

## **Key Amendments to the PFPA and Issues Raised in Consultation**

### **Key Amendments to the PFPA**

Key methodological amendments to the PFPA, approved by the PHARMAC Board, include the discount rate used when undertaking cost utility analysis (CUA) and the range of costs to be included in CUAs.

#### **1. *Discount rate***

PHARMAC's discount rate has been used consistently for investment decisions to assess both the budgetary impact and relative cost-effectiveness of decisions.

PHARMAC's discount rates undergo scheduled consideration annually by the PHARMAC Board, and had been set at 10% for the past few years until recently. In June 2005, the discount rate was reduced to 8%, following information that the capital charge to government departments, including District Health Boards had been reduced to that level. This and previous rates applied to both budget impact analysis and cost-utility analysis.

PHARMAC's use of the 10% (becoming 8%) discount rate was also the source of considerable debate amongst the health sector. This had included high-profile debate in public forums (at conferences and in the New Zealand Medical Journal) questioning the rationale and appropriateness of PHARMAC's use of the 8-10% discount rate in its cost-utility analyses.<sup>1 2 3</sup>

#### **PHARMAC View**

PHARMAC staff met on a number of occasions to discuss the different approaches for determining the discount rate – the social rate of time preference, social opportunity cost, weighted average of social discount rate, shadow price of capital, and 'bottom up' approach.

PHARMAC staff considered that the social opportunity cost rate (i.e. current market cost of capital) was not appropriate as it is likely that the discount rate in the public sector is lower than that in the private sector (if it was not there would be no need for government provision of health care and private insurance markets would be more dominant). It was also noted that applying the current market cost of capital to benefits is difficult to justify. These arguments also apply to the other approaches of determining the discount rate (weighted average of social discount rate, shadow price of capital, and 'bottom up' approach) as they all use variations of the cost of capital.

PHARMAC staff therefore agreed that the social rate of time preference was the most relevant approach for PHARMAC as it reflects social preferences not just financial sector considerations. It was noted that the long-term government bond rate is often used an

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<sup>1</sup> Milne R. Valuing prevention: discounting health benefits and costs in New Zealand. N Z Med J. 2005 May 6;118(1214):U1443. <http://www.nzma.org.nz/journal/118-1214/1443/> PMID: 15886738

<sup>2</sup> Metcalfe S, Brougham M, Moodie P, Grocott R. PHARMAC responds to Richard Milne on discounting health benefits and costs. N Z Med J. 2005 Jul 29;118(1219):U1600. <http://www.nzma.org.nz/journal/118-1219/1601/> PMID: 16059415

<sup>3</sup> Milne R. Richard Milne responds to PHARMAC on discounting future health benefits and costs. N Z Med J. 2005 Aug 12;118(1220):U1620. <http://www.nzma.org.nz/journal/118-1220/1620/> PMID: 16132078

approximate for the rate at which society is willing to exchange present for future consumption.

PHARMAC staff considered whether it was more appropriate to adjust the discount rate for risk and therefore whether to use the risk-free or risk-adjusted long-term government bond rate. It was noted that PHARMAC currently uses a risk-adjusted rate. The main argument for using a risk-adjusted rate was that it reflects the risk of the investment and the compensation for covering this risk (e.g. risk of an uncertain future). However this risk can be managed by including higher costs and/or lower benefits in the sensitivity analysis, and it was considered that it was inappropriate to use the discount rate to compensate for this risk.

PHARMAC staff therefore considered that the discount rate should not be used to compensate for the risk associated with an investment, and that it is more appropriate for risk to be taken into account in the sensitivity analysis by varying the model inputs.

The draft version 2 of the PFFA therefore recommended that the discount rate used for cost-utility analysis should be based on the five-year average real risk-free long term (10 year) government bond rate (3.5%).

### Consultation Responses

PHARMAC consulted on the proposal to reduce the discount rate to 3.5%. There was wide support for the proposed discount rate (3.5%) from economists, pharmaceutical suppliers, and the government sector.

### Amendments to the PFFA

All costs and benefits in CUAs will now be discounted based on the five-year average real risk-free long-term government bond rate, and the PFFA recommends that a rate of 3.5% be the base rate used over the next five to ten years.

Rates of 0%, 5%, 10% will be included (without exception) in sensitivity analyses to enable comparison with analyses undertaken in other countries (5%), past PHARMAC analyses (10%), and the impact of the discount rate (0%).

Importantly, the PFFA also stresses that the discount rate for budget-impact analyses (BIA) will not be adjusted, but rather will remain at the risk-adjusted rate (8%). The main reason why PHARMAC considers that different rates may be required relates to the treatment of risks, the importance of capital costs and inflation:

- BIA focuses on the financial aspects of proposals within a limited timeframe (usually 1-5 years) and is used to determine if PHARMAC can afford to fund a treatment given the current budget. Investment decisions are often associated with substantial uncertainty even in the short term – within the next few years pharmaceutical prices may decrease or PHARMAC's budget may change. With an uncertain future (and the associated risks), it is therefore reasonable that a higher discount rate be used. This is particularly the case when forecasts indicate that PHARMAC has very tight budget constraints.
- CUA differs in that it is not used to make an investment decision, but rather to determine the relative ranking of pharmaceuticals. It therefore is not considered necessary to capture the risk in the discount rate. In addition, CUA is not purely a financial analysis, but also involves the quantification of health benefits. In some cases significant health benefits occur in the future (for example, with childhood

immunisation), in which case a lower discount rate is necessary for these benefits to be realised in the results of the analysis .

- Equally, while CUA evaluates real costs and benefits, BIA focuses on actual (i.e. nominal) expenditure. Furthermore the capital costs have no obvious relationship to benefits, but a strong significance to any budget decision.

## **2. Estimating costs – inclusion of generic pharmaceutical prices**

Historically the price of pharmaceuticals included in CUAs has not included the lower price of generic pharmaceuticals that may be introduced in the future. This was because PHARMAC has used a relatively high discount rate, hence lower future prices would have had little impact on the CUA result.

However, with the change to the discount rate, it was considered that the lower prices that PHARMAC is able to receive when generic pharmaceuticals are introduced should be included in cost-utility analyses in order to represent the true cost of the pharmaceutical. This is especially important when there is only a short length of patent life remaining.

### Consultation Responses

The proposal to include generic pharmaceutical prices in CUA was not supported by Pharmaceutical Suppliers. They did not consider this proposal to be feasible and considered that it would require many assumptions regarding whether a generic substitute would be available, the contractual arrangements and by how much the price would change (particularly for biologicals and products where no generic is anticipated).

A reviewer also considered that including future expected prices adds additional uncertainty and complexity to the analysis. He considered that the pharmaceutical appraised should be judged on its own merit, and sensitivity analysis used to model the future effects of generics.

### PHARMAC View

PHARMAC staff noted that including generic prices would favour pharmaceuticals where prices are expected to decrease within the next few years, compared with those pharmaceuticals where a generic is unlikely to be available (or unlikely to be available for some time). PHARMAC staff considered that this information needs to be included in cost-utility analyses, as it is more likely to reflect the true cost-effectiveness of a pharmaceutical. However, the estimates would need to be conservative (both in timing and amount) to allow for the risk of generic entry being significantly delayed.

### Amendments to the PFFA

The PFFA has been amended to recommend the following:

*“When calculating pharmaceutical costs, consideration should also be given to the length of the pharmaceutical patent and time until a generic pharmaceutical is likely to become available. It is recommended that in cases where the patent expiry is within 10 years from expected date of pharmaceutical funding, the expected time and price reduction from a likely generic pharmaceutical should be included in the analysis. If the patent expiry is after 10 years from expected date of funding, a conservative proxy should be used for the estimated time until the introduction of a generic pharmaceutical and subsequent price reduction (e.g. 25 years until expiry and 70% price reduction with introduction of generic)”.*

### **3. Costs included in CUAs – direct patient healthcare costs**

To date the costs included in CUAs have been restricted to direct health sector costs (i.e. those paid for by District Health Boards). However, direct patients costs are 'real' costs and it is also one of PHARMAC's decision criteria.

#### Consultation Responses

The majority of consultation responses supported the proposal to include direct patient healthcare costs in CUAs. However several considered that PHARMAC's definition of direct patient costs was too restrictive. Additional costs that were suggested included travel and accommodation costs to attend hospital or specialist services (these are paid for by the government or the patients depending on distance and number of specialist visits); physiotherapy and rehabilitation costs (Accident Compensation Corporation (ACC) fund many rehabilitation programmes); time lost in receiving treatment (if likely to be significant); and non-subsidised pharmaceuticals funded by ACC.

#### PHARMAC View

PHARMAC staff discussed in detail whether CUAs should include direct patient healthcare costs. It was noted that direct patient costs are one of PHARMAC's decision criteria, and therefore should be considered. It was also noted that including the full patient cost of GP visits (as opposed to the cost to government) is more likely to represent the true cost of GP time.

It was also considered appropriate that the cost of home and continuing care (rest home or private geriatric/psychogeriatric care) be included in CUAs, independent of who is paying for this service (i.e. the family, DHB, ACC, or Ministry of Social Development). This cost is often paid directly by the DHB (hence is a cost to the health sector), and is an appropriate proxy cost for the disutility associated with having home care.

PHARMAC staff also discussed whether any additional costs should be included above those already specified. It was noted that direct patient costs included in CUAs are restricted to health sector costs (i.e. Vote: Health), as this is consistent with PHARMAC's decision criteria. This means that costs paid by ACC (such as rehabilitation and physiotherapy) are outside the scope of PHARMAC analyses.

#### Amendments to the PFFPA

All CUAs will now include direct patient healthcare costs. These costs should be restricted to healthcare costs that government partially subsidises, and should be based on the cost to government plus the additional cost to the patient. These costs include General Practitioner visits, pharmaceutical co-payments, and home or continuing care.

#### **4. Review of clinical evidence**

In November 2006 PHARMAC staff organised for Professor Rod Jackson (Professor of Epidemiology, University of Auckland) to provide further training in advanced critical appraisal. As a result of this training PHARMAC staff considered that the use of further critical appraisal tools, such as GATE (Graphic Appraisal Tool for Epidemiology)<sup>4</sup> should be encouraged more widely.

The GATE framework involves the following five steps:

1. asking focused questions based on PECOT (population, exposure, comparison, outcome, time);
2. searching the literature for best available evidence;
3. appraising the study by 'hanging' on the GATE frame to determine study validity and quality of the evidence using RAAMbo (representativeness, allocation, adjustment, accountability, measurement, blinding and objectivity);
4. assessing study quality; and
5. applicability of evidence in practice.

#### PHARMAC View

PHARMAC staff considered that the use of GATE should result in improved consistency between evaluations of the clinical evidence, and also ensure that all key issues are considered in a systematic manner when critiquing a clinical trial.

#### Amendments to the PFFA

The revised version 2 of the PFFA recommends the use of GATE, and also contains substantially more information on the data sources for deriving relative clinical efficacy, and obtaining and assessing clinical data.

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<sup>4</sup> Jackson R, Ameratunga S, Broad J, Connor J, Lethaby A, Robb G, Wells S, Glasziou P, Heneghan C. The GATE frame: critical appraisal with pictures. *Evid Based Med.* 2006 Apr;11(2):35-8. <http://ebm.bmj.com/cgi/content/full/11/2/35>

## **Key Issues Raised in Consultation**

The key issues raised in consultation (in addition to the issues noted previously) are outlined below.

### ***1. Measuring quality of life – health-related quality of life instrument***

For the past six years PHARMAC has used the New Zealand EQ-5D utility weights to measure changes in health-related quality of life (HR-QOL) associated with a new pharmaceutical. Advantages of the EQ-5D include the fact that it is the most widely used and validated instrument internationally, there are weights available that are specific to the New Zealand population (hence representing health state preferences of New Zealanders), and its validity and reliability has been established in the Maori population.

However, it is a coarse scale (5 dimensions of health and 3 levels of ability/impairment), and is often unable to measure small changes in quality of life such as those that result from side-effects. PTAC was concerned with the weight PHARMAC placed on the New Zealand EQ-5D utility weights; in particular whether the results were representative of the general population (including Maori and Pacific patients) and the significant limitations associated with the EQ-5D.

### **Consultation Responses**

There was also substantial feedback from consultation on the recommended HR-QOL instrument. Responders had mixed views on which was the most appropriate instrument to use. However, overall the majority supported the use of an instrument where NZ preferences are available (the EQ-5D), but requested that PHARMAC further investigate the use of other instruments.

The main concerns regarding the EQ-5D included:

- lack of sensitivity to detect changes in some conditions (especially towards the ceiling of full health);
- it is deficient in aspects of mental health as it does not include cognition;
- use of Visual Analogue Scale rating of health states – these do not reflect society preferences as they do not require individuals to make trade-offs between quality of life and survival (this trade-off is considered using other rating scales);
- small sample size; and
- it does not explicitly consider impact of disability.

The main reasons given for supporting the use of the EQ-5D included:

- NZ weights are available;
- simplicity;
- wide use (used in approximately 48% of published CUAs).

Several suggestions were given for other HR-QOL instruments that PHARMAC could consider. These included the following:

- SF-6D/SF-36 – based on an algorithm that converts the scores of the SF-36 and SF-12 into utility scores. Advantages include a large number of health states and studies, and that it is widely used in research (including in New Zealand). Disadvantages include the fact that the worst surviving health state is 0.35 before death, and that the preferences are those of the UK population (weights are currently being developed for the Australian population). PHARMAC staff were particularly concerned about the small range in which the SF-6D weights varied (for poor health

states the SF-6D was consistently higher compared with the EQ-5D, and for healthier states the SF-6D tends to be lower than the EQ-5D). This would disadvantage pharmaceuticals where the sole benefit was improvements in quality of life. Even though an advantage of the SF-6D was that it has 6 levels within each dimension, as PHARMAC has tended to use mid-values of the EQ-5D in the recent past, in effect this means that the EQ-5D has 5 levels within each dimension.

- HUI3 – this is a widely used instrument, is comprehensive, includes cognition, and is more sensitive to detecting moderate changes in health. However it is also complex and utility weights have not been developed for the New Zealand population.

### PHARMAC View

PHARMAC staff considered that other instruments for measuring HR-QOL should be further reviewed. However, until a better instrument is available, PHARMAC staff recommended that changes in HR-QOL should continue to be measured using the New Zealand EQ-5D utility weights, with allowance for the use of other instruments providing their use is well justified.

### Amendments to the PFPA

No further amendments on this issue have been made to the PFPA from the earlier draft of version 2 that was circulated for consultation. However, PHARMAC staff are seeking ongoing further advice on the methodological differences in the various HR-QOL measurements, and the use of Time Trade-Off methodology compared with Visual Analogue Scale and Standard Gamble methodologies.

## **2. Measuring quality of life – mapping health states**

PHARMAC staff usually obtain utility values for input into cost-utility analyses through a process of mapping health states to the EQ-5D. The mapping is usually done by several (blinded) staff members and/or clinicians. The main reason PHARMAC staff have used this technique (as opposed to conducting a survey of patients, clinicians, and the general population) is due to time constraints. In cases where the results of analyses are shown to be sensitive to the utility values, further work is undertaken to obtain more accurate values.

### Consultation Responses

The method PHARMAC uses for mapping health states was criticised by one respondent who considered that this process is unacceptable. They considered that patient-derived weights from clinical trials should be the preferred data source, and if that is not available, the next preferred source would be expert panels of relevant health professionals.

### PHARMAC View

The main problem with using patient-derived weights is that they are not representative of the general population. Patients have a higher tolerance for a health state, and their focus is on how much their quality of life improves (as opposed to the valuation of avoidance of disease). The use of patient-derived utility values would therefore be less likely to favour a pharmaceutical. Clinical trials do however provide useful information regarding how many patients are in each health state with and without the pharmaceutical intervention.

### Amendments to the PFPA

No further amendments on this issue have been made to the PFPA from the earlier draft of version 2 that was circulated for consultation. However, PHARMAC staff are currently investigating options for improving the mapping of health states, including the creation of a database of health states and utility values.

### **3. Estimating costs – deflation of pharmaceutical prices**

In the draft PFPA it was proposed that pharmaceutical prices be deflated by 2% per year in order to account for inflation in non-pharmaceutical costs over time, whereas pharmaceutical prices tend to either decrease or remain fixed over time. This adjustment for inflation had not been included in analyses historically due to the relatively high discount rate resulting in future costs being given a lower value.

### Consultation Responses

This proposed amendment was not supported by Pharmaceutical Suppliers who considered that if other prices are expected to increase, these specific prices should be inflated. It was pointed out that deflating pharmaceutical prices by 2% assumes all other costs will inflate, which is not always the case (e.g. contracted services such as laboratory testing).

### PHARMAC View

PHARMAC staff noted and discussed these concerns. It was noted that the proposal to deflate pharmaceutical prices by 2% was only intended to be a proxy for inflation. PHARMAC staff agreed however that it may be more appropriate to include this in the sensitivity analysis (either by deflating pharmaceutical prices by 2% or inflating all other prices), rather than the base-case analysis.

### Amendments to the PFPA

The PFPA has been amended to recommend that pharmaceutical prices be deflated by two percent per year in the sensitivity analysis (not the base-case analysis) as a proxy for inflation in other prices.

### **4. Exclusion of indirect patient costs**

Indirect costs are those costs relating to lost productivity of a patient due to treatment, illness or death, or that of family members if they attend to patients. These include the cost of patient time off work (i.e. lost wages) and reduced productivity costs, cost of premature mortality; and intangible costs (e.g. pain and suffering experienced as a consequence of a treatment).

PHARMAC has never included indirect patient costs in CUAs, for the following reasons (as specified in version 2 of the PFPA):

- including indirect costs would result in double-counting, as the impact of treatment on pain, suffering and inability to work is taken into account when estimating health-related quality of life;
- these costs are often difficult to quantify correctly and require unrealistic assumptions (e.g. a zero rate of unemployment) which may invalidate CUA results (this is particularly important when working in a pragmatic public policy environment where cost-effectiveness is part of the decision criteria);

- incorporating differential earning levels will result in valuing one group of individuals more than another (for example, they tend to bias against those who are not in the labour force which may result in treatments for women or the elderly being less cost-effective);
- the actual production loss for society from sickness is likely to be significantly lower than indicated by *a priori* estimates (for example, work can be covered by the unemployed);
- PHARMAC's objective is to maximise health gains from health sector funds. If societal costs were included in analyses, this could result in PHARMAC considering issues it has no control over (for example, an analysis including indirect costs could favour those with high incomes and hence suggest that it would be cost-effective to further subsidise education);
- it would be time-consuming and thus inefficient to include these costs in CUAs, as it would result in significant opportunity costs in terms of staff time. Given fixed analytical capacity at PHARMAC, by increasing the complexity of analyses there would be a trade-off in terms of numbers and timeliness of assessments. This in turn may cause delays to the listing of beneficial pharmaceuticals.

### Consultation Responses

There were varied views from consultation regarding whether PHARMAC should include indirect patient costs. One responder considered that including indirect patient costs makes the analysis more complex and suspect in its conclusions due to the number of assumptions required. It was also noted that the inclusion of these costs would result in double-counting as most indirect costs are included in HRQOL and/or life expectancy estimates.

However, others considered that indirect patient costs should be included in analyses, or at least considered in the decision criteria.

### PHARMAC View

PHARMAC staff considered that cost-utility analyses should not include indirect patient costs, for the reasons outlined above. Indirect patient costs can be incorporated in the QALY estimates through the utility values. This has the advantage of not needing to weight the QALYs according to whether the patient is working, and also doesn't require as many assumptions in the analysis.

### Amendments to the PFFPA

No further amendments on this issue have been made to the PFFPA from the earlier draft of version 2 that was circulated for consultation. The revised PFFPA recommends that indirect patient costs be incorporated in the QALY estimates through the utility values.

## **5. Inclusion/exclusion of statistically significant events in economic analyses**

The draft version 2 of the PFFPA recommended that in most cases only statistically significant events (95% confidence interval does not include 1.00,  $p < 0.05$ ) should be included in the base-case analysis. At the time it was considered that economic analyses should be based on 'real' clinical effects, and that the inclusion of clinically insignificant events would not only make the analysis more complex but may make the results of the analysis more questionable.

### Consultation Responses

Several responders to consultation disagreed with the recommendation to exclude statistically insignificant clinical events from CUA. One respondent considered that if an event was clinically and/or economically significant, it should be included in the base-case analysis regardless of statistical significance, as some trials are not sufficiently powered to determine statistical significance. Others considered that the exclusion of non-significant events was dangerous and could lead to counter-intuitive results. They considered that clinically meaningful events should generally be included irrespective of statistical significance, unless there is no difference in survival (and any differences in mean events favours the comparator), or if the event occurs at the same rate between treatment arms and is not expected to differ in clinical practice. It was noted that in some cases composite endpoints are used in clinical trials in order to achieve statistical significance, however when undertaking an economic analysis the individual endpoints need to be used.

### PHARMAC View

PHARMAC staff sought expert advice on this issue. PHARMAC staff were advised that rather than focusing on statistical significant (defined as  $p < 0.05$ ), the magnitude of the difference is what is important, especially when the p-value is close to 0.05 (an arbitrary cut-off). In addition, it is important to check whether statistical significance has been demonstrated in more than one study – if it has been demonstrated in more than one study, this should give the analyst confidence that the events are not due to chance.

### Amendments to the PFFA

The PFFA now states that for clinical events with a p value close to 0.05, consideration should be given to the magnitude of effect; whether the results are likely to be clinically significant; the relevance and validity of composite measures; and also whether statistical significance has been demonstrated in an independent study. Accounting for these factors will mean that in some cases a result considered to be 'statistically non-significant' (i.e. p value equal to or greater than 0.05) should still be used because the magnitude of clinical relevance overrides the statistical aspects. Likewise, in some cases a result considered to be statistically significant (p value less than 0.05) should not be used because it has no meaningful clinical effects.

## **6. Recommended treatment comparator**

The draft PFFA recommended that the comparator(s) used in analyses should be "current clinical practice". This is consistent with the comparator used in past PHARMAC analyses, is relevant to the perspective of the analysis (i.e. the funder), and relates to the decision problem which initiated the analysis (i.e. do the additional benefits of the new drug compensate for the higher cost compared with what is currently funded).

### Consultation Responses

One respondent considered that the comparator should be defined as the treatment that is "most likely to be replaced in clinical practice". They considered that current practice may not be appropriate in areas where practice is changing rapidly. They also noted that most clinical trials compare an intervention to the gold standard of treatment at the time, however the trial may be conducted over a number of years and treatment protocols may change during this time. A pharmaceutical supplier recommended that consideration should be given to both current clinical practice and likely future practice, and that submissions include all relevant comparators (particularly relevant if there is an extended period of time between initial application and funding). Another responder noted that

PBAC specify that the main comparator should be the 'analogue prescribed for the largest number of patients' and the 'therapy that most prescribers will replace in practice'.

In addition, several responders considered that wider clinical opinions from expert panels should be used to select the appropriate comparator for economic analyses, particularly where the disease area requires a very specific knowledge of the current NZ treatment protocols.

### PHARMAC View

PHARMAC staff considered the scope of economic analyses, including what comparator should be used in economic analyses. PHARMAC staff agreed that the comparator for economic analyses needed to be further defined in the PFPA. PHARMAC staff also agreed that clinical advice should be obtained on the appropriate comparator to use in an analysis, and that this is usually addressed by PTAC.

### Amendments to the PFPA

The definition of a comparator in the PFPA has been amended to the 'treatment that most prescribers would replace in practice at time of pharmaceutical funding AND treatment prescribed to the largest number of patients'.

The PFPA also notes that is important to consider likely future practice (i.e. treatment regimens at the time the pharmaceutical is likely to be funded). This allows for any changes that may occur in treatment regimens over time (including pharmaceuticals that are currently in development).

In cases where treatment regimens differ throughout New Zealand, the PFPA now recommends that a range of comparators be used in the analysis. The results of the analysis using the different comparators should be reported separately, as well as reporting a weighted-average (weighted by patients numbers prescribed comparator treatment) of the cost per QALY result.

## **7. Perspective of analyses**

PHARMAC undertakes CUAs from the perspective of the funder (i.e. originally the four regional health authorities, which became the Transitional Health Authority and then the Health Funding Authority, now the 21 District Health Boards), as PHARMAC has a separate budget from other government sectors, and it is consistent with PHARMAC's primary objective.

Version 1 of the PFPA stated that "the perspective taken by PHARMAC in conducting CUAs is that of the health sector, in accordance with PHARMAC's primary objective (achieving the best health outcomes possible from pharmaceutical treatment)".

### Consultation Responses

There was general support from consultation for PHARMAC to continue to undertake analyses from the perspective of the funder. However, several responders stated that PHARMAC should also consider a wider perspective (i.e. whole of government and/or societal) when the effect on non-healthcare sectors and/or individuals is significant. This is argued on the basis that the 'funder' is actually the government (as opposed to PHARMAC or DHBs), hence any costs and/or savings that accrue to the government should be considered in the analysis.

It is noted that there are good reasons for using a wider perspective. A wider government perspective would ensure that costs and savings to other government organisations were considered.

#### PHARMAC View

PHARMAC staff considered that for the interim, such wider costs can be considered in a qualitative manner in the Technology Assessment Reports (TARs) of detailed analyses. It was also considered that it would be useful to review these analyses in the near future.

#### Amendments to the PFPA

The PFPA now states that wider costs may be considered qualitatively in PHARMAC reports.

## **Areas for Further Work for the PFPA**

The main areas for further work for the PFPA include:

1. Further review various HR-QOL instruments (HUI, SF-6D, EQ-5D).
2. Create a database of health states and utility values.
3. Several responders to consultation requested that PHARMAC publish a standard list of costs to be used by Pharmaceutical Suppliers in economic evaluations (similar to the Manual of Resource Items published by PBAC). This would ensure that suppliers preparing submissions can be confident that all other submissions are referring to the same set of costs, hence improving transparency. PHARMAC staff consider that there would be benefits in publishing a manual of resource items. Initially the costs included in the manual would be limited to those costs that are most frequently used in CUAs, and also costs that are relatively stable. This would be published as a separate document (linked from the PFPA), to enable frequent updates.
4. Further review the usefulness of probability distributions. Currently PHARMAC staff use central (point) estimates (i.e. the probability of an event occurring is based on a particular value) as opposed to probability distribution (where the probability of an event occurring is based on a distribution of values). However several academic health economists consider that the use of probability distributions is necessary in order to quantify uncertainty. PHARMAC notes that including probability distributions adds significantly to the complexity of analyses (hence reducing the number of analyses that can be undertaken). It is also unclear whether the inclusion of probability distributions is likely to change the results of analyses, and the relative cost-effectiveness of pharmaceuticals.

## **Process for the Review of the Prescription for Pharmacoeconomic Analysis**

Version 2 of the PFPA has been developed through the following process:

### **1. Internal review of cost-utility analysis methodology**

A Technology Assessment Group (TAG) was formed in late 2004 to review the methodology used in conducting economic analysis and the content of the PFPA. The group consisted of Matthew Brougham, Rachel Grocott, Rico Schoeler and Dr Scott Metcalfe. Several new analysts have subsequently joined the group, including Ginny Priest, Cameron Hall and Matthew Poynton.

Topics covered in the review have included:

- clinical evidence;
- economic modelling;
- measurement of health-related quality of life;
- measurement of costs;
- sensitivity analysis and reporting of results;
- discounting and discount rate; and
- other relevant issues not previously covered.

For each topic a literature review was conducted and discussion documents were drafted summarising the information obtained from the literature review and PHARMAC's current practices.

A series of meetings was organised for the TAG to discuss the information in the discussion documents and address specific questions. At the completion of each meeting a consensus document was drafted that outlined the decisions reached. Drafting of version 2 of the PFPA was started in late 2005.

### **2. External review of the draft Prescription for Pharmacoeconomic Analysis**

The draft version 2 of the PFPA has had input from economists, clinicians and consumers. Following internal review of the draft PFPA, PHARMAC staff contracted four prominent national and international economists to review the draft version 2 of the PFPA. The Pharmacology and Therapeutic Advisory Committee (PTAC), and the Consumer Advisory Committee (CAC) also reviewed the document in 2006.

PHARMAC staff contracted the following four economists to review the PFPA and answer specific questions on CUA methodology:

- Professor Mark Sculpher – Professor of Health Economics, Director of Programme on Economic Evaluation and Health Technology Assessment and Member of the National Institute for Health and Clinical Excellence (NICE) Technology Appraisal Committee, Centre for Health Economics, University of York, United Kingdom.
- Dr Paul Hansen – Senior Lecturer, Department of Economics, University of Otago, Dunedin.
- Professor James Raftery – Professor of Health Technology Assessment, Director of National Coordinating Centre for Health Technology Assessment, Southampton, United Kingdom.
- Dr Bryce Williamson – Director, Capital Economics Limited, Wellington.

As a result of the reviews a number of amendments were made to the draft version 2 of the PFPA.

In June 2006 the PHARMAC Board resolved that PHARMAC staff consult on the PFPA. Further expert advice was obtained from Dr Graham Scott (Director, LECG) and Professor Paul Scuffham (Professor of Health Economics, Griffith University, Brisbane, Australia).

### 3. External consultation

PHARMAC staff consulted widely on version 2 of the PFPA. A copy of the revised PFPA with a personalised letter was sent to the following groups and individuals:

- national and international health economists;
- Ministry of Health;
- District Health Boards and District Health Board New Zealand;
- National Health Committee;
- The Treasury;
- Accident Compensation Commission; and
- Land Transport Safety Authority.

A notification letter alerting organisations to the revised PFPA on the PHARMAC website was sent to all pharmaceutical companies and all interest groups on our consultation list (including clinical and patient groups). In addition, a letter was published in the NZMJ alerting readers to the document and inviting consultation responses. Presentations were also held in Wellington and Auckland to discuss the revised PFPA with key stakeholders.

### 4. Consideration of consultation responses

All consultations were collated and discussed in detail by the Technology Assessment Group, and subsequent amendments were made to the PFPA. The consultation responses were also provided to the PHARMAC Board.