature Search

A wide variety of popular, academic, industry and official government literature was accessed through library resources, electronic databases and the internet. We restricted the main literature search to a two year timeframe of Jan 2000-Dec 2001, as biotechnology and other targeted therapies is a recently developing field. However, widely regarded key references before this period were also identified. We primarily used the following electronic database search engines: Current Contents, Medline, and ProQuest. We used a two-pronged approach to identifying relevant material. First, we reviewed the past two years issues of key medical and pharmaceutical journals and periodicals. These included: international journals – the British Medical Journal, Lancet, New England Medical Journal and the Journal of the American Medical Association, Drug Development Research, Pharmacoeconomics, and Health Economics; and the Australian journals - Australian New Zealand Journal of Public Health, Australian New Zealand Journal of Medicine, Medical Journal of Australia, Australian Health Review, (New Zealand Medical Journal), Australian Prescriber and the Australian Journal of Hospital Pharmacy. We also searched popular 'magazines' such as The Economist, New Scientist and Times Magazine. Second, we searched on key words including drugs/prescribed medicines/pharmaceuticals, biotechnology and drugs/targeted/innovative therapies, drug/pharmaceutical approval, the pharmaceutical industry, and the PBS. In addition, we searched on drug names. These searches yielded an extensive amount of material – the results were then scrutinised for their direct relevance and applicability to the position paper.

We were also directed to or provided with key papers and documents by interested stakeholders.

2.2 Consultation with Stakeholders

Structured interviews were held with 23 stakeholders. Potential interviewees were selected from the list of invitees to the Collaborative Forum to represent a range of interests and to cover all major stakeholder groups i.e. health consumer organisations, health professionals, industry and government.

A list of questions and topics for discussion were generated on a priori basis from the literature and exploratory discussions with several key informants. Three interviews were conducted as a pilot. Potential interviewees were contacted principally by telephone but a small number were also approached by email/fax/or mail and invited to participate. The list of final participants is provided in Appendix B1. The background to and reasons for the interview were explained and participants asked to sign a consent form for their responses to be used as input into the position paper (see Appendix B2).

The interviews were conducted either by telephone or in person, and were generally of a reasonably informal nature, interviewees being asked to comment on as many questions as were relevant to their interests and background. The list of questions is given in Appendix B3. Interviews were conducted mainly by Dr Laurie Brown and Agnes Walker of NATSEM with additional help from Dr Lynn Robinson and Nancy Emmanuel from Med-E-Serv.

3 Key Economic Issues

3.1 Research and Development

A common claim regarding pharmaceutical R&D and the prices of prescribed drugs is that the world prices of pharmaceuticals are too high. One concern is that large multinational manufacturers are spending more on marketing than on research. Some stakeholders suggested that if they lowered their marketing effort, then the savings could be used to reduce drug prices.

While views on the marketing versus research balance might in particular instances be accurate, it is often not realised by the public that pharmaceutical companies need to spend millions of dollars to develop a new drug. Hewitt and Lowy (2001) state that, in the US, a drug company typically spends US$802 million over the 10 to 15 year period between commencing the development of a new drug and obtaining approval to market it.[3]

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[3] Calfee (2001) confirms this, stating that "most new drug development projects fail, sometimes after substantial financial and time costs". Because of the high risks and costs

Neither is it generally known that returns to R&D projects in pharmaceuticals follow patterns similar to venture capital investments. That is, a small proportion of development projects tend to generate most of the revenue needed to recover development costs. Grabowski (2000) has shown that, in the US in the early 1990's, the most profitable 10 per cent of 110 new drug entities accounted for around a half of both the sales revenue (56 per cent) and of the 'quasi profits' realised by the full sample (48 per cent). This means that each of the drugs in the other 90 per cent – that is the vast majority of the new entities studied – contributed very little to overall sales and profits.[4] The above findings are in line with the conclusion reached by the Productivity Commission (2001, p.17-8) that R&D in the pharmaceutical industry was highly risky, that company profitability depended greatly on blockbuster products, but that amongst all new drugs blockbuster status was extremely rare.

The high risks involved in R&D activities does not mean that the industry cannot be profitable – clearly it has been in the past – but it does mean that too much pressure on the industry to keep prices down could lead to significant declines in R&D effort. Unless companies are able to at least recover development costs internationally, patients may never see the potential health benefits of the vast amounts that have already been spent on the Human Genome project. The issue of how the future patterns of patient/government shares in prescribed drug expenditures might evolve is discussed in Section 3.5.

3.2 Health benefits

The potential *health benefits* of high cost biotechnology and oncology therapies appear at this stage to fall into three groups:

- therapies able to save the lives of patients who until recently have faced certain death; and
- therapies able to limit (or eliminate) some of the profoundly disabling effects of ageing (see Section 2); and
- Therapies able to halt, slow down or prevent chronic progressive diseases and thus reduce or prevent disability resulting in improved quality of life.

Drugs in the first group are likely to be used to treat a small number of patients, while those in the second group a large and rapidly increasing number of patients (reflecting the ageing

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involved, Calfee argues that price controls would not only have substantial negative effects on pharmaceutical R&D, but may also have a harmful effect on patients.

[4] The many years involved in bringing a new product onto the market also adds to the riskiness of R&D. The Productivity Commission (1996, p. 18) estimated that development times varied between 6 and 10 years, and that 2 to 3 additional years were needed before government approvals could be obtained.

of the population).[5] In his early 1990s study, Grabowski noted that "the blockbuster compounds …. generally represent significant therapeutic advances in treating a particular disease, usually one with significant market size" (2000: 23-4)

One issue regarding the health benefits of the drugs that are currently being developed is that they are at this stage uncertain and difficult to quantify. There is a lack of data on how the drugs will perform over the longer term and a lack of accurate information on the 'target' patient populations. This is of course common to all situations where rapid technological change disturbs the close to 'steady-state' equilibrium of past years, often making projections based on past trends inaccurate. It is also worth noting that traditional techniques of economic analysis tend to operate on the margin – that is they consider small deviations from what has been observed in the past.[6] Because of this, such analyses are not generally useful in situations involving rapid technological change.

Quantifying health benefits so that they can be compared with the cost of new drugs has always been difficult. One commonly used methodology is the measure of the 'burden of disease' – see World Health Organisation (2000); Mathers, Vos and Stevenson (1999). This measure has two components: premature deaths (or years of life lost) and years lived with disability. While more general use of the 'burden of disease' measure represents a significant advance on what had been attempted previously, in its current form the 'burden of disease' measure is not well suited to assessment of the benefits of many pharmaceuticals. This is because a high proportion of pharmaceuticals neither save lives nor reduce the number of years lived with disability. Obvious examples are the pain killers, drugs that bring about prevention of disease, drugs that improve the quality of life of Australians generally and the drugs that keep people 'operational' (ie at work, or allow them to function independently).

In addition, quantifying the health benefits of new drugs is harder (than for existing drugs), because there are fewer 'solid' statistics on their effects. For example, stakeholders were uncertain about the number of years that the life of a leukaemia patient could be extended by when treated with Glivec – three, five, or twenty or more years appeared all possible at this stage. We also need to keep in mind, as one stakeholder commented "*biological agents are*

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5 Australian Bureau of Statistics projections suggest that, by 2050, Australia is likely to have over 20 per cent of its population aged over 65, compared with less than 15 per cent currently. The Bureau's projections – based on traditional assumptions about improvements in life expectancies - suggests that the proportion of people aged 85 years and over will have risen from around 1 per cent of the total population in the mid 1990, to 5 per cent by 2050 (ABS 1996).

6 The types of economic evaluations required by the PBAC are described in Section **4** of this position paper. How the broader cost-benefit framework could be applied to the Pharmaceutical Benefits Scheme is covered in detail in Islam and Mak (2000). However, like most other traditional methodologies, cost-benefit analyses rely for their input data on past steady-state situations and are inadequate when studying periods in which rapid technological change takes place.

proving to be very effective because they have been targeted to operate on defined molecular mechanisms. Equally, because of their short history of use, we may not be able to accurately assess the longterm effects of this profound interference with basic molecular mechanisms". Another stakeholder commented it was important that "*we start people on these drugs and gain experience of these on our own 'home turf'* ".

Overall, because of the difficulties of quantifying the health benefits of the emerging high cost biotechnology and oncology therapies, the demand for them will probably depend much more on how the community 'perceives' their benefits; on how much patients and third party payers are willing and able to pay; and on expectations about the extent to which government(s) should be involved. These issues are discussed in later Sections.

3.3 Doctor prescribing patterns

The possible effects of doctor *prescribing patterns* on the cost and potential health impact of high cost biotechnology and oncology therapies is also important. Research has shown that in Australia the number of GP consultations is the most powerful predictor of the number of prescriptions written and that an index of the severity of illness - although statistically significant - was only a weak predictor of prescribing patterns (Pritchard 1999).[7] The rate at which individuals visit their doctors[8], and the attitudes of the medical profession towards the new biotechnology and oncology therapies, are both likely to be important factors in determining the take-up rates and usage patterns of such drugs. Stakeholders also noted that, in future, prescribing patterns for certain chronic conditions may be revolutionalised, for example, drugs that are to be used for long term treatment and that have a variable patient response may be subject to single patient (n-of-1) trials (see Nikles et al, 2000). A patient acts as his or her own control in comparing the effectiveness of a new drug with that of others. The aim is to identify the best treatment for a given individual patient (Nikles et al, 2000). This provides a way of identifying those individuals with chronic conditions who would respond sufficiently to justify the subsidisation of the high cost drug.

Widespread subscribing without fully taking account of the conditions attached to PBS listings is reported in Green and Bloch (2001). The reasons quoted are 'ethical' in nature, in that doctors attempt to do what they consider the best for their patients, regardless of the PBS rules.

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7 There is some evidence that prescribing behaviour can be influenced to some extent by educational interventions (Zwar, Britt and Henderson, 2000).

8 The number of per capita doctor visits per year has been increasing since the late 1970s. Walker and Abello (2000, p.77) found that while during 1977-78 Australians visited their doctor 6.4 times on average, by 1995 this number had increased to 7.7.

3.4 Prices of new drugs

The *prices charged for drugs* by manufacturers may also influence the potential size of the health impact of the new 'biotech' drugs. Australia has a long history of having been able to negotiate below world prices for PBS listed drugs. In this respect the Productivity Commission (2001, p. xvi) found that, as at 30 June 2000, manufacturer prices for the top 150 pharmaceuticals – accounting for over 80 per cent of total PBS expenditures – were much lower in Australia than in the US, Canada, UK and Sweden. However, for new innovative pharmaceuticals, Australian prices were found to be much closer to prices in other developed countries. This suggests that, in the case of the high cost biotechnology and oncology therapies, Australian prices are likely to be similar in magnitude to those in other developed countries.

At the individual drug level, prices that were relatively high (compared to other drugs on the local market) at the time the drug was first introduced were found to generally decline over time. This was attributed to factors such as patent expiry dates and the introduction of new improved products of a similar nature. For example, using US data (given that this is a different regulatory environment to that in Australia), Suh et al (1998) observed average price increases of 7.9 per cent a year during the patent protection period, but only 6.8 per cent per annum afterwards. For 'originators' the difference was even more marked – 9.1 per cent before patent expiration and 6.0 per cent afterwards.

Using Australian Health Insurance Commission (HIC) data, Figure 1 illustrates the pattern of price declines for the drug group mainly comprised of the anti-ulcer drug Zantac - which was the world's top selling pharmaceutical product in the 1990s (Productivity Commission, 1996, p.17). Figure 1 shows that between 1992 and 2001 the monthly average cost of the drugs in that group[9] nearly halved– a decline from around $43 to $23 a month due to generic entrants. Other price reduction methods operating for listed products on the PBS include the use of price/volume arrangements; the Pharmaceutical Benefits Pricing Authority use of weighted average monthly treatment cost calculations for products with similar effectiveness and safety; the addition of new indications; and removal of an "Authority required" restriction.

However, further investigations using the HIC data showed that, over the same period, average prices did not decline for all drug groups (noting also that prices did not necessarily increase but rather remained at much the same level). This raises the question of whether the currently very high cost of new biotechnology and oncology therapies would decline or remain unchanged over time. This issue is an important one, because it impacts on the question of the long-term affordability of these new drugs. As seen earlier, even for the

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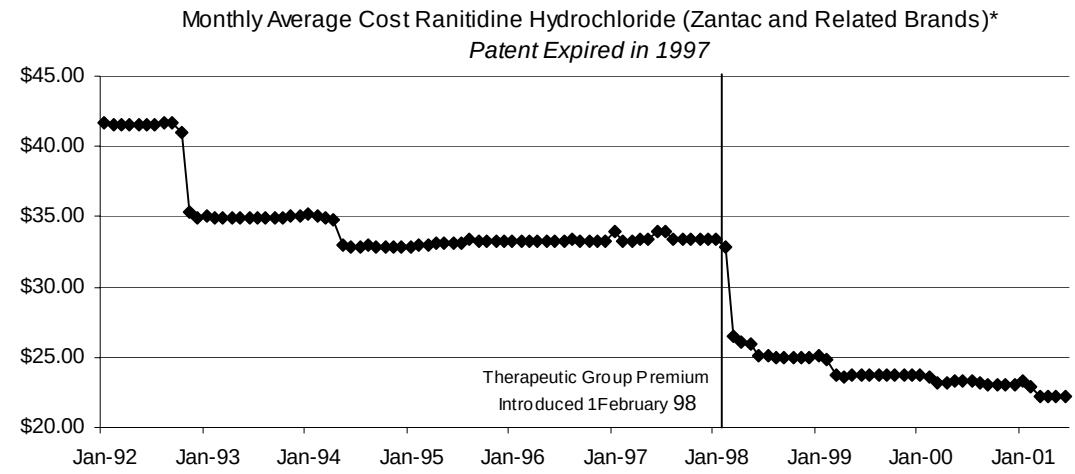
9 Monthly average cost was computed as expenditures by government and patients in that month, divided by the number of prescriptions in the same month. This average cost can be considered to be a proxy for drug prices in the group under consideration.

highly targeted disease specific new drugs, such as Glivec (which was initially used to treat patients with leukaemia), it is possible to find other uses (in this case for patients with intestinal cancer).

Figure 1 **Price Decline for Zantac and Related Brands**



Source: NATSEM computations using data available on the Health Insurance Commission (HIC) website. Note: the molecule charted comprises 12 HIC codes, which do not necessarily each have the same dosages and/or presentations.

Overall, prices of the new 'biotech' drugs could decline over time, either because additional 'target groups' had been identified; newer competing drugs have emerged; or because of economies of scale of manufacture or volume of sales.

3.5 Demand, willingness to pay and affordability

High costs, and whether such costs are likely to decrease over time, raise the issues of *consumer demand, willingness to pay and affordability.* As noted earlier, a recent survey suggested that Australians place a very high priority on health issues and were willing to pay for at least some health costs through their personal income. Similar findings have been reported for the US (Larson, 2000).

In the context of high cost biotechnology and oncology therapies a key question is the proportion of the population that might be able to afford (partially or fully) the current $80,000-$100,000 per patient per annum cost of Glivec,[10] and the proportion that would not

[10] When announcing the listing of Glivec on the PBS, the media release of 7 November 2001, the Minister for Health and Aged Care states that "Glivec treatment currently costs

be able to afford it without massive government subsidies. If government subsidies were required by most, then the issue of whether the necessary funds could be raised through additional tax revenues, or savings from other areas of the health system, arises. Some stakeholders also felt that there were potentially big savings in searching for new uses of existing low cost drugs (eg aspirin, which is now used for stroke prevention). However, such research would need public financing, as the return on investment would be too low for pharmaceutical companies (despite the considerable cost savings and health benefits arising from lower prevalence of strokes).

A recent survey of doctors in Australia, Canada, New Zealand, the UK and the US found that only in the US and New Zealand did the majority of doctors see patients' 'out-of-pocket' costs as a major problem. The US stood out on the issue of prescription drugs – with half the doctors saying that the affordability of prescription drugs was a major problem for their patients. These findings point to the type of situation that could develop in Australia if patients were to become responsible for a significantly higher share of prescribed drug costs under the PBS than currently. This issue is discussed further in Section 5.5.

Stakeholders expressed concern about the lack of price signals to consumers as to which drugs or treatments were cost-effective and suggested that lower (higher) copayments could be charged for the most (least) cost-effective drugs. Concerns about price signals have also been reported in the international literature. For example, Calfee (2000) argued for the prices for pharmaceuticals to be much more market-driven in future, because the emerging new drugs were expected to shift the focus away from the currently dominating acute care activities towards long term prevention and quality of life improvements. The reason underlying this suggestion is that Calfee sees the massive benefits of the new research as resulting mainly in 'pure consumer benefits'. In other words, while until recently prescribed drugs mainly concerned the healing of the sick, according to Calfee the emerging new drugs will mainly result in prevention of illness and/or improvements in the quality of life. Hence his conclusion that "only market-determined prices can provide adequate signals for future pharmaceutical research investment" (Calfee, 2000, p. 47).

The way this extra patient responsibility would be formulated (in a policy sense) would determine how people in different socio-economic groupings were affected, and whether particular groups would fall below the 'affordability' line. Previous studies of the distributional effects of different policy arrangements regarding pharmaceuticals include, for Canada, Crossley et al (2000) and, for Australia, Walker (2000) and Walker, Percival and Harding (2000). The latter has shown that, in Australia, it is the poorest amongst general patients (the working poor, large families, etc) who are most vulnerable. Such groups'

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around $2000 a week" and that it is "expected that over 500 Australians will benefit from this decision". The dispensed price as currently listed on the Schedule of Pharmaceutical Benefits for 600mg per day, which is the recommended dose of Glivec, for a 30 day supply is $6,745.

expenditures on prescribed pharmaceuticals were found to account for a much higher proportion of their families' take-home (or after tax) income than for those of other Australians.

3.6 Sustainability in the long run

There was strong support amongst stakeholders for the current Pharmaceutical Benefits Scheme. They noted that:

- the scheme was seen internationally as one of the best in the world;
- the 'cost effectiveness' criteria of the PBAC had generally delivered the desired outcomes. That is, drugs with large health benefits relative to costs had in most cases been listed, while those with marginal improvements relative to existing cheaper drugs tended not to be listed; and
- the current arrangements had already proved that they were able to adequately handle new biotech drugs. The example given was the new life saving drug, Glivec. Listed on 7 November 2001, approval for this drug had been 'fast tracked' - to 7 months compared with the usual 18 to 24 months. The drug, although without a comparator and with no backing through historical data, was listed despite its high cost ($80,000 to $100,000 per year). The very large health benefits (close to normal life for several years compared with certain death without the drug) and the small number of persons affected (around 500) were important factors in obtaining listing. At the same time a very strict authority had been imposed to limit possible 'leakage'.

However, several stakeholders also expressed concern that, without changes to current practices, the PBS may not be sustainable in the long run.

In a broad economic sense, long run sustainability depends on how fast PBS expenditures grow relative to Australia's GDP. The many factors that are likely to affect future GDP growth are described in Walker (1997, Section 1.3). Since 1992-93, increases in total PBS expenditures varied between 7 and 20 per cent a year [11] – a rate considerably higher than either for growth in GDP or in all health expenditures. Unless, GDP growth accelerates significantly, or PBS expenditures grow well below historic rates in the future, difficult decisions are likely to have to be made about priorities across different parts of the health sector - for example, should the costs of the new 'biotech' drugs be funded through lower allocations to primary care, hospitals, preventive policies, etc.

Several stakeholders, however, voiced an alternative view to what seems to be the prevailing attitude towards the increases in PBS expenditure. They argued that there wasn't a 'crisis' in

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[11] Department of Health and Aged Care (2001 and earlier issues).

PBS funding as commonly portrayed in the media, or projected by government and other bodies. As one stakeholder commented "*we are pandering to a sense of crisis – the PBS is under pressure but not crisis – we are still doing pretty well*" as expenditure in Australia on prescribed pharmaceuticals is low as a proportion of both government expenditure on health and GDP, and that the Australian Government has continued to secure very low drug prices by international comparison. However, stakeholders generally were concerned about the large unexpected 'over-Budget' expenditures that tended to characterise the PBS (for example in 2000-01). One stakeholder believed that "*there was an apparent lack of appreciation by the public that one element of the PBS was to protect the public purse*"**.** Another stakeholder argued that the problem is not so much the total cost of the PBS but "*that government seems incapable of predicting the volume of usage of new drugs. The average compound percentage increase over the last ten years of about 14% compares favourably internationally. Government has been able to fund the PBS even though expenditure has gone up from $1b to $3.5b in ten years. Keeping that sort of rate of increase going might be a problem in the future but it has been manageable up to now. The supposed 'blow-outs' in past years are partly due to the fact that 'Finance' has a model that says PBS costs will go up by 9% which has only occurred twice in the previous decade*". Stakeholders expressed as much concern for the apparent lack of predictability of future PBS budgets as for the absolute levels of expenditure.

Some stakeholders noted that when considering the long term sustainability of the PBS, it was important to ask questions such as : "*is it necessary to save lives*" and "*is it important to relieve extreme pain*" and "*why should 'life style' drugs be taxpayer subsidised*". While long term sustainability is outside the scope of this position paper, it is a concern that tends to be common to the various interests represented by stakeholders (ie the community, government, the medical profession, pharmaceutical companies, etc). Importantly, the use of high cost medicines may be preventative in nature i.e. be used for the primary prevention of disease, and may offset the cost of hospitalisation, other direct medical costs as well as productivity costs to society. Thus, there are potential huge cost savings of high cost biotechnology products to heath care and across other sectors of society. Such outcomes should have major implications in terms of how decision-makers assess the value of products listed on the PBS to the Australian community. This is an issue that stakeholders may wish to discuss at the 7 March Forum.

4 Review of the PBS

4.1 The Pharmaceutical Benefits Scheme

The Commonwealth Government's Pharmaceutical Benefits Scheme (PBS) aims to provide Australians with timely, reliable and affordable access to necessary and cost-effective

prescription medicines (DHAC 2001). The PBS was designed originally in 1948 to provide access for all Australians to a 'free-list' of life-saving medicines. Today, a comprehensive range of medicines is listed on the PBS. As at 1 August 2001, the PBS covered 594 generic drugs, available in 1,466 forms and strengths (items) and marketed as 2,448 different drug brands. An authority prescription is needed for 297 of these items and restrictions also apply to a further 488 items.

From 1 January 2002,

- *general* patients pay the first $22.40 for each PBS item; and
- *concessional*[12] patients pay the first $3.60 for each PBS medicine.

The PBS Safety Net arrangements protect individuals and families from large overall expenses for PBS listed medicines. For general patients, once the eligible expenditure of a person or their immediate family exceeds $686.40 in a calendar year, the patient copayment per item decreases from $22.40 to $3.60. The current Safety Net threshold for concessional patients is $187.20 and, once this threshold is reached, they pay no copayment for the remainder of the calendar year.

Patients may pay more than the copayment where a PBS item is priced above the benchmark price for different brands of the same drug, or the benchmark price for a particular therapeutic group of drugs. The Government pays the additional cost of drugs exceeding patient copayments up to the benchmark price only. Brand or therapeutic group premiums do not count towards safety nets. Patient copayments and safety net thresholds are indexed to movements in the Consumer Price Index from 1 January each year.

Restrictions on subsidised use

There are three levels of restriction that can apply to PBS items—"unrestricted", "restricted benefit" and "authority required" (Birkett et al. 2001). "Restricted benefit" restricts subsidised use to specific indications, patient groups or clinical settings that achieve the optimal clinical benefit and cost effectiveness. "Authority required" further requires the doctor to obtain prior approval from the Health Insurance Commission or the Department of Veterans' Affairs to prescribe under subsidy to the individual patient. Often the "Authority required" mechanism is used for cost containment purposes by limiting usage to fewer patients.

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12 Concessional patients include people on low incomes and sickness beneficiaries who hold a healthcare card; those holding a pensioner concession card; or c) self funded retirees eligible for the Commonwealth Seniors Health Card.

4.2 Alternative supply arrangements

Benefits are generally distributed through community pharmacies after being prescribed by medical practitioners (DHAC 2001). However, for certain groups and in certain situations, alternative arrangements are in place to ensure the most appropriate access for the community. There are also supply arrangements that fall outside the PBS. Many of the features of these schemes form the basis of the third model proposed in Section 5.3 of the position paper.

Special supply arrangements under the PBS include Section 100 of the *National Health Act 1953*, for the provision of certain highly specialised drugs for chronic conditions which, because of their clinical use or other special features, are restricted to supply through hospitals having access to appropriate special facilities (DHAC 2001). As at 1 August 2001, this service provided a range of 42 generic drugs available in 116 forms and strengths (items) and marketed as 122 drug products or brands. Expenditure in 2000–01 was approximately $271.3 million. Other supply arrangements outside the PBS include funding for lifesaving drugs, essential drugs, unapproved drugs, orphan drugs, and other.

4.3 Listing a new drug on the PBS

The criteria for listing new drug products on the PBS include efficacy and safety compared to other available therapies (including non-drug treatments), and cost-effectiveness. Submissions to list new drugs are normally made by the sponsor or manufacturer but may also be made by medical bodies, health professionals and private individuals. Guidelines and other necessary information are available for making a submission are available on the Commonwealth Department of Health and Ageing PBS web site (www.health.gov.au/pbs).

TGA approval is required for a drug to be eligible for consideration of PBS listing. A drug can only be listed on the PBS if the Pharmaceutical Benefits Advisory Committee (PBAC) has so recommended (DHAC 2001). The PBAC accepts that products included on the ARTG have established safety and efficacy adequate to allow marketing in Australia. The current legislation requires the PBAC to consider the effectiveness, cost and cost-effectiveness in its deliberations on listing of a drug (Sansom, 2001). Thus, by law, the PBAC has to assess the degree to which new drugs represent "value for money" to the Australian community. As Sansom states "*this requires a comparison with alternative therapies*" (2001, p257). The PBAC assesses the clinical place of a product compared with other products already listed on the PBS for the same, or similar, indications and cost of a proposed benefit compared to alternative therapies. Where there is no listed alternative, the PBAC considers the effectiveness, cost-effectiveness and clinical place of the product compared with standard medical care or the benefits for patients the new product will provide compared to the cost of achieving those benefits (DHAC, 2001). Sansom argues that "*the use of a cost-effectiveness approach enables equity across all diseases (and therefore the population) when considering drugs for*

listing. For example, if the total cost was the only consideration then expensive drugs used in a small group of patients or a relatively cheap unit-cost drug in a large proportion of the population would never be subsidised" (2001, p257).

On the basis of community usage, the PBAC recommends maximum quantities and repeats and may also recommend restrictions as to the indications where PBS subsidy is available.

When recommending listings, the PBAC provides advice to the Pharmaceutical Benefits Pricing Authority (PBPA) regarding comparison with alternatives or their cost effectiveness.

The Pharmaceutical Evaluation Section (PES) evaluates company submissions to the PBAC for comparative effectiveness, safety, cost-effectiveness and budgetary impact. The Economics Sub-Committee (ESC) of the PBAC largely relies on this evaluation in its review of the submission and advises the PBAC on the above matters.

The PBAC may recommend a new drug entity if:

- It is needed for the prevention or treatment of significant medical conditions not already covered, or inadequately covered, by drugs in the existing list and is of acceptable cost-effectiveness;
- It is more effective, less toxic (or both) than a drug already listed for the same indications and is of acceptable cost-effectiveness; or
- It is at least as effective and safe as a drug already listed for the same indications and is of similar or better cost-effectiveness.

In making its recommendations, the PBAC takes into account the community need or benefit of a drug. Drugs intended specifically for in-hospital use are given lower priority as the PBS is primarily for community-based patients. Drugs for the treatment of clinically minor or trivial conditions are given a "low priority" for listing.

The PBAC may:

- recommend a drug for subsidy listing as acceptably cost effective at the requested price or at a lower than requested price; or
- recommend a drug for subsidy listing with tighter restrictions than those proposed in the submission (this is known as targeting); or
- reject a drug for subsidy listing on clinical and/or cost-effectiveness grounds (Birkett et al. 2001).

Circumstances where the PBAC is unlikely to recommend listing include the following:

- A fixed combination of drugs;
- A drug which may increase problems of abuse or dependence; or

- A drug solely to treat an individual patient whose response to, or need for, a drug is unique.

The PBAC may consider a drug or drug formulation for **Restricted Benefit or Authority Required listing**:

- To limit PBS usage so that this is in accordance with the approval and registration granted by the TGA;
- To allow the controlled introduction of a drug in a new therapeutic class;
- To limit PBS usage to the indications, conditions or settings seen as appropriate for clinical, cost-effectiveness or other reasons; or
- Because of concerns about adverse effects, possible misuse, overuse or abuse.

Highly specialised high cost drugs may be recommended for availability through hospital out-patient departments, where use of the drugs for the treatment of community patients is not suitable to a community medical practice setting.

Any submission to list a new drug on the PBS must include the following information:

1. A description of the proposed drug, its use on the PBS and the therapies which will be co-administered or substituted (i.e. its comparator);
2. Data and results from all comparative randomised trials for main indication and a preliminary economic evaluation based on the evidence from these trials (i.e. a determination of value-for-money). Further, a description of the search strategies used to select the comparative randomised trials must be included;
3. A description of any modelled economic evaluation of the likely cost effectiveness of the drug versus its comparator; and
4. An estimation of the extent of use of the drug and a financial analysis from the perspective of the PBS and government health budgets.

The following process of evaluation takes place for each submission (Hill et al. 2000):

1. The Pharmaceutical Evaluation Section (PES) of the Department of Health and Aged Care[13] subjects each submission to detailed evaluation. This involves checking the literature search used in compiling the submission, verifying the trial results, validating the key assumptions in models, and confirming resource costs according to a manual of Australian costs;
2. The ESC reviews both the submission and the PES evaluation and produces a summary document outlining key issues and the implications these have for recommendations made by the PBAC; and

[13] Now Department of Health and Ageing

3. The PBAC considers the submission, the PES evaluation, the ESC report, the sponsor's response to the evaluation, and the views of its members when making its final recommendation to the federal health minister.

As well as cost-effectiveness, the PBAC takes other factors into account in making its recommendations—clinical need, equity of access, "rule of rescue" (i.e. accepting some cost-ineffective interventions for patients with rare catastrophic illnesses who have no other treatment options) and total cost to the health care system (Hill et al. 2000).

Only about 20% of all drug products registered for marketing are listed on the PBS (Cookson 2000), although these account for about 65% of prescriptions in Australia and about 80% of the Australian market by value (Evans 1995). Martyn Goddard has been reported as identifying reasons for the PBAC rejection of a drug for PBS listing as including: the company hasn't done the proper research, or its economic case is not credible, or commonly the company wants a price out of all proportion to the health benefit which the evidence shows can be credibly expected (Dow, 2002).

4.4 Review of current difficulties in listing a new drug on the PBS

Industry Criticisms

Cookson (2000) noted the following industry criticisms of the listing process:

- Cost effectiveness evidence misused for cost containment in price negotiations;
- Sometimes delays or restricts access to effective medicines for patients;
- Heavy burden of cost, delay and uncertainty on a "knowledge-intensive" industry;
- Disproportionate administrative burden for drugs with low sales volumes;
- Focus on "hard" efficacy data undervalues the indirect benefits of pharmaceuticals and other benefits to patients which are intangible and hence difficult to quantify or place a value on;
- All claims of benefits are to come directly from trial evidence. Yet, the duration of some trials would require decades of follow up (eg to measure survival) in order to meet the PBAC's direct evidence requirements. Greatly increasing time to market beyond the approximate 12 year process in place today would be ethically and morally questionable in the case of life saving therapies, including those with superior efficacy in treating chronic progressive disabling diseases that also shorten survival;
- Government evaluators are overly conservative and under-estimate benefits;
- Unfairly harsh on new drugs with highly cost effective comparators;
- Lack of accountability of the public officials involved; and

- No appeals process against PBAC rejections [*but applications can be resubmitted].*

Birkett et al. (2001) also assert that the industry believes that the criteria for choosing a comparator treatment disadvantages new drugs as they are compared with cheaper old drugs that are out of patent.

Impressions of an observer

Cookson[14] (2000) attended one PBAC meeting in 1999 as an observer and also noted the following impressions:

- The PBAC takes careful account of the disease-specific clinical effectiveness information provided, with comparative effectiveness being the priority and cost considerations only taken into account once comparative effectiveness has been established;
- Items with relatively low costs appear to be given less careful consideration than those with relatively higher total costs, particularly those estimated to have a first year cost of $10 million or more (these require cabinet approval for listing);
- Broader cost effectiveness comparisons (e.g. QALYs) between treatments in different disease areas were rarely given explicit attention in decision making;
- Consideration of "rule of rescue" sometimes weakened cost effectiveness requirements and there is no recording or monitoring of this - although Dalton (2001) notes that "economics cannot handle all dimensions of community values"; and
- While an estimation of the extent of leakage is not formally required, the PBAC does consider it informally, as leakage tends to reduce the overall comparative effectiveness and cost effectiveness.

Current Perceptions of Difficulties

As already stated, there is strong support amongst stakeholders interviewed for the position paper for the current Pharmaceutical Benefits Scheme. They note that the scheme is seen internationally as one of the best in the world, that the 'cost effectiveness' criteria of the PBAC had generally delivered the desired health outcomes, and that the current arrangements had proved to be flexible enough to accommodate some new biotechnology and oncology drugs. However, many of the problems and criticisms listed above were re-iterated by the stakeholders. Key issues noted by stakeholders, and/or reported in the recent literature, are outlined below:

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[14] Cookson also interviewed stakeholders.

Requirements for empirical and randomised trial data

The guidelines for major submissions state "*The PBAC has and will continue to consider all evidence, but will be most influenced by the results of the most rigorous randomised trials*" (2.2A). The PBAC has a strong preference for economic evaluations based on "head-to-head" randomised clinical trials (i.e. trials that directly compare the proposed drug with the main competitor). However, it does recognise that such trials will not always be available and in some cases no randomised trials may be available (DHAC 2001). Despite this, there is the perception that the PBAC does not consider "softer" evidence of the kind often used in economic modelling as trustworthy as "hard" evidence from trials (Cookson 2000). The PBAC is reported to encourage the use of economic modelling to correct for biases in randomised trial evidence and to deal with uncertainty in the cost-effectiveness estimates due to the strength or weakness of the clinical trial evidence (Cookson 2000, Birkett et al. 2001). However, the impression of stakeholders is that the Committee is heavily influenced by what it perceives to be the available 'hard' evidence. In practice, it appears that the PBAC expects pharmacoeconomic analyses to be based on direct evidence yet there are logistic difficulties in providing this data, particularly for chronic diseases that increase mortality in the longer term. As one stakeholder indicated, "*a major problem stems from the growing chasm between the PBAC's reading of the clinical trial data and what is being interpreted and extrapolated by the companies*".

Trial subject groups have specific indications and derive specific benefits but these data are being extended to a wider population group for which the evidence is not there – and the PBAC will not approve the submission in such situations. For a number of the new biotech drugs, there are no appropriate head-to-head studies, and few trials with quality of life endpoints. Cross-over and randomised trials also have been seen to be problematic because of ethical dilemmas. If the drug works in a particular patient group, is it ethical to with-hold it, and how many patients would be forthcoming and consent to being randomised to different treatment options where they may get a placebo or less effective drug.

Some of the problems related to differences over data arise in part because of the trade-off companies make between the expediency with which they want their submission assessed and the quality (extensiveness) of the information demanded by the PBAC to make an informed decision. With the application for the drug Herceptin, survival was measured from the clinical trials. However, it appeared that the PBAC wanted (empirical) data on survival over a longer-term timeframe but, as the drug was essentially still in development, such long term 'hard' data wasn't available.

Cost/Price Issues

There is a perception that the new biotech drugs are costly and anxiety from government that they will lead to unconstrained growth in PBS expenditure if listed. However, the total annual cost forecasts for these new drugs are not 'high' compared to many other drugs already listed on the PBS, and the pharmaceutical bill may be only a small proportion of total

health costs of the disorder. For example, Herceptin is estimated to cost $9m per year. Lipitor the highest volume brand had a total cost of $265.5m for the year ending June 2001 (PBS, 2001). The direct health system costs of prevention and treatment of arthritis were estimated to be approximately $2.24b, with prescription pharmaceuticals contributing to only 6% ($132.5m) of these costs (Access Economics, 2001). The issue according to one stakeholder is that "*it is not so much that these drugs are biotech rather than small molecules, but that they are very specifically targeted so you end up with a relatively small patient population. The cost of developing them is not cheaper than something else. If you have a cost of development of around $800m, and you have a relatively small group of patients, then the cost per patient will be high. This is occurring not just for biotech drugs but probably a lot of the new compounds that are targeted to very specialised groups*".

It may be apt to reimburse small molecule mass market products on a price-volume arrangement, but this economic model doesn't work for large molecules that require an expensive manufacturing process but which are highly targeted. For high cost biotechnology /oncology products, even a significant reduction in unit price will not sufficiently reduce cost risk to the PBS if prescribing controls and other supply side measures are not strengthened. For example, at one third of their current price, the cost of Herceptin and Enbrel is still several thousand dollars per patient per year.

It is also important that there are demand and supply forces operating for biotechnology products. Large antibodies such as Herceptin and Enbrel are particularly difficult to manufacture, quality assurance is complex and forecasting is rarely accurate early in the drug development process. Moreover, biotechnology plants take several years to build, so there is inevitably a period where global demand greatly exceeds supply, thus impacting on the manufacturer's ability to offer price discounts.

From time to time, the PBAC and PBPA have recommended listing of different products at lower prices. From an industry perspective, there is pressure for consistency in international price-setting. Australia has relatively cheap drugs on an international scale (Productivity Commission, 2001). Australia is, however, a small market and a low price for a drug here is seen to influence the world market and company behaviour. The industry seeks a similar price for its product on a worldwide basis - otherwise governments and other payers will exert pressure on the company to lower its price in countries where the price is higher than what it sells for elsewhere.

Cost-effectiveness

There is widespread agreement that it is the cost-effectiveness ratios of these drugs that are problematic, not their total cost – the cost effectiveness ratios are seen by all stakeholders to be challenging for the community. They expressed the view that the high development – and consequent market - costs of such drugs resulted in products for which cost

effectiveness was hard to prove. Some also noted that greater difficulties were likely to arise in cases where both high costs and potentially very large patient populations were present.

It is widely accepted that the PBAC works on a cost-effectiveness ratio of $40-50,000 per quality life year gained. This compares unfavourably to cost-effectiveness ratios used overseas, although it has to be recognised that the thresholds for assessing cost effectiveness as a basis for accepting or rejecting an application for government funding are highly controversial. Ten years ago, Laupacis, Feeney and Detsky identified tentative guidelines for using clinical and economic evaluation to ascertain how attractive a new technology had to be to warrant adoption and utilisation in Canada (Laupacis et al, 1992). Glasziou in 1995 reported that Laupacis and colleagues suggested a cost-effectiveness ratio of less than US$20,000 per quality-adjusted life year (QALY) gained was good; between US$20,000 and US$100,000 may be acceptable; and higher than US$100,000 was generally unacceptable. In the UK, a figure of £20,000 is popularly reported as the cost-effectiveness cut-off point, and in the US, the same ratios noted by Laupacis et al but in US dollars at current prices – all significantly higher than the threshold perceived to be operating in Australia.

The PBAC (and PBPA) informs the drug company whether it has met the cost-effectiveness criteria for PBS approval. If it has not done so then the drug will not be recommended for listing (unless other factors are taken into account) and the company will have to re-apply with changed costs or new indications. Many stakeholders reported that the listing of Herceptin, for example, was always going to be difficult because it had a cost-effectiveness ratio of approximately $60,000. This was seen to be in the 'danger zone' falling well above the PBAC's 'threshold' (although noting that the PBAC hasn't officially set any cost per QALY that they say is a cut-off point). Certainly the PBAC has recommended drugs with cost-effectiveness ratios higher than Herceptin. A key point of contention remains though, and that is the PBAC has been inconsistent in its handling of different drugs with high cost-effectiveness ratios, according to industry stakeholders. As one stakeholder queried '*why is Herceptin not acceptable when other drugs with higher costs per QALY are*?'

The PBAC works on evidence-based cost-effectiveness and, according to some, the Committee does this reasonably well. One of the main problems in determining cost-effectiveness is however the choice of comparator - in terms of cost-effectiveness, the comparator "*can make or break an application*". The drug company has to decide on the comparator drug. This is a crucial piece of reasoning so the company has to get it right but, according to one stakeholder, they often don't (from the perspective of the PBAC). For some new drugs, there may be no true comparative studies, and the new biotech and other targeted therapies will present high costs when compared to out-of-patent very old drugs that are very inexpensive. Some stakeholders quoted statistics indicating that "*the probability of a drug with an established comparator being listed was much greater than that of a new therapy without an established competitor*". They considered that there was a need to expand the current listing criteria to better accommodate the advent of the new biotech drugs.

One stakeholder reported that "*it is much easier for a drug to be listed if the incremental benefit is very large – i.e. it leads to a revolutionary change in the treatment paradigm*". In the case of Glivec, for example, one or two patients per 100 responded to old therapies but with Glivec this increased to 50 per 100. Even though the incremental cost is 'huge', the benefit is also substantial. If the PBAC believes some people have 'fantastic responses' but this is not representative of all eligible patients, then there will be problems in getting approval, and the cost-effectiveness will be rejected for those groups. The PBAC has in the past indicated that a drug is not cost effective at a particular price but, if the company lowers the price, then approval will be recommended for listing at the lower price (negotiated with the PBPA). However, this often is not a commercially attractive proposition for the company, which will have undertaken its submission on the basis of its own figures (such price manipulations appear to work better where price/volume arrangements operate). Most stakeholders recognise that the industry is good at manipulating the figures; if the figures on which the cost–effectiveness ratios are based are dubious or the 'numbers just don't stack up' then the PBAC will make a recommendation not to list the drug. Importantly, the PBAC may be willing to reconsider if a company comes back with a price reduction, but the revised cost-effectiveness ratios may not alter significantly and still fall into the 'grey zone' by not coming under the $40-50,000 (per QALY) threshold.

Essentially, the high price structure of targeted biotechnology/oncology therapies, and their benefits which cannot logistically all be demonstrated in the short term, do not allow the cost effectiveness ratios of these agents to fit within the 'required' limits of the PBAC. This is tantamount to "fitting a square peg in a round hole". Stakeholders further believe that the inclusion of indirect costs, such as productivity losses, in cost-effectiveness analysis is not encouraged, although these costs may show that a targeted therapy is actually cost saving to society. According to some stakeholders, the PBAC does not like cost-benefit analysis.

A further problem is that the devaluation of the Australian dollar is working against Australia in terms of its ability to purchase pharmaceuticals on an international market. Importantly, movements in the dollar are not being taken into account in calculating cost-effectiveness measures – these are now based on a '75c dollar' and it becomes arbitrary where you judge cost-effectiveness. It also appears that the public has little capacity to understand any notion of cost-effectiveness – as one stakeholder indicated "*we don't want a system where a current affairs program decides what drug gets listed*".

Leakage – Problems with Identification of Target Population and Doctor Prescribing Behaviour

The main difficulty that the PBAC has faced in controlling costs in recent years is "leakage" (i.e. clinicians prescribing drugs for a wider range of indications than those listed on the PBS) (Cookson 2000). One reason for this is that government is reluctant to impose prescribing patterns on doctors. Goddard claims that "*the system is encouraging 'good doctors to be criminals', writing anywhere up to $1bn in scripts for drugs outside their legal subsidised uses*"

(SMH, 26-27 Jan 2002, p11). There are no mechanisms in place for post-listing policing of prescriber behaviour. While some stakeholders felt that much tighter 'leakage' control was not only feasible, but necessary in future, others expressed doubt that 'leakage' control could be effective without a level of 'policing' that Australians may find difficult to accept.

Stakeholders recognise that it is often difficult to draw a line between patient X and patient Y in deciding who will and who will not get a particular drug. All stakeholders acknowledge that patient eligibility has to be clearly defined and is very important in terms of identifying the appropriate target population. At the moment, there is no capacity within the system to distinguish between, for example, the 1000th and 1001st patient . *"We need to find a system that says yes to the 1000th person but no to the 1001st"* said one stakeholder. Furthermore, a hard cap on the number of eligible patients for a particular targeted therapy is not considered an equitable option. Rather, a soft cap according to clinical need should determine the size of the eligible patient population.

While there is some dissatisfaction with primary clinical markers, and questions have been raised concerning the adequacy of screening, in general there is a strong consensus among stakeholders that these drugs, because they are targeted therapies, should not receive the open-ended commitment typical of previous PBS experiences. Leakage with high cost biotech drugs is more likely to occur to some extent on slippage of disease progression indications than prescribing for patients who do not have the key biological markers. Many of the biotech drugs have been introduced to treat well advanced stages of disease progression. There may be a tendency for doctors to prescribe to patients with early or mid-stage disease progression, who they feel may also benefit from the medication. Therefore, to prevent this form of leakage, cut-offs for various stages of disease progression will need to be clearly indicated, in addition to the basic biological makers (as already occurred for some drugs). It may be noted, however, that the irony is that the patients most likely to benefit from a targeted therapy are those whose disease is in the early stages and who thus can avoid considerable morbidity and mortality longer term.

Logistics and the Approval Process

Stakeholders were frustrated by a number of logistical and organisational problems. There were timeline issues, with delays 'in the wheels turning' and a lack of co-ordination of the stages and steps in the approval process. Application for listing of drugs could take a few months to several years. If the industry rushed their submissions then they didn't have all the information they would like. However, the system has cutoffs and deadlines that they are required to meet. They therefore had to trade-off commercial interests versus quality. While the companies wanted the best submissions they could produce, (commercial) reality is such that they felt compromises had to be made to get an application in by a certain date.

Some stakeholders regarded the reimbursement process as cumbersome. It was easy to get out of 'sync' – if you missed one meeting then there could be significant delays. Applicants perceived they were not always being treated 'properly' or equitably and that short notice

was often given for evidence required for the next meeting. This imposed time constraints on sponsors who did not always have the time to provide the data requested. As some stakeholders identified, the timeframe for approval needs to be weighed against clinical and disease pathways – the disease will progress and the clinical status of some patients will deteriorate significantly over a few months.

The PBAC is clearly well intentioned but it is seen by stakeholders to be very conservative and not to understand all the contents of some submissions and therefore not be well placed to assess some applications. High cost biotechnology/oncology drugs and the disease entities they target are highly specialised. The Committee is perceived as having limited clinical and economic expertise to deal with these new biotech drugs, to be fiercely independent, and to operate via a 'closed door' approach.

Transparency of decisions and consumer involvement

Martyn Goddard, a former member of the PBAC, has been reported as stating that the exclusive negotiation between Government and industry over drug subsidies, with no public transparency, is a fundamental problem with the current system (Dow, 2002). Under the PBS, everything the evaluators see is commercial-in-confidence but there have been calls for the PBAC to make the information publicly available at least for drugs recommended for listing (Rennie and Luft, 2000). The PBAC now publishes a list of drugs, which have been recommended for PBS listing, and this includes a short statement of the reasons for acceptance.

According to Cookson (2000), the PBAC accords a high priority to industry and expert consultation but there is limited public consultation, although there is a consumer representative on the Committee. Dow (2002) reports that many people argue that the mathematical formula for determining cost-effectiveness is opaque, and there is no obligation on the PBAC or the PBPA to explain its actions to the public. One stakeholder believed that "*the public confidence in the process was undermined when negative decisions were debated in the media. This led to 'smoke and mirrors', and a lack of clarity on the actual decision and decision-making processes*".

Another stakeholder said "*it is difficult if the PBAC will not talk with you during the process… The way the PBAC wants to operate is exceedingly difficult – be aloof, not meet you, also dictate what the PBPA should do … the PBAC should be prepared to meet and discuss the issues*".

Consideration of equity and intangible benefits

There are no requirements for submissions to include or quantify informal equity arguments to support their case and there is no guarantee that the PBAC takes equity considerations into account in a systematic manner (Cookson, 2000). Intangible benefits may be taken into account informally by the PBAC.

5 MODELS

All the models presented below are based on the view that leakage through difficulty in specifying the target population and inappropriate prescriber behaviour is the main cause of cost blow-outs. Therefore mechanisms to clearly identify and define patient and/or prescriber eligibility are key constructs of the models proposed. The general view of stakeholders interviewed was that changing the price of these 'high' cost drugs would not significantly alter their chances of being PBS-listed. Their cost-effectiveness ratios are sufficiently high that reductions in price, even by say 10%, would not reduce their ratios to a level acceptable to the PBAC. Thus, while price is clearly an important factor, the models below do not specifically focus on finding ways to contain costs through price control. In each of the models, it is assumed that standard national drug prices will be established through normal negotiations with suppliers via the Pharmaceutical Benefits Pricing Authority (PBPA).

5.1 A "Quality Use and Outcomes Measurement for Biological Agents" Registry Approach

Model Description

As stated in the previous section, the high cost of targeted biological agents is creating special problems regarding authorisation for use under the PBS. Two of the main problems are the risk of leakage and the risk of potentially wasteful continuation of therapy when no objectively measurable or worthwhile improvement has been achieved in response to the therapy. The current systems for authority prescribing do not address these risks adequately.

This model seeks to address these risks by establishing objective assessment and outcomes measurements by means of a Quality Use and Outcomes Measurement for Biological Agents Registry. The model is based on the proposal to establish the **Quality Use and Outcomes Measurement for Biological Agents for Rheumatoid Arthritis (QUOM-BARA) Registry**, developed in preparation for the introduction and proposed PBS subsidisation of novel biological agents for the treatment of rheumatoid arthritis. In particular, a group of stakeholders developed the proposal to support the application of etanercept's subsidisation for a limited targeted patient group. Stakeholders included the Australian Rheumatology Association (ARA), Arthritis Australia, Med-E-Serv Pty Ltd, and Wyeth Australia. The QUOM-BARA Registry was intended to address the complex and ongoing issues involved in providing high cost treatments in a highly targeted population of patients most likely to significantly benefit. It was intended that the QUOM-BARA Registry would provide a model which might be applicable to other situations where small numbers of patients with serious disease could benefit from expensive but effective novel agents.

In general, a 'QUOM' Registry aims to:

- Ensure appropriate patient selection for subsidised prescription of the drug based on objective criteria and assessment in a way which removes any prescriber bias;
- Ensure that patient response to the drug can be measured;
- Ensure continuation of therapy is based on objective response to treatment criteria;
- Ensure quality use of biological agents over time based on high quality data collection and analysis; and
- Use the data to continue to optimise treatment (selection criteria) guidelines.

A central registry would form the organisational and logistical hub of the model and ensure that the model achieves its aims. The central registry would have custody of a database, on behalf of appointed steering committees, that would hold data related to the project. The central registry would, for example:

- Collect all data required from patients, specialists and independent clinical assessors (health practitioners) e.g. metrologists;
- Hold all data and preserve confidentiality within the guidelines established;
- Facilitate patient appointments with clinical assessors;
- Preserve a 'blinded' referral process;
- Administer the contracting of the clinical assessors and arrange payments;
- Arrange visits of clinical assessors to non-metropolitan and rural areas;
- Ensure data quality and integrity;
- Administer the budget according to budgetary guidelines;
- Distribute information kits for doctors and patients and manage on-line information services;
- Provide reports to stakeholders;
- Transmit data to the HIC so that a decision can be made as to whether an authority will be issued in regard to a particular patient;
- Administer a process that will enable individuals to access their own data in accordance with Privacy Legislation; and
- Provide or secure the provision of the hosting and service delivery of the technical infrastructure for the Registry.

Etanercept and the QUOM-BARA Registry

Nearly 5% of Australians are taking some form of medication for arthritis. Rheumatoid arthritis affects approximately 2-3% of the population and is acknowledged as one of the main health reasons for individuals retiring from the workforce early (Access Economics, 2001). Access Economics estimated the direct cost of rheumatoid arthritis at $173m in 1999-2000. Enbrel (Etanercept) is a new biological disease modifying antirheumatic drug (DMARD) used for the treatment of active rheumatoid arthritis. Wyeth Australia achieved 'signoff' from the peak medical and consumer bodies involved with arthritis on a proposal to limit the funding of Enbrel (an anti-TNF alpha agent) to a select subgroup of patients with rheumatoid arthritis who meet very stringent eligibility criteria. In spite of achieving 'in principle' support from senior government officials, the proposal was rejected by the PBAC. The annual cost per patient for Enbrel is estimated now at $22,000 but stakeholders involved in the arthritis field argue that, despite having a 'high' prescribing cost, it is a very cost-effective drug. In contrast, Don Birkett (former Chair of PBAC) is reported as saying *"It's a clever drug and does seem to work in resistant rheumatoid arthritis. It is one of those cases where there is a benefit for those taking the drug but it is not cost-effective compared with other treatments"* (BRW, 6 Sept, 2001).

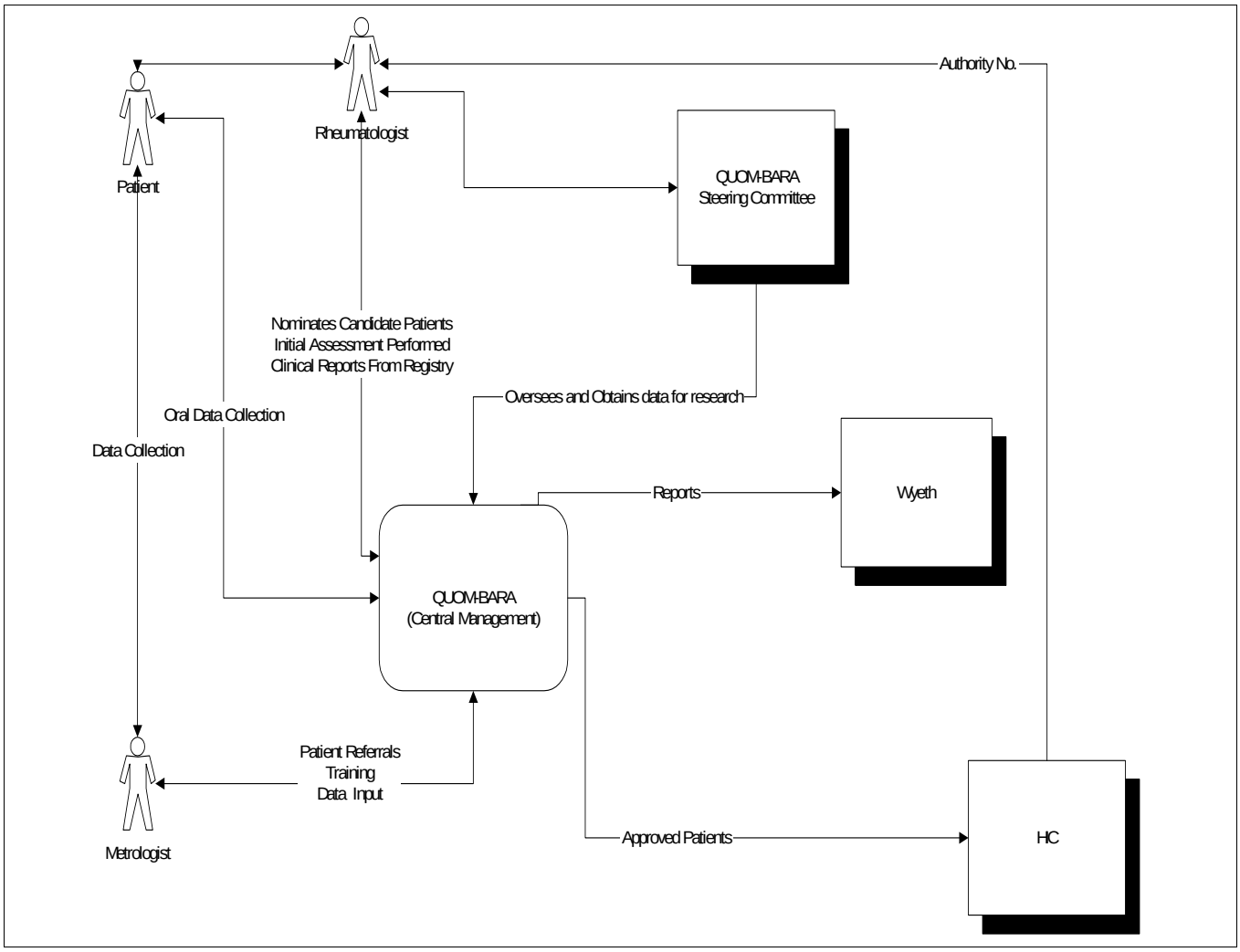
The principles of the Registry are that rheumatologists, patients and trained, independent (blinded), metrologists will supply information that will be matched against eligibility criteria in real time. The objectivity of the data would be ensured by the use of independent and blinded professionals. All data collected and independent assessments would be available in real time to the treating doctor and patient for the purposes of tracking and monitoring care. With appropriate privacy and consent processes in place, additional high quality data can be collected which will provide a longitudinal view of outcomes of patients prescribed etanercept.

A concept diagram of the QUOM-BARA Registry is provided in Figure 2. From the perspective of the PBAC, PBS and HIC, the Registry would put a system in place which would maximise compliance with agreed patient selection criteria for initial and continued subsidised prescription of etanercept, and which is based on consistently applied, verifiable, objective assessment. For clinicians, the Registry would provide a mechanism that allows them objective assessment as to which of their patients are eligible for prescription of etanercept via the PBS, and assists in the collection of data that will improve the treatment management of their patients. And, patients would gain access to etanercept via the PBS. It was assumed that 1300 new patients would be eligible for etanercept each year, reaching steady state at 5 years after PBS listing.

Baseline data would be collected and used to determine initial eligibility for etanercept. Continued eligibility for etanercept would be based on a second assessment at 6 months from commencement which demonstrates objective improvement of at least 20% using

indicators based on the American College of Rheumatologists arthritis response measurement (ACR-20).

Figure 2 **Concept Diagram of the QUOM BARA Registry**



Data source: Med-E-Serv Pty Ltd.

A further assessment at 12 months would determine continued eligibility. Those patients in whom there is no demonstrable improvement at 12 months from baseline will not be eligible for continued use unless they have been subject to a withdrawal challenge of 4 weeks after which time it can be demonstrated that in the absence of etanercept treatment they have scores (on a combination of parameters) of 20% worse than their most recent assessment score while using etanercept. Patients also may need to undergo a withdrawal challenge if deterioration of 20% or more has occurred between the 6 month and the 12 month

assessment. A deterioration of more than 20% after a four week withdrawal challenge in these patients will indicate a continuing objective benefit of etanercept therapy and will restore their eligibility to treatment with etanercept.

The Health Insurance Commission would be able to use the data from the QUOM-BARA Registry in real time to make determinations before issuing authority numbers.

A Steering Committee, under the auspices of ARA and with representation from all stakeholders, would continue to monitor the longitudinal outcomes such that the evolution of prescribing guidelines would be informed by the growing body of data from the field.

Discussion

This model is based on an initial proposal for the subsidisation of biological agents for rheumatoid arthritis, of which Enbrel was the first. However, the funding of other products in the 'high cost biotechnology and other targeted therapies' category from other manufacturers also could be structured under this approach. Enbrel is used only to illustrate the option. The procedures outlined in the model aim to ensure that only those patients who fulfil stringent predetermined diagnostic and disease activity criteria will be granted access to the proposed biological agent. The procedures also ensure that approval for continuation of the agent will only be granted to patients who have responded adequately to the therapy according to set criteria. The system will capture high quality data that can be used to analyse responses and outcomes. The model involves a fixed cost in establishing the registry and then ongoing operating costs.

Advocates of a registry model, argue that it will promote the cost effective distribution in Australia of treatments that have been shown to benefit groups of patients who are unresponsive to or intolerant of current drugs available via the PBS. It will allow the collection of outcome data which may provide further clinical insight into the rational use and outcomes of these biological agents. Importantly, both the patient Registry option and clinical trial option discussed in Section 5.2 may provide data indicating that *increased* utilisation of a particular targeted therapy would be beneficial from an overall economic perspective. This is a possibility given that the evidence based approach based on randomised clinical trials frequently has limited scope to show the complete benefits of a new targeted therapy and thus does not yield the cheapest therapy.

The QUOM-BARA proposal has undergone a detailed feasibility study and costing. The cost per patient of QUOM-BARA is between $200 and $400 per year or the equivalent of approximately one week of therapy. If the Registry saved the PBS from one prescription which was unworthy against the prescribing criteria, this would recoup the cost of the QUOM-BARA Registry and related processes for approximately 40 patients. It is anticipated that, once demonstrated to be an effective instrument, QUOM-BARA would be funded directly by PBS.

A modified version of this approach was recently adopted by the British Department of Health in a 'groundbreaking' scheme for the funding of expensive drugs for the treatment of multiple sclerosis (MS). Under this scheme, the manufacturers of the drugs will only be paid in full if the treatment 'lives up to its promise' (Timmins, Financial Times, 2002). Under a 10 year agreement, the NHS will pay the full £6,600 - £12,000 a year price for beta-interferon and glatiramer acetate, but the patients receiving the drugs will be monitored and an assessment made of whether the drugs are effective (performance being measured against an agreed set of outcomes). If they are, the companies will be paid in full - if they are not, then payments will be reduced on a sliding scale. This reimbursement approach shares the risk between the companies and government (Timmins, Financial Times, 2002). Not all patients with MS are eligible for the scheme – patients with relapsing remitting MS and those with secondary progressive MS in which relapses are the dominant clinical feature are the 'main' targets of the program (Woodman, Reuters, 2002). The scheme was developed after the National Institute for Clinical Excellence (NICE) concluded that the treatments were not cost-effective enough for the NHS to adopt them routinely.

5.2 Staged 'Clinical (and Economic) Trial' Model

Model Description

This model represents a staged approach to the approval process, in that proposed drugs enter a clinical trial as a provisional listing mechanism before full listing is granted. The model stems from current drug registration processes where clinical trials play a fundamental role in establishing quality, safety and efficacy. The model also draws on the TGA's scheme that allows the supply of unapproved therapeutic goods through clinical trials (TGA, 2001). This option also has its derivations in an earlier proposal by Professor Paul Glasziou (1995). Glasziou argued for a new authority category for the PBS, namely an authority to prescribe within a controlled trial. Glasziou suggested that therapeutic products that showed promise but for which conclusive evidence of long term effectiveness and advantage over comparators or standard treatments was lacking, or drugs targeting new indications, could be prescribed within a randomised trial. The PBS would fund a substantial proportion of the trial costs. However, the problem Glasziou specifically addressed was that of a promising treatment where the clinical trial evidence was weak (i.e there was

insufficient available data). As indicated in Section 4.4 'Current Perceptions of Difficulties, Requirements for empirical and randomised trial data' (p23), this is often the case for high cost biotech therapies, but it is not always so. Rather, the main stumbling block to PBS listing for new biotech targeted therapies appears to be their high cost-effectiveness ratios and fear of leakage with subsequent blow-out in costs. The clinical trial is one mechanism whereby doctor prescribing can be controlled, patient access carefully regulated and monitored, and an accurate assessment of costs gained.

Under this option, subsidisation is recommended only for patients enrolled in a formally approved and registered prospective 'PBS' clinical (-economic) 'trial'. The trial acts as a mechanism for provisional listing of the drug onto the PBS. Full listing would be recommended or rejected on the review of pre-determined and negotiated end-points and outcomes of the trial. In other words, this is a naturalistic trial collecting real life cost data.

Historically, clinical trials have been a central part of the drug registration and regulatory processes. The initial goals of clinical trials were to establish safety and efficacy, but these have been extended to address a range of new questions – questions set within the 'real world' context (Jones, 2001). Assessment of financial risk, cost-minimisation, cost-effectiveness, cost-benefit analyses and quality of life studies have been incorporated into phase III trials (Jones, 2001). The PBAC already uses a hierarchy of clinical trial evidence to evaluate PBS submissions (Sansom, 2001). Use of trials as a staged PBS funding mechanism is just an extension of current practices and can be seen as formalising activities otherwise undertaken as part of phase IV and postmarketing surveillance [15].

Expertise already exists in conducting and overseeing (supervising) clinical trials in Australia, through the TGA's unapproved drug supply scheme — but, also, for example, through the NHMRC's Clinical Trials Centre (CTC) at the University of Sydney. The CTC is a leader in clinical trials research in Australia, promoting evidence-based medicine through co-ordinating its own and assisting others in conducting large scale multicentre clinical trials (www.ctc.usyd.edu.au). The main focus of CTC's work is cancer and cardiovascular trials but the Centre also conducts other research. This includes quality-of-life research, economic evaluations, biostatistical research, prospective meta-analyses and operating the National Clinical Trials Registry.

The National Prescribing Service (NPS) could also act as an independent co-ordinator of these trials. Although it is part funded by the Commonwealth Department of Health and Ageing, the NPS is a non-profit organisation that operates 'at arms length' from government and the pharmaceutical industry. Its main aim is to improve the health of Australians

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[15] Clinical trials are classified according to the phase of the medicine's development. For generally accepted definitions of the different phases see TGA, Access to Unapproved Therapeutic Goods – Clinical Trials in Australia, May 2001, p9-10

through quality prescribing of medicines. The NPS was launched in March 1998, initially to undertake work in Quality Use of Medicines (www.nps.org.au).

Acting as a national co-ordinator of these trials would be consistent with its current roles and activities. The NPS currently provides access to timely, independent, balanced, critically appraised information on new and existing medicines to both prescribers and consumers. This information: is based on critical analyses of current evidence; is consistent with nationally recognised guidelines; and is reviewed by independent researchers and experts in clinical pharmacology, medicine, general practice and communication (www.nps.org.au). The NPS runs a number of programs including: the Prescribing Practice Review (PPR) which provides evidence-based information and individual prescribing data to assist doctors in reviewing their prescribing habits; clinical audits and case studies; decision support program and practice visits aimed at translating evidence on therapeutics into day to day practice; and policy support to government and other stakeholders including as one initiative the selective removal of authority requirements to prescribe particular PBS medicines in pilot projects to assess the viability of doctor self-regulation (www.nps.org.au).

The precedent and logistics for clinical trials as a supply mechanism are already well established with the:

- TGA's Clinical Trial (Exemption) (CTX) Scheme, which requires assessment of data by the TGA prior to approval on to the ARTG, or
- the Clinical Trial Notification (CTN) Scheme under which responsibility for assessment lies with institutional Human Research Ethics Committees (HREC).

These schemes are used for clinical trials involving any product not entered on the ARTG or use of a registered or listed product in a clinical trial beyond the conditions of its marketing approval. Some of the features of the CTX and CTN schemes that could form the basis of this model are outlined below.

Exemplars: Clinical trials for unapproved products

All CTN and CTX trials must have an Australian sponsor. The sponsor is that person or body that organizes the trial or the institution which takes overall responsibility for the conduct of the trial. The sponsor usually initiates, organises and supports a clinical study and carries the medico-legal responsibility associated with the conduct of the trial (TGA, 2001).

The **CTN Scheme** is a notification scheme. As such, all material relating to the proposed trial, including the trial protocol, is submitted directly to the HREC by the researcher at the request of the sponsor. The TGA does not review any data relating to the clinical trial. The HREC is responsible for assessing the scientific validity of the trial design, the safety and efficacy of the medicine and the ethical acceptability of the trial process, and for approval of the trial protocol. The institution or organisation at which the trial will be conducted is

referred to as the 'Approving Authority'. It gives the final approval for the conduct of the trial at the site, having due regard to advice from the HREC (TGA, 2001).

In comparison, the **CTX Scheme** is an approval process. A sponsor submits an application to conduct clinical trials to the TGA for evaluation and comment. The TGA reviews the information about the product provided by the sponsor, including overseas status of the medicine, proposed Usage Guidelines, a pharmaceutical data sheet, a summary of the preclinical data and clinical data. A TGA Delegate decides whether or not to object to the proposed Usage Guidelines for the product. If an objection is raised, trials may not proceed until the objection has been addressed to the Delegate's satisfaction. Even if no objection is raised, the Delegate usually provides comments on the accuracy or interpretation of the summary information supplied by the sponsor. If no objection is raised, the sponsor may conduct the trial at any number of sites under the CTX application without further assessment by the TGA, provided use of the product(s) in the trials falls within the original approved Usage Guidelines. Each trial conducted must be notified to the TGA (TGA, 2001)

A sponsor cannot commence a CTX trial until written advice has been received from the TGA regarding the application and approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted.

Components of a PBS Trial

The PBS trial becomes part of the application process for PBS listing. Two approaches could be implemented: 1) the sponsor (company) submits a PBS drug approval application as a listing for clinical trial use only as part of their initial submission to PBAC; or 2) they submit their application as per normal and wait the decision of the PBAC. An option then available to the PBAC would be to recommend listing for clinical trial use only. The company would then be invited to submit an appropriate clinical trial protocol for review and approval.

The PBAC would establish appropriate guidelines on trial protocols and document the requirements for PBS trials with components being agreed upon between the PBAC, sponsor, conducting investigators and host institutions. Codes of practice for designing, conducting, recording and reporting of clinical trials are well established (e.g. the NHMRC guidelines). Trial protocols would need to be approved by independent external review and appropriate Ethics Committee.

As with the TGA trials, PBS trials would need to be centrally recorded and administered. A register of approved institutions in which these trials could be conducted could be established. Again like the TGA trials, the primary responsibility for monitoring a PBS clinical trial would rest with the sponsor, the institution in which the trial is being conducted and its HREC, and the investigator (TGA, 2001, p8). As stated above, an independent body would act as the national co-ordinator of these trials.

The PBS would provide payment for the drug for enrolled patients. Like all the models proposed, this is a mechanism for Commonwealth Government subsidisation of the supply of drugs. Patient access to medicines under this model would not be free-of-charge. Patients would be expected to make a financial contribution to costs through normal PBS copayment arrangements.

PBS trials would need:

- clearly identified and well established criteria for patient entry;
- stringent baseline data requirements;
- specification of objective measurable endpoints and outcome measures;
- good follow-up and detailed documentation;
- appropriate duration (to maximise observation of outcomes and therefore statistical power);
- quick turnaround time with authority to supply; and
- clear rules concerning the disclosure of information found in the trial (what findings should remain confidential and what, if any, should enter the public domain).

Glasziou also identified the need for a randomised control group. Uncontrolled clinical trials have been widely criticised and the disadvantages widely debated. While perhaps being desirable from a scientific point of view, having a control group may not be feasible nor ethical for many of these new drugs. Jones (2001) states "we must agree that different types of drugs and different diseases require entirely different approaches to clinical trials … drugs developed on a basis of sound theoretical models and animal trials should not follow the same route as a compound without such a basis. Therefore flexibility in drug assessment would be a required part of the new process of clinical trials and drug registration" (p922). If for example these drugs are 'life-saving' drugs where there are no direct comparators then it may not be ethical to randomise patients to treatment, placebo or standard treatment where the chance of death in the control group approaches 100%. Thus, a key element that would have to be agreed upon between the PBAC and sponsor would be the type of trial – a properly blinded randomised controlled trial or uncontrolled prospective trial, for example. Blinded randomisation may not be possible. The nature of the trial would in part reflect the questions the PBAC particularly wanted addressed by the company. The legislative basis for PBS trials would need to be enacted, including revisions to the National Health Act, but an exemplar of necessary legal arrangements can be found in the CTN and CTX schemes.

Example

There are no direct examples of this approach. However, the Australian Human Growth Hormone (hGH) program illustrates many elements of the model. The Australian hGH program is primarily concerned with the growth-promoting effects of hGH. The program

also allows for the indication of neonatal hypoglycaemia associated with growth hormone deficiency. The aim of hGH therapy for children under the Australian program is to allow a trial of treatment with hGH and possible ongoing hGH therapy in children who are likely to achieve specific benefits. One of the specific aims of the program is to ensure hGH therapy is safe. The national Australian database 'OZGROW' collates data on all patients receiving hGH, which is used for research into and evaluation of growth hormone use under the program (DHAC, 2001).

The program is administered by the DHA with the assistance of the Growth Hormone Advisory Committee (GHAC), an independent panel of experienced paediatric endocrinologists appointed by The Australasian Paediatric Endocrine Group. An officer of the Department, who is a pharmacist, administers the program on a daily basis according to the guidelines. The GHAC deliberates on cases that do not clearly fulfil the guidelines and where eligibility is uncertain, or where there is dispute about an eligibility decision.

Through this program, Somatropin (recombinant human growth hormone) is supplied directly by the manufacturers under Section 100 to eligible patients (very short children and children with chronic renal failure, Turner Syndrome and hypoglcaemia). hGH is available as a pharmaceutical benefit only for patient groups included in the 'Guidelines for the Availability of Human Growth Hormone (hGH) as a Pharmaceutical Benefit' When an application to commence treatment is approved, a *Growth and Treatment Record* is sent to the treating physician. This form lists the required data for assessing a patient's response to treatment. In order to continue treatment, patients have to be reviewed by the treating physician every three months and the information requested on the *Growth and Treatment Record* containing the three monthly data provided to the Department every six months (approximately 4 weeks before supplies are due to run out). A radiological assessment of skeletal age must be submitted every twelve months. Applications to continue treatment are assessed by the pharmacist according to the set response criteria outlined in the Guidelines. More difficult cases are referred to the GHAC.

Patients meeting approved eligibility criteria are not required to make any copayment for this drug (although State and Territory charges may apply for dispensing Somatropin). In 2000-01, the expenditure on this drug item was $21m (DHAC, 2001).

Discussion

This is a prudent strategy as it provides access to new drugs for patients in clinical need and a mechanism for collecting appropriate information for future decision-making without wasting time and money on otherwise unhelpful options. Glasziou argues that it would be better to spend a proportion of the PBS budget for new drugs on appropriate trials to determine the most effective medications than to randomly approve full listing of some 'promising' drugs that may subsequently be shown to have no effect or a net harmful effect compared with standard treatment, while risking rejecting others that may confer significant

benefit. In the mid-1990s when Glasziou proposed his clinical trial model, scientific evidence suggested that only about half of the new drugs proposed for PBS listing would clearly show a net benefit compared with standard therapy. While proponents of the new biotech drugs and other targeted therapies argue vehemently that they confer clear and substantial benefits over existing comparators, assessment on a trial basis could allay the fears and concerns of those who believe there is insufficient clinical or economic evidence to warrant full PBS listing.

Bell (1995) suggests that such a clinical trials approach would be seen by large international pharmaceutical companies as an additional barrier to entry into the Australian market and they may well reconsider Australia as an unfavourable regulatory environment. The model may prove to be a larger barrier to entry for some manufacturers than for others. For example, companies with a small (or no) clinical trial presence in Australia may find the scheme relatively difficult to work within. It is a demanding approach for the industry but companies are highly motivated by their desire to gain government subsidisation of their product. Further, as Dalton (2001) notes, drug companies could assume a potentially powerful strategic position if they are the ones who instigate the design, conduct and collection of the clinical trials that form the basis of submissions to the PBAC.

Some of the advantages and disadvantages of this option are listed in Table 1. Two major issues that would need to be resolved are determining how many and which patients would be allowed to enter the trial. Sample size and power calculations are usually used to identify the number of subjects that need to be enrolled in a trial to have confidence in being able to observe the putative effects of the drug. A dilemma arises if you need, for example, only 300 subjects but there are 500 patients who would meet eligibility criteria. How do you ensure equity of access to the drug? Second, what happens if the results are equivocal? Little informative data will have been gained from the investment in running the trial.

Conducting the clinical trial does add costs to the existing process. Informal estimates by several stakeholders have placed the additional cost of running such a trial at 10% of estimated prescribing costs. Glasziou (1995) however argues that such a scheme overall will provide greater health benefits from the same limited budgetary resources. He believes that the cost of supporting prescriptions in trials would be offset by the savings through delaying the general listing of some new medications (presumably those which prove to be less effective in the longer term).

Table 1 **Clinical Trial Option**

Advantages	*Diasadvantages*
Provides high quality clinical and cost data on which to base decision for full listing.	Adds to complexity of PBS
Restricts doctor prescribing	Administrative burden and logistical problems
Patient access and costs carefully regulated and monitored	Impacts on day-to-day clinical practice
Data in an Australian setting	Delay in full-listing
Spreads the risk of non-listing more evenly among companies and consumers	Additional costs for conducting clinical trial
Provides opportunity to gather postmarketing data on long term safety and adverse events	Additional 'barrier to entry' into Australian market
Coherent, rigorous and consistent approach	Possible inequities in patient access

Adapted from Glasziou 1995

5.3 Special Supply Scheme Model

Model Description

An argument put forward by stakeholders (akin to Jones' view that different types of drugs need different types of clinical trials) is that high cost biotechnology and other innovative targeted therapies are different to the small molecule drugs traditionally funded through the PBS and therefore different arrangements should be put in place for their funding. As one interviewee commented "*its like treating orphan drugs as mainstream or making disabled Olympian athletes compete in the able-bodied games*".

This model stems from the views of a number of stakeholders, particularly from their knowledge of Section 100 of the *National Health Act 1953* and recent experience with the breast cancer drug Herceptin and the funding mechanism that has been recently put in place for its supply. The model draws on the special supply arrangements under the PBS for 'highly specialised drugs' (HSDs). Section 100 and other 'special' arrangements are existing mechanisms that have been used to provide consumers with access to several high cost biotech and targeted drugs. At the present, however, there is no consistent process for granting pharmaceutical benefits under special arrangements to this category of medicines.

The existing special supply arrangements, especially the HSDs program, could be broadened to encompass the submission for all high cost biotech and other targeted therapies, or alternatively, a new parallel scheme be introduced specifically for this category of medicines. As one of its key roles, the Highly Specialised Drugs Working Party (HSDWP) is currently supposed to monitor new drugs that potentially might come under these HSD funding

arrangements (the roles of the HSDWP are given in Appendix C1). A special arrangement scheme would help to evaluate these drugs as members of a particular drug group. Concern was raised by stakeholders that there was no consistency in the way in which individual drugs were being processed and that each drug was being treated as a special case when it came up for approval, and not part of a wider class of therapies.

Two other special supply arrangements currently operating outside the PBS also provide support for such a model. For example, with the Lifesaving Drug Program, the Commonwealth Government provides funds under an appropriation item which was established for the specific purpose of assisting access by individuals to expensive and lifesaving drugs accepted by the PBAC as clinically effective, but not available as pharmaceutical benefits because of a failure to meet cost effectiveness criteria (DHAC 2001). Financial assistance for such drugs is approved in accordance with specified eligibility criteria and is subject to certain conditions as agreed by the Ministers for Health and Ageing, and Finance. The criteria and conditions applied to requests for financial assistance for access to expensive lifesaving drugs not available as pharmaceutical benefits are given in Appendix D. This arrangement presently funds the expensive lifesaving drug Imiglucerase[16] (Cerezyme®) for a number of patients suffering Gaucher's disease. Expenditure in 2000–01 was $12.5 million (DHAC 2001).

The Orphan Drug Program also operates outside of the PBS. It is administered by the TGA, and allows for the availability of a range of drug treatments for rare diseases as part of the Australian evaluation process through an agreement on drug evaluations with the FDA's Orphan Drugs Program (DHAC 2001). The program is designed to assist manufacturers to overcome the high costs of developing and marketing drugs which usually are not commercially viable because of small patient populations and therefore small financial returns relative to costs (TGA,1998). The Orphan Drug program is not a funding mechanism as such for subsidising patient costs. Rather, the TGA waives its evaluation fees incurred in registering the drug in Australia in order to secure supply. Orphan drugs still have to be assessed by the PBAC if patients are to receive a pharmaceutical benefit for these drugs.

Many of the organisational mechanisms needed for a special supply arrangement model already exist in the HSD program. Some of the key features of this program are noted below:

Highly Specialised Drugs Program – Section 100

Highly Specialised Drugs "*are medicines for chronic conditions that, because of their clinical use or other special features, are restricted to supply through hospitals having access to appropriate*

16 Accepted by the PBAC as clinically effective for these patients but not cost effective at over $100,000 per life year gained (Commonwealth of Australia 1998 – DHFS PBS Anniversary Edition 1998, cited in Cookson 2000).

specialist"[17] (DHAC, 2001). The drugs are provided in accordance with restrictions identified under Section 100 of the National Health Act 1953. The Commonwealth Government meets the cost of these drugs, in excess of the patient contribution, for patients in the community or attending day services. The States and Territories meet the costs of in-patient supply and costs associated with the administration of these drugs. All community patients are required to pay a financial contribution in respect of each supply of medication. Patient co-payments are comparable to charges levied on medications received through PBS or the Repatriation Pharmaceutical Benefits Scheme (RPBS) (DHAC 2001; TGA, 2002). Some HSDs have a brand price premium, the additional cost having to be met by the patient (the premium continued to apply after changes were introduced to private hospital prescribing and dispensing of highly specialised drugs on 1 November 2000) (TGA, 2000).

Drugs are listed for subsidy under this program following recommendations by the HSDWP and the PBAC and approval by the relevant Federal Ministers (TGA, 2001). The procedures for adding, or varying, an item subsidised under the HSD program are given in Appendix C2. There are two main differences in the listing of drugs on the HSD program compared to the general schedule listing process: the HSDWP must support the listing of each application, and, for public hospitals, the States and Territories must also agree to the Commonwealth's offer of subsidy, prior to the drug being available in that State or Territory (HSDs typically have significant inpatient and associated costs). The HSDWP is not a technical committee but considers the policy and administrative aspects of the supply of certain specialised drugs through the hospital system. Once the HSDWP makes a recommendation in support of the application, the approval process by the PBAC is the same as for other pharmaceutical benefits. Hence, applying for funding for high cost biotech drugs under Section 100 will have no beneficial outcomes if the problems in listing are with the PBAC. Previously, in cases where the annual expenditure for the new listing of a drug on the HSDs program exceeded $10m, the Federal Cabinet may be required to approve the listing. This threshold was reduced recently with any new drug with an estimated annual cost to Government of between $5-10m requiring support from Finance.

Criteria for selection of Highly Specialised Drugs: Drugs recommended for special supply arrangements under the PBS must satisfy the following criteria (DHAC 1999, TGA, 2001):

- Ongoing specialised medical supervision is required (this should not preclude treatment in a community setting and should be interpreted to include specialist initiated treatment where ongoing treatment may be under the supervision of a community general practitioner but involve periodic reference to the specialist facility);

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[17] URL for this: http://www.health.gov.au/pbs/pubs/pbbexp/pbjun/bookp49.htm

- Treatment is for longer-term (chronic) medical conditions, not episodes of in-patient treatment or treatment of acute conditions (the intent is to assist the ongoing maintenance of patients in the community setting);
- The drug is highly specialised and there is an identifiable patient target group;
- Recommendation is subject to marketing approval by the TGA and specific therapeutic indications covered by the terms of the marketing letter from TGA; and
- The drug has high unit cost (high unit cost is interpreted as a cost beyond the normal financial capacity of individuals and imposing significant financial burden on specialised institutions).

Eligibility Issues: To gain access to a drug funded under this program, a patient must attend a participating hospital (either public or private) and be a day admitted patient, a non-admitted patient or a patient on discharge, be under appropriate specialist medical care, meet the specific medical criteria and be an Australian resident in Australia (or other eligible person) as defined in Section 3 of the Health Insurance Act 1973 (TGA, 2000). HSDs are dispensed through hospital pharmacies that participate in the HSDs program. From 1 November 2000 changes were introduced to the prescribing and dispensing of HSDs supplied through private hospitals. For HSDs to be prescribed through private hospitals, a prior authority approval is required from the HIC, and prescribers have to write scripts on "PBS/RPBS authority prescription" pads.

HSDs are restricted to supply through public and private hospitals having access to appropriate specialist facilities. A staff, visiting, or consulting hospital specialist may initiate therapy if they are associated with an approved hospital. Medical practitioners not affiliated with these specialist hospital units cannot prescribe these drugs as benefit items. However, hospital based doctors and general practitioners may prescribe HSDs to provide maintenance therapy under the guidance of the treating specialist in situations where it is impractical to obtain a prescription from the treating specialist, or where the State/Territory and Commonwealth agree on a specific arrangement. A general practitioner or non-specialist hospital doctor may also be accredited to prescribe HIV/AIDS medication following State or Territory approval (TGA, 2001, 2002).

Private hospital prescriptions for HSDs can be dispensed by either a s94 approved private hospital dispensary or any s90 approved community pharmacy. From 1 November 2000, all s90 approved community pharmacies are able to supply HSDs. This is important as access to an approved hospital dispensary is a problem for many patients (TGA, 2002).

As at 1 August 2001, this program provided a range of 42 generic drugs available in 116 forms and strengths (items) and marketed as 122 drug products or brands. Expenditure in 2000–01 was approximately $271.3m (DHAC, 2001). A list of the drugs funded on the HSDs program and public hospital national expenditure on each of these for 2000-01 financial year is given in Appendix E. Many of the new high cost biotech drugs now available, or coming

on to the market, meet the criteria for the HSD program. Two recent examples of applications for Section 100 listing are presented in Table 2. Kaletra was successfully listed on Section 100 after re-submission by Abbott. As several stakeholders commented this recommendation came "*after major delays in the approval process*". In contrast, Novartis had requested Section 100 listing for Glivec but this was listed as 'a highly restricted Authority drug' on Section 85 (HIC, 2001) - doctors being able to request supply of Glivec to their eligible patients from 1 December 2001.

Table 2 **Kaletra and Glivec - Positive Recommendations made by the PBAC**

DRUG AND FORM	DRUG USE AND TYPE	PURPOSE OF APPLICATION	PBAC RECOMMENDATION
Lopinavir with ritonavir capsule 133.3 mg-33.3 mg and oral solution 400 mg-100 mg per 5 mL, Kaletra® - Abbott Australasia Pty Ltd Re-submission (rec. Dec 2001)	A combination treatment for HIV/AIDS.	Section 100 for treatment of HIV infection in patients with CD4 counts less than 500 per mm^3, or viral load greater than 10,000 copies per mL.	Recommended for listing on a cost-effectiveness basis, as requested, for use in combination with 2 or more other anti-retroviral drugs.
Imatinib mesylate* capsule 100 mg, Glivec® New listing (rec. Sept 2001)	An anti-cancer drug	Section 100 listing for treatment patients with chronic myeloid leukaemia expressing the Philadelphia chromosome or the transcript, *bcr-abl* tyrosine kinase. Patients must be in: The chronic phase where the use of interferon alfa- has failed or is inappropriate; the accelerated phase; or blast crisis.	Recommended for listing with an authority required restriction for treatment of adult patients in the accelerated phase or in the blast phase of chronic myeloid leukaemia expressing the Philadelphia chromosome or the transcript, *bcr-abl* tyrosine kinase. Recommended for listing on the basis of acceptable, but high cost-effectiveness ratios in these patient groups.

Source: Department of Health and Aged Care,© Pharmaceutical Benefits Scheme, 21 September 2001 and 28 December 2001. URL: http://www.health.gov.au/pbs/listing/pbacrec/pbacrecsept.htm

* Note Kaletra was listed on Section 100 and Glivec was listed on Section 85 with authority required restriction

Herceptin (Trastuzumab) - A 'Special' Arrangement

Herceptin is a monoclonal antibody used to treat metastatic breast cancer. The drug selectively targets the human epidermal growth factor receptor 2 protein (HER2). Over-expression of HER2 is observed in approximately 25-30% of cancers (Australian Prescriber, 2001). On 1 December 2001, following ministerial intervention by Dr Michael Wooldridge,

the HIC implemented a new program to finance the drug costs of Herceptin to eligible patients (HIC, 2002). This is a 'unique' program administered completely separately to the PBS. Roche Products Pty Limited had applied unsuccessfully three times to the PBAC for PBS listing of Herceptin, despite a widely held view that this was a very clinically effective drug for a subset of patients where there was no other prime treatment alternative.

To obtain Herceptin under the new HIC program, doctors are required to register their patients on the Herceptin program, providing evidence to the HIC that their patients meet the eligibility criteria (these criteria are given in Appendix F). Once patients are enrolled in the program, registration has to be confirmed every six months by the prescribing doctor. HIC is required to obtain signed consent forms from the prescribing doctor and the patient, principally to access patient and provider information already held by HIC. Once eligibility has been established and the consent forms received, HIC directly places an order for Herceptin with Roche. Roche then is responsible for the delivery of the product to the prescriber. The prescribing doctor determines, on a monthly basis, the supply of the drug required for each patient treatment (there are restrictions on the maximum supply for both initial treatment and continuing monthly treatment) (HIC, 2002).

Essentially, this funding mechanism continues as though the drug was listed under a special arrangement scheme within the PBS. It is an audited program, the criteria for patient inclusion are exactly as proposed to the PBAC, and some information is provided in the public domain. The scheme however circumvents the PBAC – its introduction avoided a direct ministerial over-rule of the PBAC decision to decline listing, a PBAC decision that a number of stakeholders would argue lacked commonsense. One problem that the PBAC apparently worried about was the cost-effectiveness ratio in that there was no definite end-point to treatment, other than treatment stopping when there was no sign of cancer or the disease progressed. The average duration of treatment is currently estimated at 9 months at a cost of approximately $32,000 per patient. The total cost to government was estimated to be $9-10m pa. Approximately 190 patients are currently receiving Herceptin through the HIC program. The target population for the drug was identified at 1000 patients. Like other targeted therapies, it is argued that the government budget could not blow-out with this drug, as there are only so many patients that have metastatic breast cancer and are HER2 positive. If patients don't over-express HER2, they will not get benefit from using Herceptin, and there is no point in a doctor prescribing the drug. Problems of leakage arise when a doctor prescribes for an indication outside those specified.

Discussion

As one stakeholder said *"we are not exploring the range of mechanisms [special arrangements] currently available, we are not optimising criteria already there for inclusion"*. On the surface, it would not take much effort to introduce a special supply arrangement mechanism designed to assess high cost biotech and other targeted therapies. Many of the organisational

mechanisms are already in place in existing programs. The criteria for the drugs and therapies (specifications, types of compounds, manufacturing, types of indications, treatment regimens, costs etc) that would be eligible for consideration under a 'high cost biotech and other innovative targeted therapies' special funding arrangement would have to be carefully stipulated and agreed upon by all stakeholders. Importantly, issues of patient access would need to be addressed as, although a significant number of these drugs are related to hospital or specialist treatment (akin to Section 100 drugs), many could and should be dispensed through community pharmacies.

A model based on the special funding arrangement approach could provide a transparent and consistent process for assessing and funding these drugs. The Herceptin Program illustrates the ability of Government to introduce special funding arrangements. However, many stakeholders believe that this particular program was not a good precedent and that it undermines the PBS. While politically expedient, in the longer term it would seem to be more advisable (and acceptable) to establish a program within the existing PBS framework that can encompass many drugs and not just a single item.

Also when considering the cost-effectiveness of a high cost drug, the 'supply chain' does need to be taken into account. The price of a drug listed on Section 85 includes a wholesaler margin and a pharmacist mark-up but these are excluded if the drug is listed on Section 100. The difference in the estimated dispensed price between Section 85 and 100 for one high cost biotechnology drug that was being submitted for PBS listing amounted to 14%. As one stakeholder indicated "*in some instances, this could turn a drug from not being cost effective to being marginally cost-effective (and vice versa)*".

5.4 Incremental (Evolutionary) Organisational Reform Model

Model Description

No stakeholder voiced the need for a 'revolutionary' overhaul of the existing PBS system. However, stakeholders believed that many of the problems outlined in Section 4.4 could be overcome by change to the prevailing organisational culture of the PBAC (and associated committees), and evolutionary (incremental) administrative reform to the ways in which the PBAC operates and conducts the approval process. As one stakeholder said *"If the process worked properly, it would work well"*. Stakeholders want a **rational, consistent** and **transparent process** for determining what drugs get PBS listing.

As one stakeholder commented "*we need structural change to ensure the objectives of the PBS are achieved as they were set-up*". This option basically identifies improvements that could be made to the approval process within the existing PBS organisational-administrative framework. Three main areas of change have been identified. These are: 1) organisational

issues including logistics and transparency**;** 2) assessing cost effectiveness; and 3) improvements to the quality of submissions.

PBAC and the Approval Process – Organisational Issues, Logistics, Transparency

Lloyd Sansom (2001) acknowledges that there need to be closer working relationships between all stakeholders, particularly those involved in the quality use of medicines. Currently, two members of the PBAC are nominated as the discussants of a proposed drug – their role is to lead the discussion after reviewing all submission documents and supporting evidence. The remaining committee members read summary papers along with any material provided from the ESC. The perceived lack of expertise and knowledge of PBAC members on highly technical issues could be overcome and the current system improved by either: 1) broadening the representation of the PBAC to include the use of an expert subcommittee to comment on highly specialised applications; and/or 2) inviting an expert or industry representative to attend on the day of assessment to be there on standby to answer any questions if they arise. In fact, the PBAC does very occasionally invite non-industry individuals to brief it on particular issues before it makes a decision – this is not well known or formalised, but the Committee has recognised it is at a disadvantage if no member has specific knowledge of a drug or its indication. This behaviour, as it currently stands, is problematic as it raises a question of equity in that such an opportunity for discussion is not afforded to all companies submitting a drug for approval. It is, however, a practice that stakeholders would like to see regularly implemented if it were done in a formal manner.

The PBAC recently established guidelines "to provide for meetings between PBAC and stakeholders where there is an application for a drug which treats a serious, disabling or life-threatening condition, where there are no other realistic treatment options for that condition, but where insufficient cost-effectiveness prevents PBAC from recommending listing…The aim of these meetings is to inform stakeholders of the situation, to seek their views, and if possible to define a listing restriction acceptable to the parties which will give the best possible cost-effectiveness, even if at a level which would normally be unacceptable (the "Rule of Rescue"). The meetings are not intended as an appeals mechanism, but as a "without prejudice", non-adversarial process in order to facilitate a re-submission to PBAC by the sponsor or manufacturer" (PBS, 2002)[18].

The timeframe for processing submissions also could be reviewed further and some processes streamlined. The PBAC was reviewed in 2000 and some 15 recommendations made, one of these being the introduction of a 'fast-tracking' mechanism. Some stakeholders interviewed for the position paper endorsed the idea of a 'fast tracking' mechanism particularly for life threatening disorders. This has been advocated for some time by HIV/AIDs organisations where the immune status of patients can change rapidly within the

[18] URL for this http://www.health.gov.au/pbs/listing/pbacguidelines.htm).

timelines of drugs being assessed for subsidisation. Thus, in theory a process of fast-tracking exists but greater practical use could be made of it.

While stakeholders recognised that sponsors of drugs need to 'jump through the same hoop', it was generally agreed that there was need for flexibility in the system. Overcoming current difficulties, according to one stakeholder, is "*primarily a matter of [the PBAC] being more flexible and willing to discuss if they have a problem, what that problem is, and what we can do to overcome it*".

Professor Lloyd Sansom, Chair of the PBAC (2001, p257) acknowledges that "*the degree of understanding by health professionals and the general public of the processes that are used to evaluate submissions is extremely low*". Stakeholders share the belief that the current committee needs to provide more transparency over the approval process and that there could be more room for open exchange of information with consumer organisations, health professionals and the pharmaceutical companies. However, the process of transparency needs to 'cut both ways'. For example, at the present, it would appear (from the views of some stakeholders) that when an application is rejected then the industry doesn't want public disclosure as to why the drug has been declined for PBS-listing. All stakeholders need a greater understanding as to why drugs are rejected or recommended. However, as one stakeholder commented, the need for transparency has to be weighed up against the PBAC getting pushed into a corner. The "*PBAC still needs a fair degree of discretionary movement*" and flexibility in its decision-making processes.

How can the actual decisions and the decision-making processes become more transparent? Stakeholders thought first, by a greater and more open exchange of information between the PBAC and the sponsors of the drugs and, second, by bringing some of the processes into the public domain — for example, by holding public hearings on submissions. The Committee could ask questions of the company, consumer groups and medical/scientific experts in a public forum. While their final deliberations could remain 'behind closed doors', this would increase participation in and openness of the approval process. A precedent exists with the FDA, which holds public hearings for drug approval in the US. Information that was of a commercially sensitive nature could be heard in camera. While improving issues of transparency, such a change could have major resource implications, as currently the PBAC assesses around 30 applications in two days. This turnaround would not be possible if public hearings were to be introduced for all applications. However, public hearings could be held for marginal cases only - where the decision to recommend or decline a submission was equivocal. Clear criteria would have to be established as to when a hearing was or was not warranted.

Assessing Cost Effectiveness

From 1 Jan. 1993 onwards, submissions for PBS listing have been required to include cost-effectiveness analyses. As mentioned earlier, guidelines are provided to the industry on appropriate methodology and interpretation, with the PES and ESC providing advice to

PBAC on the validity, economic model assumptions, implications etc. However, 'cost-effectiveness' is a highly contentious issue and probably the main stumbling block to PBS listing of high cost biotech drugs. The PBAC works on an evidence-based system, so clinical trial data are the starting point on which cost-effectiveness is measured. As one stakeholder commented "*most stakeholders can't agree or disagree to support a particular drug as we cannot enter into an informed open debate because much of the available data is 'commercially in confidence' and is not in the public arena*".

Drugs are being rejected if their cost is not commensurate with their benefit but the threshold on which such decisions are being made has not been made explicit and is debatable. As stated earlier (Section 4.4 'Current Perceptions of Difficulties, Cost effectiveness, p24), the criteria for assessing cost effectiveness as a basis for accepting or rejecting an application for PBS funding are highly controversial and, in terms of the PBAC, not at all transparent. The commonly held view is that the PBAC uses a threshold of between $40,000 and $50,000 and that there has been strong downward pressure on this threshold. The threshold used by PBAC has apparently been in the economic literature over the last 7-8 years. It does not appear to have been updated, and there is uncertainty among stakeholders as to whether this was even empirically based or where it derived from. Stakeholders say this threshold needs to be discussed. However, they warn of the dangers of advertising or making explicit what is an acceptable threshold since drug prices can be manipulated in the economic evaluation of a new drug to ensure the cost-effectiveness ratio comes under the threshold. Also having 'a decision rule to list' removes the flexibility and discretionary powers of the PBAC, the retention of which stakeholders see as important (as long as this is exercised in a consistent, responsible and transparent manner). Furthermore, cost-effectiveness could be measured in terms of international currency or some weighted basket so that the figures included in submissions don't vary with fluctuations in the Australian dollar.

The immediate advantage of traditional cost-effectiveness analysis is that it allows policy-makers to compare distinctively different procedures and treatments – to compare 'apples with oranges'. However, if it is to be a really effective tool for the PBAC then perhaps as Menzel et al (1999, p7) argue it has to "be recalibrated so that it better reflects some of our widely held beliefs about the merits of different kinds of treatment". The advantages and disadvantages of cost-effectiveness techniques in health care are widely debated in the academic literature. The point Menzel and colleagues (1999) make is that conventional cost-effectiveness analysis when assessing a treatment disregards or underestimates: "the initial severity of the illness; any unique value of lifesaving or other treatment in the face of death; the fact that patients' limited potential for increased health may be a longterm identifying characteristic of their lives, and age (not the effect of age on duration of the health improvement but age itself)"(p8). They argue that cost-effectiveness analysis should explore how social values might be better incorporated into the "effectiveness" side of the economic analysis.

Furthermore, public utility options in applying cost-effectiveness ratios, such as determining 'the greatest good for the greatest number', are not without their problems. In 1990, the Oregon Health Services Commission produced a draft of a priority list of health procedures and treatments that would be included in a Medicaid program expanded to cover 'all' poor Oregonians, but only services deemed to be of relatively high priority were to be covered. The initial list was met with widespread criticism and a second version generated. "Some doctors and consumer groups were highly critical of the draft list, asking why some procedures they deemed to be beneficial or lifesaving were placed below routine procedures like headache treatment" (cited in Hadorn, 1991, p2218). High cost high benefit services posed a particular dilemma for the priority listing. Traditional cost-effectiveness techniques (assigning priorities by relating the cost of a service to a measure of the health benefit it provides e.g. QALY) resulted in high-cost procedures with significant benefits having similar priority rankings to low-cost procedures with minimal quality of life benefits. "Specifically, the cost-effectiveness analysis approach used to create the initial list conflicted directly with the powerful "Rule of Rescue" – people's perceived duty to save endangered life whenever possible … people cannot stand idly by when an identified person's life is visibly threatened if effective rescue measures are available" (Hadorn, 1991, p2218). As Hadorn states "even if suffering and denial are fairly allocated, individual instances of suffering and denial are extremely difficult to accept" (1992, p1455).

In addition, the Oregon Plan may have violated the *Americans with Disabilities Act*. Utilitarian efforts, as encapsulated in the Oregon experience, run the risk of discriminating against individuals with medical disabilities. The two key elements in such priority setting – estimation of health outcomes and assignment of preference values to these outcomes – are open to the charge of discrimination. "Medical outcomes expected in disabled individuals and the values they place on those outcomes may differ from the general public" (Hadorn, 1992, p1454). Hadorn (1991,1992) believed that the lesson to be learned from the Oregon experience was that the use of cost-effectiveness analysis was unlikely to produce a socially or politically acceptable definition of 'necessary' care, and that priority setting efforts must avoid the appearance and reality of discrimination. Cost-effectiveness approaches based on a utilitarian philosophy tend to give inadequate attention to the individual person and too much to the aggregate good, and are insensitive to issues of distributive justice involving the least advantaged (Menzel et al, 1999). These issues need to be taken into account in considering the broader debate surrounding the PBS funding of new high cost biotechnology and oncology therapies.

Improving the Quality of Submissions

Hill et al. (2000) found that 67% of submissions to the PBAC between 1994 and 1997 had significant problems with their pharmacoeconomic analyses, which may have influenced the PBAC's recommendation. While the existence of such problems probably reflects the complicated synthesis of data from a variety of sources and the fact that judgement calls/assumptions have to be made, they also imply the need for the industry to be as

rigorous as possible in their submissions. Cookson (2000) also notes that PBAC assessments are not as comprehensive as they could be because there is no requirement for submissions to include the following:

- An estimation of the extent of possible leakage [*for current submissions, the PES does estimate leakage outside the proposed indications in anticipation of leakage*];
- An evaluation of the cost per QALY that would enable comparisons between disease areas as well as within disease areas (although cost per QALY is not possible to obtain for some drugs). The PBAC has a preference for patient relevant outcomes to quantify increases in health benefit and to weigh them against increases in cost (Birkett et al. 2001); or
- Cost effectiveness data on historical decisions about other drugs, which would help to put the submission's data into perspective (but is not available to industry).

Provision of this information could assist in allaying the Committee's fears on cost blow-outs and in determining a more balanced assessment of cost-effectiveness.

Increasing transparency may also help in getting better quality submissions in the future. Disclosure of the PBAC's views, for example, on an appropriate comparator and why, would be highly beneficial to companies in preparing submissions and understanding why a drug may not have been approved. However, no advice provided to manufacturers prior to lodgement of a submission is binding on the PBAC.

Discussion

Of the six options proposed, this would seem to be the most expedient in terms of implementation and immediate benefits that could be gained. However, the changes proposed are not targeted specifically to the listing of high cost biotech drugs but rather address general problems with the PBS approval process. Incremental changes to the current operations of the PBAC and approval processes, as outlined above, would go 'some way' to improving both the assessment of submissions and the uneasy relationship as perceived by stakeholders that currently exists between consumers, medical professionals, industry sponsors and the PBAC. Importantly, increased transparency would help overcome the perception that the PBAC does not operate in an equitable fashion in its decision-making. The most substantial addition to current costs would be the introduction of a public hearing scheme. Otherwise, this would not seem be an expensive option to implement.

5.5 Differential Copayments and Public Subsidy Arrangements

Model Description

This option puts forward alternative copayment arrangements as a mechanism for government to share the cost of existing and new pharmaceutical medicines with prescribed drug users. As the Adam Smith Institute (ASI) in the UK suggested with respect to the reform of the NHS, "*there are a number of steps that can be taken to move us in the right direction. For example, better use could be made of copayments: sensitively structured, these need not harm equity and will encourage the more responsible use of health services*" (ASI, 2001, p2). Modelling changes in the patient copayment policy of the PBS and a number of different cost containment policies have been a recent focus of the Australian Pharmaceutical Manufacturers' Association (APMA). Different copayment arrangements are also considerations of the Department of Health and Ageing, and were raised as an alternative option by various stakeholders interviewed for the position paper.

As described in Section 4.1, Australia currently has one fixed rate of copayment for concessional patients ($3.60 per prescription item) and another for general patients ($22.40). Eligibility to concession cardholder status depends on an individual's or family's welfare position, and in this way can be regarded as being 'means tested'. For the last financial year (2000-01), patient copayments contributed to only 16.3% of the total PBS pharmaceutical bill (Table 3). Government subsidisation of drugs prescribed for concessional patients amounted to $3,020m (66.3% of total costs excl. doctors bag) and general patients $790m (17.4%). A number of consumer, industry, medical and government stakeholders stated it made little sense to continue to operate a system of public subsidisation of prescribed drugs based on this fixed (i.e. flat) rate of patient copayment. As one stakeholder commented "*Patient contribution to the pharmaceutical bill in Australia has waned over time as a proportion of total PBS expenditure – with Government missing the opportunity of maintaining proportionate patient contribution*".

Pharmaceutical subsidy arrangements operate in most developed countries. As the Productivity Commission (2001) has identified, the major differences are with respect to four key elements: 1) the eligibility criteria i.e. what section and proportion of the population is covered; 2) level of public subsidy i.e. the size of the drug list and level of patient copayment; 3) the type of subsidy list – positive, negative or both; and 4) the mix (balance) of coverage provided by public versus private schemes. The latter of these will be discussed in the next section of the paper.

Table 3 **PBS Prescription Volume, Government Cost and Patient Contributions, year ending June 2001**[a]

Category	Volume	Govt Cost	Patient Payments	Total Cost
	No. of Scripts	$	$	$
Concessional Non Safety Net	99,284,880	2,359,644,872	337,378,069	2,697,022,941
Concessional Safety Net	25,420,093	660,301,391	0	660,301,391
Total Concessional	*124,704,973*	*3,019,946,263*	*337,378,069*	*3,357,324,332*
General Non Safety Net	18,526,030	662,096,086	392,430,174	1,054,526,260
General Safety Net	4,340,355	128,173,669	14,353,807	142,527,476
Total General	*22,866,385*	*790,269,755*	*406,783,981*	*1,197,053,736*
Total	**147,571,358**	**3,810,216,018**	**744,162,050**	**4,554,378,068**

[a] excludes doctors bag. Source: PBS, 2001.

Table 4 describes the type of subsidy arrangements operating in a number of selected countries. Essentially, there are two kinds of copayment systems (subsidisation schemes):

1. **fixed** rates of patient copayment, as currently operating in Australia, and

2. **proportional** copayments where patient contributions (and government subsidies) are proportional to final drug prices (or reimbursement). There are basically two approaches to proportional copayment:

   - a sliding scale by drug category, and
   - other sliding scales e.g. by individual or family expenditure on prescribed medicines, patient characteristic or drug price.

Countries operate subsidy lists as a means of controlling access to subsidised products. Both list types - positive and negative lists - have the same aim of eliminating less effective drugs from public subsidisation. As seen in Table 4, the majority of Governments of OECD countries operate a positive list – governments identify the drugs that will be subsidised. However, a few countries such as the UK and Germany, have negative lists where the government decides which therapeutic products will not be subsidised. Other countries operate a combination of the two. Burstall et al (1999) state that positive and negative subsidy lists appear to have similar outcomes in reducing the proportion of prescriptions that are reimbursed. However, while positive lists tend to indicate a more considered approach, it is difficult politically to deny reimbursement to popular drugs of doubtful efficacy.

Table 4 **Prescribed Pharmaceutical Subsidy Arrangements in Selected Countries**

Country	Copayment Arrangement	Subsidy List
Australia	fixed	positive
Austria	fixed	positive
Belgium	proportional	positive
Canada	proportional	positive
Denmark	proportional	combination
Finland	proportional	positive
France	proportional	positive
Germany	proportional	negative
Ireland	fixed	positive
Italy	proportional	combination
Netherlands	proportional	combination
New Zealand	fixed	positive
Portugal	proportional	positive
Spain	proportional	combination
Sweden	proportional	combination
UK	fixed	negative
US	Mixed- Prop/fixed	positive

Source: Burstall et al, 1999; Productivity Commission, 2001.

Several countries operate fixed copayment systems similar to Australia's PBS copayment policy, and as in Australia, these usually involve some form of 'means-testing'. There are, however, some differences. For example, while the British Government operates a system of fixed copayments, it prefers a negative subsidy list. It subsidises all new prescription drugs once approved for marketing except those placed on its negative list. A large range of drugs (some 3000 pharmaceutical products – most over the counter (OTC)) is listed on Schedule 10 - the 'Black' list (Kanavos, 1999). Patients pay a fixed amount per prescription. In 2001, the standard charge was £6.10 irrespective of the cost of drug (Productivity Commission, 2001). Significantly, only a small number of scripts actually attract this copayment - 85% of prescriptions dispensed at community pharmacies are free to patients (Senior, 2001). Exemptions are widespread, being granted to the elderly, pregnant women, students and people on low incomes.

In Ireland, where a fixed copayment system also operates, copayment depends on income with reimbursement being selectively applied to patients according to their financial and medical status. About one-third of Ireland's population is entitled to receive free medications under the General Medical Service (GMS) Scheme or the Long Term Illness (LTI) Scheme (Barry et al, 2000). Similar to Australia's concession cards, patients eligible to the GMS are issued medical cards. Eligibility is means tested and dependent on a number of factors including age, marital status, living alone or with family, and allowances. The LTI scheme

entitles patients suffering from one of fifteen chronic conditions to full drug reimbursement irrespective of income. Approximately, 2% of Ireland's population are eligible under this scheme.

The remainder of the population, whose drug consumption amounts to about 33% of the annual drugs bill, have to make copayments up to a maximum payment of IR£42 in any calendar month (as from 1 July 1999). The Irish Government also introduced a 'common medicines list' for all schemes – GMS, LTI and drugs payments scheme (introduced July 1999 for non medical cardholders) – to ensure equity between the schemes. This list is basically the list of items reimbursable under GMS (Barry et al, 2000).

Within OECD countries, however, the predominant form of drug subsidy arrangements is where subsidisation and patient contributions are proportional to drug price. There are basically two approaches under proportional copayments: the first is where medicines are allocated to different drug categories and different co-payments are required in each; and the second is based on sliding scales of individual or family expenditure on prescribed drugs.

The first of these proportional copayment systems operates in Belgium, Denmark, France, Italy and Portugal for example (Table 5). Under these schemes, subsidisation ranges from 100% subsidisation of life-saving and essential drugs to 50% or less for 'comfort', lifestyle and non-essential drugs. A number of stakeholders interviewed for the position paper thought Australia should introduce this type of drug subsidy scheme. In fact, one stakeholder reported that "*although the official interpretation of the relevant clause in the National Health Act, as determined by Dr Blewett when Minister of Health, is to the contrary, some legal experts in Australia would argue that the Act does provide for differential copayment*".

Belgium provides a good example of these drug subsidy arrangements. In Belgium, the third party payer system is applicable to the dispensing of prescribed reimbursable medicines. Nearly all Belgians are covered by compulsory health insurance. The system is financed through social security (public funding by six national sickness funds), patient copayments and contributions by federal and regional authorities (Annemans et al, 1997). In Belgium, in the mid-1990s, patient copayment contributed on average to 24% of the cost of prescription drugs. Prescribed reimbursable drugs accounted for about 71% of the total expenditure on pharmaceuticals; non-reimbursable prescription drugs 11% and OTC medications 18% (Annemans et al, 1997). In Belgium, a patient copayment has to be paid for reimbursable pharmaceuticals dispensed through retail pharmacies according to drug category.

The basis for drug reimbursement in Belgium is the so-called 'grid of categories'. Every category is categorised by a given level of subsidisation (and thus copayment level) (see Table 5). Classification in the grid of categories reflects the therapeutic and social value of the drug. Where a new drug corresponds to an already existing 'acceptance criterion', it is assigned to a therapeutic class (a group of comparators) and hence to a category (Annemans et al, 1997). Originally, there were three reimbursement categories A, B and C but for cost-

savings reasons, two further categories (Cs and Cx) with lower reimbursement levels were added. In all countries identified in Table 5, category A medicines, which include life saving drugs, are totally subsidised (no patient copayment). Categories B and C have a subsidisation of 75% (25% copayment) and 50% (50% copayment) of the retail price respectively.

In France, a national health insurance fund subsidises prices of pharmaceuticals to all French citizens (Productivity Commission, 2001). Drugs on the Government's positive list (where medical benefit or therapeutic value has been accepted) are classified into one of three categories, which determines their level of reimbursement and patient copayment. Approximately, 72% of products are in the middle class of drugs (Productivity Commission, 2001). Drugs in this category have a patient copayment of 35% of drug price.

Table 5 **Public Subsidy Arrangements for Selected Countries**

Belgium	Denmark	France	Italy	Portugal
5 groups:	3 groups:	3 groups:	3 groups:	3 groups:
100% A. Life-saving drugs e.g. anti-neoplastics, insulin, antiepileptics	100% e.g. insulin & drugs to control chronic diseases	100 % Life saving medicines e.g. drugs to control diabetes, AIDS, cancer and chronic diseases	100% Group A. Essential drugs	100% Essential drugs
75% B. Essential medicines e.g. antihypertensives, antibiotics, antirheumatics, antidepressants	75% drugs for treatment of well defined life threatening diseases e.g. cardiovascular, antiasthmatic, oral hypoglycaemic agents, opoid analgesics, antiepileptics, neuroleptics	65% reimbursement for essential and indispensable drugs (majority of products - those not in 1 or 3) eg infectious diseases	50% Group B. products of significant therapeutic interest	70% important drugs
50% C. Comfort drugs e.g. drugs targeted to discomfort diseases or drugs with limited efficacy	50% medicines for definite and valuable effect e.g. antibiotics, analgesics, corticoids, antihistamines, antacids	35% non-essential drugs used for non-serious conditions and disorders	0% Group C. Other drugs including OTCs	40% for drugs of recognised therapeutic value
40% Cs. Comfort drugs e.g. Antihistamines and some vaccines				
20% Cx. Drugs support well-being e.g.oral contraceptives and cerebrovascular agents				

Source: Burstall et al, 1999; Productivity Commission, 2001

In Denmark, until the early 1990s, patients had to pay for all their prescribed drugs up to an annual limit (in 1990-91 this was US$137). This limit was relatively high, being set at slightly below average per capita consumption (approx. US$150) (Burstall et al, 1999). According to Burstall and colleagues (1999), this angered individuals who rarely demanded pharmaceuticals and who had to pay in full for any occasional prescription item. This system was replaced by the scheme identified in Table 5 where patients have to pay the balance between the price of the drug and its reimbursement level, the latter depending on the category in which the medicine is allocated. Copayments cover about 33% of the Danish drug bill (Burstall et al, 1999).

Italy has relatively high patient copayments. In 1996, copayments amounted to about 50% of spending on reimbursed medicines (Burstall et al, 1999). Italy, like Denmark, France and Portugal, has three reimbursement categories (Table 5). Approximately 45% of drugs are in Group A, which are fully subsidised. About 50% of drugs are, however, in Group C (no subsidy) and only a few are in the middle category (50% subsidy). In Italy, a fixed copayment is also charged for the first prescription item and a second flat rate for two or more items, with an upper limit on copayment per prescription (Burstall et al, 1999).

Countries like Sweden, Spain and Finland also operate proportional subsidy arrangements but these countries use a number of different types of sliding scales to determine the levels of proportional copayment. In Sweden, for example, all prescribed medicines are placed on a positive subsidy list (known as Drug Benefit Scheme) after marketing approval has been granted and the retail price decided. Sweden also has a negative list, which contains products such as cough remedies, nicotine substitutes, hair restorers, obesity and erectile dysfunction therapies (Productivity Commission, 2001). Patient copayments were introduced in 1990 – all consumers of prescribed drugs are required to make a financial contribution, the only exemption is insulin which is free. Consumers pay the full cost of their prescribed drug use up to the threshold where their total expenditure on pharmaceuticals, over a 12 month period, exceeds SKr900 (A$173). When purchases exceed this level, the cost is subsidised with a progressive reimbursement rate until a ceiling of SKr1800 (A$346) per annum is reached. Once expenditure is above this threshold then any additional drug costs are fully subsidised (Productivity Commission, 2001; Senior, 2001). There are no exemptions on socio-economic grounds (Senior, 2001).

As in Australia, prescription drugs in Spain are subsidised under a national scheme with universal coverage to the population for a wide range of products (Productivity Commission, 2001). Prior to 1993, all prescription medicines were automatically granted subsidisation, but in 1993, some 800 products were removed and placed on a negative subsidy list, and more were removed and added to the negative list in 1998 (Kanavos, 1999). However, copayment arrangements in Spain differ markedly to those in Australia. In Spain, most patients make a financial contribution towards the cost of prescribed medicines based on a proportion of the drug price:

- individuals aged less than 65 years pay 40% of the price of the reimbursable pharmaceutical;
- persons with chronic or life threatening illnesses pay 10% (with a maximum up to Pst439 (A$4.20) per prescription item; and
- the disabled, people aged 65 years of age and over, hospital patients, and those with work related injuries are exempt from copayments (Productivity Commission, 2001).

Discussion

The idea was put forward by some stakeholders with respect to the provision of price signals, that "*if the patient was not prepared to pay (assuming they were able to afford to pay), then it was not appropriate to ask taxpayers to subsidise such drugs*". Stakeholders believe there is a need for greater patient awareness of the costs of the PBS drugs that they use and greater patient responsibility for such costs. At the moment, the majority of prescribed drug users are concessional patients whose out-of-pocket payments contribute to only 7.4% of the total expenditure on PBS listed drugs.

What is wrong with a fixed copayment system as is currently operating in Australia? There are several problems with flat rates for user part charges, as Senior (2001) identified with regard to the British system:

- As a way of raising finance for the Government to pay for prescribed medicines, it is a failure. In England in 1989, prescription charges financed 26.5% of community prescription costs. Since then the percentage has drifted down to 19.6% in 1999. (Stakeholders reported that Australia has experienced a similar trend);
- As a way of containing demand for medicines, it is ineffective. Rates of copayments have increased but the number of prescribed items have also continued to rise;
- A flat rate denies consumers knowledge of the cost of their medicines, and therefore denies them the possibility of choice between, for example, a new higher priced medicine and an older cheaper drug;
- If a flat rate is thought of as a form of social solidarity, it fails when a worker on £5 per hour pays the same for a given medicine as the next patient earning £50 per hour (Senior, 2001); and
- Fixed copayment arrangements also tend to favour consumers of expensive drugs and of items dispensed in large packs i.e. with a flat copayment per prescription item, high cost users of drugs are cross-subsidised by low cost users (Burstall et al, 1999).

There are of course some advantages with these types of subsidy arrangements – they are easy to understand and administer for example – but as Senior would argue these tend to be outweighed by the system's failings.

While there are equity concerns with both fixed and differential copayment schemes, there are a number of subsidy arrangements that the Australian Government could explore as an alternative to the existing mechanism with the view towards long term sustainability of the PBS. Although shifting to a proportional copayment system would add to the complexity of current PBS system, as shown, there are well established precedents in other countries. Countries operating public pharmaceutical subsidy schemes are similar in that they provide universal coverage, subsidise most products, and require some financial contribution to cost from patients. However, as the Productivity Commission (2001) noted, subsidy arrangements that provide universal coverage and subsidise an extensive list of drugs are more likely to stimulate demand for pharmaceuticals than narrower subsidy schemes. Governments typically have mixed objectives and will make trade-offs in trying to provide access to necessary medicines at the lowest possible costs.

There is a strong relationship between public subsidy and cost-containment arrangements. Usually, the policy focus of drug price and reimbursement systems is on cost containment strategies within the pharmaceutical budget, achieved through a mix of price, reimbursement and volume controls. These controls include supply side measures such as the positive and negative subsidy lists, reference pricing, generic substitution, and demand side measures of patient copayments and drug budgets for general practitioners (Annemans et al, 1997; Burstall et al, 1999). No country relies on a single instrument, and as shown, there are variants within each approach (Burstall et al, 1999).

Patient copayments have two effects: they transfer some of the burden of drug expenditure to the patient and may reduce the overall level of consumption (Burstall et al, 1999). An aim of copayments is to reduce unnecessary or excessive consumption by making consumers aware of and bear some of the costs of purchase – they are intended as an incentive to deter unnecessary or marginal utilisation (Hitiris, 2000; Productivity Commission, 2001). The relevance to the funding of high cost biotechnology and oncology therapies is that patients can make a financial contribution to the cost of these drugs, and savings from reduction in the consumption of existing subsidised drugs can be used to help fund new drugs. Thus, copayments, if implemented appropriately, may generate additional revenues that can be 'ploughed back' into essential services (drugs).

However, reduction in consumption will only occur if the elasticity of demand for drugs is relatively high - Burstall et al (1999) report estimates ranging between -0.1 and -0.6 i.e. a 10% increase in price decreases consumption by 1% to 6%. In the UK, Hitiris (2000) reported estimated elasticities of between –0.22 to –0.50. Price elasticity will vary for different groups of consumers since different groups of individuals will have different demand characteristics and responses to price changes. Furthermore, the effect is reduced by the fact that, as shown

above, a sizeable proportion of each country's population is exempt from copayments. Also, elasticity is dependent on the perceived efficacy of the drug – elasticity is low for more important and efficacious drugs and higher for marginal drugs (Hitiris, 2000).

As identified by Hitiris (2000), there are three important issues to consider in deciding upon drug subsidy arrangements: whether a reduction in consumption from the introduction of (higher) copayments would be substantial; would a reduction in drug use have delayed or flow-on effects on other parts of the health system or on future budgets; and what are the distributional impact on selected groups in the population. As Annemans and colleagues state "Although the Belgian category grid system guarantees better reimbursement to more efficacious drugs, it doesn't recognise sufficiently the links between the different elements in health care" (p1997, p206). Pharmaceuticals should not be considered as a 'stand alone' budgetary item but an integrated part of the health care system. As one stakeholder said "*we need a 'whole' of system approach*". There are negative consequences of cost containment through increased patient copayment. Higher patient financial contributions may lead to reduced drug consumption but higher use of other parts of the system, for example, people who stop using drugs may have increased hospital admission or visits to the doctor, especially the poor and elderly (Tamblyn et al, 2001).

Proportional copayment schemes are not without their own difficulties. As Senior (2001) comments, using the Swedish system as an example, proportional copayment still leaves a relatively low paid individual paying the same as a highly paid one. However, Senior (2001) identifies two main benefits in the Swedish system: it has brought in new private money to pay for medicines. Since its introduction in 1997, Swedes have had to pay about 25% of the cost of their medicines compared with 22% previously; and for the majority of patients without chronic and expensive conditions, it has sensitised people to the cost of their medicines, and consequently has opened up the possibility of 'genuine' choice in drug use. If additional funds can be injected into Australia's PBS system then some of the difficulties in funding new biotechnology and oncology therapies arising from budgetary limitations may be removed or at least reduced.

Theoretically, there are a number of ways of introducing a sliding scale for patient copayments, including sliding scales by category of drug and drug price as outlined above. Stakeholders may wish to discuss at the 7 March Forum other alternatives such as:

- Sliding scale of reimbursement based on severity of illness;
- Sliding scale of reimbursement based on the indication;
- Sliding Scale of reimbursement based on ability to part charge;
- Sliding Scale of reimbursement based on effectiveness of treatment;

plus

- Means testing for patient part charge; and
- Tax rebate for those who pay for high cost biological agents.

5.6 Cost Sharing with Third Party Payers – Expanding the Role of Health Insurance Funds

Model Description

This option raises the possibility of shifting some of the cost of prescribed pharmaceuticals to third party payers through increased use of either social insurance schemes or private health insurance funds. Private insurance schemes cover a large proportion of both the US and Canadian populations, and play an important role in a number of other countries including France, Germany, Ireland and Spain by providing part coverage to certain segments of these countries' populations. Many European countries' health systems, including their pharmaceutical reimbursement schemes, are based on compulsory social insurance. The topic of third part payers in health care funding, however, is extensive and therefore only some of the key issues can be touched upon here.

The debate of moving towards a more mixed public-private system is not unique to Australia. Members of the ASI (2001) argue that the UK too should take note of the world's experience and move towards a pluralistic insurance-based funding model, along the lines of those used by many European countries. The ASI believes that the UK should adopt compulsory social insurance in which people can choose between different funds. This, they argue, is compatible with an increased role of private insurance through which choice would be extended further. The ASI states that the UK should not rely on tax funding alone as public expenditure cannot keep pace with rising demand and upward pressure on costs of health care. These arguments have parallels in Australia.

In Australia, private health funds currently play a very minor role in the funding of prescribed medicines. Private Health Insurance (PHI) ancillary (or extras) cover usually only includes coverage of prescribed non-PBS listed drugs. The PHI funds vary with respect to benefit limits paid per person in any calendar year as shown in Table 6. In the three months to December 2001, private health funds paid out $14.6 million in benefits for pharmaceutical related expenses (PHIAC 2001). This accounted for only 3% of total benefits paid from ancillary tables in that quarter.

The current Liberal Commonwealth Government has demonstrated its support of PHI funds in financing health care in Australia through its private-public partnership policies. The '30% Rebate' and 'Lifetime Health Cover' are two initiatives introduced by the federal Government to address declining private health insurance membership and the problem of increased pressure on the public health system.

The 30% Rebate was introduced on 1 January 1999 to make private health insurance more affordable. All Australians who are eligible for Medicare, and who are members of registered health funds, are eligible for the rebate irrespective of family type or income. It is available on hospital cover, ancillary cover or combined cover. The rebate is claimed in one

Table 6 **Private Health Insurance Pharmaceutical Cover, Selected Funds**

Fund	Cover	Limit on pharmaceutical benefits paid per person per calendar year
MBF[(a)]	MBF Young Cover	$700 maximum per membership
MBF[(a)]	Premium Extras	$250 per person in first year; $500 for any two consecutive years
NIB[(b)]	Quality Extras	$600 maximum
NIB[(b)]	Safeguard, Singles Plus and Couples Plus	$45 per script to a limit of $450
Medibank Private[(c)]	Blue Ribbons Extras and Extras Plus	$600 maximum
HCF[(d)]	Extras Multicover, General Extras Family Option and General Extras Sports Option	Maximum of $50 per drug per script to a limit of $500 per person per year

(a) For prescribed non-PBS listed drugs where prescribed specifically for the treatment of an ailment or illness. However, MBF may, on special application, provide benefits for PBS Authority or Restricted drugs, but only if prescribed for illnesses which do not meet the PBS Authority or Restricted requirements and therefore are rejected under the PBS before being prescribed. MBF will only provide benefits for drugs approved for sale in Australia which by law require a prescription and are so prescribed. Contraceptives and anabolic steroids are not covered unless prescribed for an illness. MBF will pay a benefit for the PBS patient contribution where the drug is intrinsic to hospital treatment covered by MBF.

(b) For prescribed non-PBS items only. Excludes contraceptives and items not related to a medical condition. Benefits are paid on cost above non-concessional PBS copayment. Benefits per script not payable for prescriptions dispensed in pharmacies located within a hospital.

(c) For prescribed non-PBS items only. Excludes oral contraceptives. Benefits are paid on cost above non-concessional PBS copayment.

(d) For prescribed non-PBS items only. Benefits are paid on cost above PBS copayment.

Sources: http://www.mbf.com.au; www.nib.com.au; www.medibankprivate.com.au; www.hcf.com.au.

of three ways—through a premium reduction; direct payment from Medicare; or as a tax rebate.

Lifetime Health Cover was introduced on 1 July 2000 to encourage people to take out private health insurance earlier in life and to maintain their cover. The scheme allows health funds to charge different premiums based on the age of each particular member when they first take out cover with a registered health fund. People pay a 2% loading on top of their premium for every year they are aged over 30 years of age when they first take out hospital cover. The maximum loading a person is required to pay is 70%. However, people who were aged 65 years and over on 1 July 2000 are exempt.

The rationale behind the initiative is that it would improve the overall health profile of health insurance members, which would contribute to making premiums more affordable for all members. These schemes provide a precedent for a joint collaborative approach to funding prescribed medicines.

What types of health insurance (third party) schemes operate overseas? While private insurance schemes cover a large proportion of the US and Canadian populations, there are public pharmaceutical subsidy schemes which provide cover for certain segments of the

population. In the US, Medicaid provides coverage of prescribed pharmaceuticals for the poor and Department of Veteran Affairs subsidies drug expenditure by military veterans (Productivity Commission, 2001). Medicare, the public health insurance program for the elderly and certain disabled persons, does not provide reimbursement for most community dispensed prescription or OTC drugs (Hansen, 2001).

Most Americans are enrolled in public health insurance schemes which provide subsidised pharmaceuticals to their members, or are uninsured and have to purchase drugs at market prices. Pharmaceutical reimbursement has been incorporated into managed care plans. Copayments are usually required and most schemes have some form of drug formulary (reimbursement list) which lists pharmaceuticals that are preferred for use and are subsidised by the plan (Productivity Commission, 2001). Formularies are reviewed and modified regularly. Rates of patient copayment may vary according to the nature of the fomulary. An incentive based formulary offers enrolees lower copayments for preferred products and part subsidisation of non-listed products with higher copayments. In contrast, a 'closed' formulary limits coverage to selected pharmaceuticals and requires enrolees to pay full cost of non-listed medicines (Productivity Commission, 2001). Third party payers operate both fixed and proportional copayment arrangements.

In the US, drug prices are established through arrangements between the manufacturers and a variety of public and private sector purchasers (including insurers, Health Maintenance Organisations (HMOs) and other managed care plans). Significantly, pharmaceutical companies have traditionally sold the same prescription drug at different prices to different purchasers (Hansen, 2001). In the US, price negotiations are influenced not only by price-volume mechanisms that may be in place - bigger price discounts will be exchanged for larger volumes of sales – as is the case in Australia, but also by the price sensitivity (elasticity of demand) of the different purchasers. HMOs are, for example, price sensitive as they can channel use to the particular drugs that they purchase and list on their formularies (Hansen, 2001).

As the ASI (2001) identifies what differentiates the US from other insurance-based health systems is the level of compulsion – obtaining insurance in US is not mandatory, and many individuals chose not to, or are unable to afford to, purchase cover. Perhaps more importantly though, while the federal government does not regulate doctor prescribing practices or direct doctors to adhere to specific practice guidelines, private insurers, HMOs and managed care plans typically do. The managerial techniques common to these providers (funders) help control prescription drug costs.

Control over doctor prescribing behaviour has also been trialled through drug budget holding. Drug budgets for GPs exist in France, Germany and the UK. In Germany, regional budgets for prescribed medicines were introduced in the early 1990s. Cost over-runs were to be deducted from doctors' fees. As Burstall and colleagues (1999) report, the effects were immediate and considerable, with a 17% reduction in drug volume and 24% reduction in

spending. However, the effects were not lasting as it was difficult to enforce collective sanctions. The scheme was replaced by indicative budgets for individual practices – doctors who exceed their budget by more than 15% are audited and those by more than 25% have to repay the excess or face delisting. GP budget holding was introduced in the UK in 1991. The incentive for doctors to participate was that any savings on drugs could be re-invested in the practice. Non-budget holders were also given budgets but these were indicative rather than formal, however, those exceeding these budgets were subject to review. The effects derived from budget holding on reducing pharmaceutical costs were however overwhelmed by other factors such as generic substitution. Budget holding was abolished on the grounds that it infringed the principle of equality by imposing group sanctions, and because doctors by being able to reinvest any savings were directly profiting from the scheme (Burstall et al, 1999; Senior, 2001). As Senior highlighted "should doctors have an incentive to prescribe cheaply and benefit financially at a later date?" A doctor's practice is an asset that a doctor expects to sell at some point in time.

Private health insurance also dominates the Canadian health system. Federal schemes for subsidising pharmaceutical costs are limited, for example, to the First Nations and Intuit, war veterans, members of Armed Forces and Royal Canadian Mounties (Productivity Commission, 2001). The provinces and territories operate their own schemes with varying arrangements and coverage to seniors and welfare recipients. Multiple payers finance prescription medicines in Canada, mostly insurance companies and employers as employee benefits. In 1995, 62% of prescriptions were funded by private plans, 19% by provincial plans, 7% both and 12% of Canadians were not covered (Productivity Commission, 2001). Over 20% of elderly Canadians have some form of supplementary private health insurance – elderly and welfare recipients are estimated to account for approximately 33% of total spending on prescribed medicines in Canada.

France provides a good example of a national social health insurance system. The main social insurance scheme covers employees and pensioners (and their families) and covers about 80% of the French population. It is funded through employer and employee contributions, patient copayments and taxes. Employers pay a levy of 12.8% of gross salaries and employees a levy of 6.8% of gross salaries. This contribution is similar to Australia's Medicare levy arrangements. General taxes contribute approximately 40% of health insurance funds. In addition, 87% of the population are members of voluntary, supplementary sickness funds or private health insurance funds. This cover subsidises out-of-pocket pharmaceutical expenses (Productivity Commission, 2001).

Some countries in Europe either allow or force their citizens to opt out of their social insurance systems and take their taxes and wage contributions with them to purchase private health insurance (Belien, 2001). This is similar to operating a sliding scale of reimbursement based on ability to pay, or means testing. Both Germany and the Netherlands operate such schemes. Germany allows citizens whose incomes exceed a threshold to opt out of the national sickness fund. These individuals are no longer required

to pay a percentage of their earnings to the sickness fund but they must purchase private health insurance. Over 10% of the German population have taken this option (Belien, 2001).

The Dutch social insurance system is similar but high income earners are legally excluded from statutory public health insurance. If these individuals want to have their pharmaceuticals reimbursed then they must hold private health insurance (ASI, 2001). The income threshold is lower than in Germany, with about a third of the Dutch population being privately insured. Private insurance is affordable to a larger proportion of the Dutch population because the high risk, very expensive health problems (so called catastrophic health care needs) are covered under a separate nationwide scheme - catastrophic health insurance is mandatory and is financed through income taxes (Belien, 2001).

Discussion

Increasing the involvement of private health funds through collaborative initiatives has the potential to bring additional resources into the reimbursement of pharmaceuticals which is unlikely to happen within the existing system (ASI, 2001). Increases in public expenditure can be achieved in two broad ways; first through higher taxes, and second by increasing health's (and in particular the pharmaceutical budget's) share of current levels of government expenditure i.e. by changing the priorities for public spending (or a combination of the two). Increasing taxes are not popular with voters and, as a number of stakeholders commented, this is very unlikely to happen. Increasing the pharmaceutical budget is also difficult as it requires strong political will to cut other areas of government expenditure (ASI, 2001). Where can funds be released? Again this is not a politically attractive option, and would need strong support from the electorate.

Under social insurance schemes, the majority of funding comes from payroll taxes levied on employees and employers. These taxes are set as a proportion of income and are independent of individuals' health risks. The advantage over income taxes is that these funds are explicitly tagged for health – the contributions don't get lost in general revenues. Usually, social insurance schemes have several competing funds which are separate from government and are non-profit organisations (ASI, 2001).

The economic argument for private sector involvement relates not only to cost-sharing but also to increasing consumer choice, responsiveness and price regulation through market competition. For consumers to demand, participate in and pay for private health insurance then the coverage the schemes provide has to be 'good', reasonably priced and give value for money. With a number of competing schemes, there is opportunity for differentiation through choice in premiums and coverage.

However, an important issue with mixed public-private drug reimbursement arrangements, in which the role of the private sector is extended, is the risk of developing an inequitable two-tiered system. One tier exists for individuals and families who can afford to pay twice

(once through income taxes and once through insurance premiums) and one tier for those who cannot afford to pay for private sector coverage. Individuals and families who cannot afford private health insurance therefore are limited in their choice of schemes and the levels of cover and subsidisation they can obtain for their pharmaceutical consumption.

Private health insurance policies currently provide for some reimbursement of pharmaceutical costs in Australia but limits are set very low and are unrealistic for most of the costs of these new biotechnology and oncology drugs. Health Funds could provide a valid alternative to the current PBS, with funding of prescribed medicines being collaboratively split between Health Funds and Government. It is assumed that Health Funds in part funding prescribed medicines would also implement mechanisms similar to those used by the PBAC, or outlined in the other options, to assess cost effectiveness, patient eligibility, copayment arrangements etc.

6 Conclusions

As one stakeholder aptly summarised "*beyond the initial listing, there are currently no effective methods of monitoring the use and outcomes of new agents on the PBS and nothing which would create a feedback loop to inform ongoing policy and decisions about the use of these agents in the field (as compared with controlled trials.) This is relevant to the concerns about "leakage". More involvement of the community (clinicians and patients) is required. Better use could be made of community processes (including Divisions of General Practice) to allow clinicians to monitor (peer review) the appropriateness and effectiveness of treatment using expensive agents. Some drugs which are subsidised are used in an unfettered way and consume too much of the PBS budget*".

However, providing patients with access to medically effective drugs at affordable prices is a challenging task for any society. The need for effective review of submissions to the PBAC has to be balanced against the urgency for drug access. The PBAC's reliance on cost-effectiveness as the principle measure for making recommendations means that access to effective but not cost effective medicines for certain patients is reduced. The ethical question is how far society has a duty of care for these patients, regardless of cost, even though the consequence is that money will not be available to care for other patients who stand to gain more in terms of health gain (Cookson, 2000).

The significant growth of new pharmaceutical and bio-medical techniques means that there is an increasing need "*to have good methods of making just and humane resource allocation decisions, especially in relation to pharmaceutical drugs*" (Harvey 2001). Limits to the amount that society is willing to pay for health care mean that in the future not all drugs that provide significant quality of life improvements will be able to be funded. Reducing the cost of drugs would be one way of making the budget go further, thereby delaying the time when tradeoffs have to be made. However, new biotechnology drugs and other innovative

oncological targeted therapies are often high cost treatments, and there is little room for manipulation in prices. The fact that the PBS is an open-ended scheme (i.e. there is no explicit budget constraint) has posed a fundamental problem because, over time, successive PBAC decisions have enabled manufacturers to infer a threshold price at which the government is willing to "purchase" more quality life-years (i.e. through price-volume arrangements, manufacturers of the more traditional small molecule drugs are better able to price their drugs so that they achieve a favourable cost-effectiveness result) (Viney 2001). The new biotech drugs have high cost-effectiveness ratios but what is the upper limit on the value of life? In the mid-late 1990s, some HIV/AIDS drugs were seen to be very costly, but the costs government feared did not eventuate - rather there were significant improvements in cost-effectiveness ratios as life was extended and affected individuals returned back into the workforce.

Cookson (2000) noted that industry representatives continued to argue that evaluation methodologies relied too heavily on clinical trials rather than wider sources of data and modelling; and that officials argued that trial-based evidence was easier to scrutinise for bias and potentially exaggerated claims of effectiveness. However, health economists continued to complain about the lack of requirement for standardised cost-utility evidence to make comparisons between disease areas. The most widely voiced criticism, however, was that the PBAC did not make evidence used in decisions publicly available nor did it have a public relations strategy for communicating the reasoning behind decisions to clinicians, patients and the wider public (Cookson, 2000). These findings were re-iterated by the stakeholders interviewed for this position paper.

Six possible funding options have been proposed here: a patient registry model; a clinical trials model; special funding arrangements approach; organisational change; differential drug subsidy arrangements (patient copayments), and cost sharing with third party payers. These are not mutually exclusive, each coming with advantages and disadvantages. It has not been possible, within the timeframe available to prepare the position paper, to cost these options. A cost-benefit analysis that would allow comparison of the expenditure required to implement each of these six options versus the benefits gained is a next step in the way ahead. Such an analysis would provide further key input into an informed decision and policy-making process on the future of the PBS. A main point of contention remains the discrepancy between the cost-effectiveness figures produced by the sponsors (predominantly the pharmaceutical companies but also health professional and consumer groups) of these high cost biotech and other targeted therapies, and those generated or believed by Government (either the PBAC, PBPA, or Departments of Health and Ageing, and Finance and Administration). A comparative study of the costs put forward by the companies, by government, and of the actual costs that eventuate once drugs are listed either within or outside PBS arrangements — and why differences may exist between these three sets of figures — also would go a significant way in helping to resolve difficulties being encountered in getting these new drugs listed on the PBS.

Essentially, there are two basic sets of issues that need to be addressed in discussing the funding of pharmaceuticals. The first is ensuring equity of access to drugs at affordable prices to those in clinical need. This debate centres on 'controlling' access and cost - ensuring individuals in need are not deprived of safe and efficacious drugs that are available on the world market but, at the same time, minimising the risk of the two main problems currently affecting the PBS — namely, leakage where drugs are prescribed for a wider range of indications and patient populations than those listed on the PBS, and waste through either the continuation of therapy when no objectively measurable or worthwhile improvement has been achieved in response to the therapy, or the over-supply of medications. The first four of the six models outlined above address this first set of issues. They are proposed within the existing contextual funding framework as mechanisms operating either within or outside the PBS.

However, as a number of stakeholders voiced, these models and the first set of perhaps more practical issues need to be located within the wider public debate of 'How much is Australia prepared to pay for pharmaceuticals, who should pay, and what drugs do Australians want subsidised?' However, public utility options, such as 'the greatest good for the greatest number', are not without their problems as illustrated by the Oregon Medicaid experience.

It is generally agreed that the PBAC has an unenviable task. In many ways, this Committee has become the custodians of part of the public health budget. Is this fair or reasonable? Many of the difficulties encountered by the PBAC and Industry may lie with the fact that the Committee has to balance a number of competing tasks. Would decisions on listing be different if, for example, the current climate of economic rationalism, limited budgets, cost containment and avoiding cost blow-outs at 'all cost' were not so prevalent? As one stakeholder commented "*the PBAC has been made responsible for managing the growth of the pharmaceutical budget but this is outside 'a whole of government approach' to public spending. The PBAC is doing a good job given that they have to work with a set budget*".

Several stakeholders believed that the PBS was not in [financial] 'crisis' and that the total pharmaceutical budget as a proportion of either government expenditure or GDP was relatively small on an international scale. Australia has been very successful in securing low prices for the purchase of its pharmaceuticals. However, the debate needs to be had as to the extent Australia is prepared to pay for these new drugs as well as for existing items, and how our society might meet these costs.

This broader debate introduces options five and six (increasing the financial contribution from patients through new copayment arrangements and increasing the role of third party payers via health insurance). Both these approaches involve wider implications for society in terms of cost-sharing and in particular cost-shifting away from government. In the context of this broader debate, there are at least two other economic options available to the Australian society:

- the community at large could decide there should be re-direction and re-allocation of existing government resources to support the pharmaceutical budget; and
- an income based levy similar to Medicare could be introduced to quarantine funds to pay for medicines 'wanted' by the Australian population.

These options fall outside the scope of the position paper, but they represent fundamental economic alternatives that need to be placed on the public agenda for open discussion as to the future of the PBS and the best way forward.

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APPENDICES

A Correcting susceptibility patterns with new drugs

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www.abc.net.au/rn/talks/bbing/stories/s444193.htm,

p 7 of 12.

"This whole business of genetics and knowing susceptibility patterns, and possibly being able to do something about them, has enormous cost implications. Let me describe the sort of experiment that's being done in a lot of labs right now. Remember we're in Australia and the United States if 15 hours behind us. Cells are taken say from a tumour and from adjacent normal tissue. These experiments are being done here as well as in the US and in Europe. You extract the messenger DNA from the tumour, and then you interrogate for the gene chips. …. After some sophisticated computer analysis and the help from people who are specialising in the new science which is called informatics, we learn which elements of the DNA are expressed in the cancer but not in the normal cell. This may lead us to the identification of a defective protein or protein pathway. Something's broken, maybe the capacity of a regulatory protein to bind to another protein that regulates cell division. We're thinking about cancer. Cancer is basically a disease of unregulated cell division. We can't stop the cells dividing, they keep dividing, they get bigger and bigger and so forth. If we found that defect, if we could identify the protein that's defective, then we could take the normal protein and the other protein and make large quantities of them, see how they fit together. The way we'd see how they fit together is we'd get a protein chemist to grow us up a lot of protein, and then we would go to a crystallographer who would crystallise the structure, the way the two proteins fit together, then he'd put it into a synchrotron. ….. Then the crystallographer could tell us what sort of structure between these two proteins. We might be able to mimic, say with a small molecule that could do the same job. So instead of having two whopping great proteins coming together we could get a little molecule that would fit in that site and do the job with the other protein, and ***that's what we call a small molecule mimic, or what we'd call a drug. And if we can make that synthetic drug, then we're starting to think about a new treatment for this thing that maybe will kill the tumour or block the tumour.***

B Structured Interviews With Stakeholders

B.1 List of Participants

D. Baxter	Chief Executive Officer, Australian Federation of AIDS Organisations, Sydney
M. Blackmore	Executive Director, Consumers' Health Forum of Australia, Canberra
Dr F. Boyle	Medical Oncologist, Royal North Shore Hospital, Sydney
Mr P. Cross	Pharmaceutical Industry Adviser, Minister of Health, DHA, Canberra
Prof R. Day	Director, Clinical Pharmacology & Toxicology, St Vincent's Hospital, Sydney
Mr A. Evans	Chief Executive Officer, Australian Pharmaceutical Manufacturers Association, Canberra
L. Fong	Director of Biotrax Division, Schering Plough Pty Ltd, Sydney
Prof P. Glasziou	Centre for General Practice, University of Queensland
Dr J. Hyde	Director, Health Policy Unit, Royal Australian College of Physicians, Sydney
Dr D. Kingston	Medical Director, Roche Products Pty Limited, Sydney
B. Kirkham	Chief Executive Officer, Arthritis Australia, Sydney
A. Kolivos	Health Outcomes Manager, Wyeth Australia Pty Ltd, Sydney
Assoc. Prof. G. Littlejohn	Director of Rheumatology, Department of Medicine, Monash Medical Centre, Monash University, Melbourne
A. McEvoy, AM	Managing Director, Australian Crohn's and Colitis Association, Melbourne
Assoc. Prof. A. Mant	School of Public Health and Community Medicine, University of New South Wales, Sydney
L. Swinburne	National Co-ordinator, Breast Cancer Network Australia, Melbourne
Dr J. Thomson	Acting Medical Director, Health Services, Australian Medical Association, Canberra
V. Toulkidis	Health Policy Unit, Royal Australian College of Physicians, Sydney
C.Ward	Policy Analyst, Australian Federation of AIDS Organisations, Sydney
M. Wonder	Health Economics Manager, Novartis Pharmaceuticals Australia Pty Ltd, Sydney

Several Stakeholders wished to remain anonymous

B.2 Information and Consent Form

UNIVERSITY OF CANBERRA

NATSEM
National Centre for Social and Economic Modelling

Director: Professor Ann Harding

Funding High Cost Biotechnology and Other Innovative Targeted Therapies under the Pharmaceutical Benefits Scheme

Information and Consent Sheet

Introduction

The current Pharmaceutical Benefits Scheme is under increasing pressure to fund new high cost biotechnology and other innovative targeted therapies for the prevention and treatment of previously unmanageable diseases. In most cases they represent major advances in prevention and treatment. Interviews are being conducted by staff of the National Centre for Social and Economic Modelling (NATSEM) of the University of Canberra and Med-E-Serv with key stakeholders to obtain input into a position paper on this issue. The aim of the position paper is to outline possible options for the funding of these new drugs under either current PBS mechanisms or new or modified supply arrangements. The position paper will be presented for discussion at a stakeholders' forum scheduled for early March 2002. Please note that there is no intention for the position paper or the stakeholders' forum to undermine Medicare or the Pharmaceutical Benefits Scheme.

We wish to canvass your views on topical issues, problems and possible solutions to the equitable and affordable funding of these new drugs. NATSEM does not have a position as to whether or not these new high cost biotechnological and other targeted drugs should be included on the PBS. Although not necessarily the views of NATSEM, we are however assuming for the purposes of the position paper and as a starting point that difficulties are being encountered in getting these new drugs PBS listed. If you have any inquiries about the research or any concerns regarding the way the research is or has been conducted, please contact Professor Ann Harding, Director NATSEM (02 6201 2780) or Dr Laurie Brown, Senior Research Fellow NATSEM (02 6201 2770).

Consent

I understand that my participation in this research is voluntary, I am free to refuse to participate and I am free to withdraw from the interview at any time. My refusal to participate or withdrawal of consent will not affect my involvement in this project or in the forum in any way.

I understand that the data collected from my participation may be used for the position paper. I consent for it to be used in this manner, subject to my review and approval of the text derived from this interview.

Signed ..... Date ...../...../.....

Name (please print) .....

Postal Address: NATSEM University of Canberra ACT 2601 Australia Location: 170 Haydon Drive BRUCE ACT 2617
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B.3 Interview Questions

Funding High Cost Biotechnology and Other Innovative Targeted Therapies under the Pharmaceutical Benefits Scheme

Structured Interview Framework

NOTE: Not all questions below may be applicable to your background and interests.

1. Disease-drugs

Specify disease/health problem and related high cost biotech drug(s) if appropriate.

2. What Concerns-Problems with PBS?

What do you perceive are the main problems in getting these new drugs PBS listed?

What's different about these drugs to traditional small molecule medicines that makes it difficult to them get subsidised?

What are your perceptions about the cost of these drugs and what factors have shaped those perceptions?

How would you define "cost-effective"? Do you think these drugs are cost-effective?

What economic data are available on these drugs? Do these data deal mainly with short term cost-effectiveness vs long term benefits?

What are your views on the quality of the empirical clinical data? Are there problems with the randomised control trial study methodology and results (from perspective of PBAC and cost-effectiveness)?

In your view, would having quantitative data on long term cost effectiveness and quality of life issues (if it does not exist) make any difference to the chance of getting these drugs subsidised?

What are your views on how these drugs should be priced?

In your opinion, would lowering the price make any real difference to the likelihood of getting the drug subsidised?

What general criteria should be used for assessing whether or not a drug should be listed on the PBS? Would you please rank these criteria in order of importance.

3. What Possible Solutions?

Do you have any suggestions on possible mechanisms to overcome current problems?

a) within PBS system

b) outside PBS – new arrangements

What are your views on controlling and monitoring

a) doctor prescribing behaviour

b) patient eligibility

How willing are consumers to pay for these new therapies? e.g.

a) pay higher copayments for these medicines

b) pay higher taxes (income, Medicare etc) to fund PBS

c) income-tested: subsidised on the basis of ability to pay

Are trade-offs possible? What would you forego to have these new drugs PBS-listed (if anything)?

4. Size of the Problem

How many individuals are likely recipients of these particular drugs (size of target population)? and as a proportion of all persons with disease/health problem?

How successful is screening/identification of the target population?

What is the annual treatment cost per patient and likely total costs?

C Highly Specialised Drug Program Under The PBS

C.1 Role of Highly Specialised Drugs Working Party

The Highly Specialised Drugs Working Party (HSDWP) was established to consider issues relating to the provision of drugs under the Highly Specialised Drugs Program and to provide subsequent advice to the Australian Health Ministers' Advisory Council (AHMAC) and the PBAC. It contains representatives from the Commonwealth and Health Departments of each State and Territory, with the Commonwealth as chair.

The HSDWP is not a technical committee but considers the policy and administrative aspects of the supply of certain specialised drugs through the hospital system.

The role of the HSDWP is to:

- identify drugs which might be suitable for funding under the Highly Specialised Drugs arrangements and provide supporting information and advice to the PBAC;
- provide advice to the PBAC about applications made directly to the PBAC for supply as Pharmaceutical Benefits under these specialised supply arrangements;
- monitor new drugs which potentially might come under the funding arrangements;
- monitor the quality use of drugs supplied under these arrangements; and
- investigate and make recommendations on procedures to monitor drugs supplied by public hospitals under the HSD arrangements to patients in community settings.

C.2 Procedures for Adding a New Drug or Varying a Current Listing

Drugs are listed for subsidy under this program following recommendations by the Highly Specialised Drugs Working Party (HSDWP) and the Pharmaceutical Benefits Advisory Committee (PBAC) and approval by the relevant Federal Ministers.

Applications considered by the HSDWP must address the criteria for selection and provide a summary of the drug similar to the executive summary provided with the PBAC submission. Where possible, all applications are to be discussed in a 'face to face' meeting, or a teleconference, of the Working Party prior to the PBAC consideration. For an application to be recommended to the PBAC it must be supported by the majority of the Working Party members. The process of incorporating new drugs into the Highly Specialised Drugs arrangements is identical to the process for general benefits listing, with two exceptions. The HSDWP must support the listing of each application, and for public

hospitals the States and Territories must also agree to the Commonwealth's offer of subsidy, prior to the drug being available in that State or Territory.

Sponsors of applications should also be aware that many HSDs have significant in-patient and associated costs that are met by the States and Territories. In cases, where there are likely to be significant costs to the States it is in the interest of the sponsor to provide costings of the likely in-patient costs and any costs of administering or monitoring the product. State and Territory Governments would need to assess the financial impact versus the patient benefit prior to agreeing to the Commonwealth's offer of subsidy should the drug be approved.

Once the recommendation supporting an application has been forwarded to the PBAC the application and approval process is the same as other Pharmaceutical Benefits. The criteria for selection of Pharmaceutical Benefits are contained in section 7 of this document. Applications to list or vary HSDs may also be lodged with the PBAC prior to HSDWP consideration to assist in timely consideration. In these cases the HSDWP would assess suitability to the HSD criteria following PBAC consideration.

Following recommendations for listing from both the HSDWP and the PBAC the product is then considered by the Pharmaceutical Benefits Pricing Authority (PBPA) for negotiation of an agreed price between the Commonwealth and the supplier. If an agreed price is mutually acceptable then the recommendation is sent to the Federal Ministers for Health and Finance for their approval. In circumstances where the annual expenditure for the new listing exceeds $10m the Federal Cabinet must also approve.

Once Ministerial/Cabinet approval is granted, drug assay and packaging requirements are finalised and the States and Territories accept the Commonwealth's offer of subsidy then the drug is included under the supply arrangements for HSDs. The Commonwealth and the States and Territories have agreed that there be a one month advance notice provided to the States and Territories once approval is granted. This is to allow time for advice to be disseminated to hospitals and appropriate arrangements be put in place. HSD subsidy commencement is determined by the publishing timetable of the Schedule of Pharmaceutical Benefits.

The current Commonwealth policy precludes listing products dually as General Benefits and as Highly Specialised Drugs where the approved indications are the same. Where the indications for subsidy differ then it is possible to have a product listed in the general schedule and under the HSD program.

Source: TGA HSD Industry Document, 2001

D Lifesaving Drugs Scheme (PBS Alternative Supply Arrangements)

Criteria And Conditions Applied To Request For Financial Assistance For Access To Expensive Lifesaving Drugs Not Available As Pharmaceutical Benefits

CRITERIA

Financial assistance for access by an individual to a particular expensive lifesaving drug may be approved where a Senior Medical Officer of the Department of Health and Aged Care confirms that:

1. There is a rare but clinically definable disease for which the drug is regarded as a proven therapeutic modality, i.e. approved for that indication by the Therapeutics Goods Administration.

2. In epidemiological studies, the disease has been associated with a significant shortening of expected age-matched lifespan for those suffering from the disease and there is evidence to expect that a patient's lifespan will be extended as a direct consequence of the use of the drug.

3. A patient with the disease can be identified with reasonable diagnostic precision.

4. The patient should not be suffering from any other medical condition, including complications or sequelae of the primary condition, that might compromise the effectiveness of the drug treatment.

5. The drug must have been accepted by the Pharmaceutical Benefit Advisory Committee as clinically effective, but rejected for Pharmaceutical Benefits Scheme (PBS) listing because it failed to meet the required cost effectiveness criteria.

6. There is no alternative drug listed on the PBS or available for public hospital in-patients which can be used as lifesaving treatment for the case under consideration.

7. There is no alternative therapeutic modality (e.g. surgery, radiotherapy) which is recognised by medical authorities as a suitable and cost effective treatment for this condition.

8. The cost of the drug, defined as the cost per dose multiplied by the expected number of doses in a one year period for the patient, would constitute an unreasonable financial burden on the patient or his/her guardian.

9. The patient must be an Australian resident who qualifies for Medicare.

10. Where required, the patient must satisfy also any other specific criteria which may relate to a particular disease under these arrangements.

CONDITIONS

1. Financial assistance will only be provided where the patient agrees to participate in the evaluation of efficacy of the treatment by periodic medical assessment as directed.

2. If, depending on the natural course of the disease, there is no evidence of

a. substantial clinical improvement in the patient, or
b. stabilisation of the patient's condition

as assessed not later than 12 months after commencing therapy with the subsidised drug, then the patient's continued eligibility for financial assistance under these arrangements will be reviewed.

3. Where the patient fails to comply adequately with treatment or measures taken to evaluate the effectiveness of the treatment, financial assistance under these arrangements will be withdrawn.

4. Financial assistance will be provided to cover only the cost to the Commonwealth for the purchase of the drug from the approved sponsor at a price to be satisfactorily negotiated by the Commonwealth with the sponsor according to guidelines established by the Pharmaceutical Benefits Pricing Authority. Where appropriate, the price may include a factor for importation and transportation of the drug by the manufacturer direct to the place of administration to the patient. Benefits under this arrangement are not payable for costs associated with other transport, storage or administration, or any other hospital or medical expenses associated with the use of the drug or the management of the disease.

Source:
Department of Health and Aged Care

URL: http://www.health.gov.au/pbs/supply/criteria.htm

E HSDs Program - Public Hospital National Expenditure, 2000/2001

Note: Private hospital expenditure up until 31 October 2000 are included in these figures

Drug Name	Total Cost
ABACAVIR SULFATE	$4,089,663
APOMORPHINE HYDROCHLORIDE	$372,248
AZITHROMYCIN	$167,751
BACLOFEN	$272,609
CIDOFOVIR	$43,200
CLARITHROMYCIN	$212,791
CLOZAPINE	$22,076,291
CYCLOSPORIN	$29,801,567
DELAVIRDINE MESYLATE	$179,473
DESFERRIOXAMINE MESYLATE	$4,344,244
DIDANOSINE	$4,003,742
DISODIUM PAMIDRONATE	$11,530,979
DORNASE ALFA	$6,571,100
DOXORUBICIN HYDROCHLORIDE	$203,338
EFAVIRENZ	$3,164,653
EPOETIN	$48,793,333
FILGRASTIM	$23,165,716
FOSCARNET SODIUM	$63,201
GANCICLOVIR	$1,689,077
INDINAVIR SULFATE	$4,426,817
INTERFERON ALFA-2a	$773,019
INTERFERON ALFA-2b	$4,461,819
INTERFERON GAMMA-1b	$402,569
LAMIVUDINE	$9,346,914
LAMIVUDINE AND ZIDOVUDINE	$11,369,864
LENOGRASTIM	$2,068,449
MYCOPHENOLATE MOFETIL	$8,708,271
NELFINAVIR MESYLATE	$5,032,450
NEVIRAPINE	$6,889,846
OCTREOTIDE	$1,591,115
OCTREOTIDE ACETATE	$6,990,150
RIBAVIRIN & INTERFERON ALFA-2b	$4,524,733
RIFABUTIN	$116,633
RITONAVIR	$1,877,362
SAQUINAVIR MESYLATE	$3,092,935
STAVUDINE	$13,418,240
TACROLIMUS	$6,227,763
VALACICLOVIR HYDROCHLORIDE	$393,851
ZALCITABINE	$242,496
ZIDOVUDINE	$1,201,317
TOTAL	**$253,901,588**

Source: TGA - PUBLIC HOSPITAL NATIONAL EXPENDITURE REPORT - FINANCIAL YEAR 2000/2001

F Herceptin – Patient Eligibility

Eligible patients are Australian Residents, persons eligible under the Reciprocal Health Care Agreements (RHCA), and Department of Veterans' Affairs entitlement holders who are eligible under the following criteria:

- for the treatment of HER-2 positive patients with metastatic breast cancer, in combination with taxanes for patients who have not received chemotherapy for metastatic disease; or
- for the treatment of HER-2 positive patients with metastatic breast cancer, as monotherapy for the treatment of those patients who have received one or more chemotherapy regimen(s) for metastatic disease.

In patients who have either:

a) immunohistological evidence of HER-2 protein at the 3+ level; or

b) immunohistological evidence of HER-2 protein at the 2+ level, subsequently confirmed as exhibiting HER-2 gene amplification by fluorescence *in situ* hybridisation (FISH);

c) exhibiting Her-2 gene amplification by fluorescence *in situ* hybridisation (FISH).

Patients who show immunohistological evidence of HER – 2 protein at the 1+ level or less and who subsequently test positive to the FISH test will not be considered eligible under the Herceptin program criteria.

Source: HIC, 2001, *Herceptin.* www.hic.gov.au/CA2568D90003F3AF/page/Forms-Herceptin?OpenDocument&1=18-Forms~&2=45-Herceptin~&3=~