

## **RMI Submission on PHARMAC's Guidelines for Pharmacoeconomic Analysis**

### **1. Introduction**

The Researched Medicines Industry Association (RMI), representing New Zealand's researched-based pharmaceutical industry, makes the following submissions regarding PHARMAC's draft guidelines for pharmacoeconomic analysis. It is however noted that the Government has agreed to the development of a National Medicines Strategy and it is the RMI's view that New Zealand's system for determining the relative merits of pharmaceuticals and which offer value for money should form an important part of that policy development.

As such our approach to this consultation exercise conducted by PHARMAC has been to simply critique the guidelines as they have been presented and reserve further commentary regarding the system until these policies are being considered and debated as part of the National Medicines Strategy development.

### **2. Submissions on the Recommendations.**

PHARMAC's proposals are summarised in their 24 recommendations on Pages 6 and 7 of the draft document. The following recommendations are commented on Recommendations 1, 2, 4, 5, 7, 9, 14, 15, 16, 17, 18, 21, 22.

#### **2.1 Recommendation 1 - CUA as a Preferred Technique**

PHARMAC proposes to continue using CUA as the preferred technique for economic analysis of pharmaceuticals. The advantages of CUA<sup>1</sup> are:

- It provides a method by which various disparate outcomes (such as life extension, quality of life, side-effects etc) may be combined into a common outcome measure for all interventions,
- It provides a method to attach values to the outcomes so the more important outcomes are weighted more heavily,
- It can be used to make comparisons across a broad set of interventions,
- It enables decision-makers to compare programs on the basis of their cost-effectiveness.

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<sup>1</sup> Drummond et al. Methods for the Economic Evaluation of Health Care Programmes, 3<sup>rd</sup> ed

Given PHARMAC's current framework, cost-utility analysis is therefore an appropriate technique for application in this policy setting. However, there are issues to be considered in PHARMAC's methods used in CUA that are raised later in this response.

Another economic analysis technique that has the advantages outlined above is cost-benefit analysis. Cost-benefit analysis requires valuation of the programme consequences in monetary units thus enabling a comparison between the programme incremental costs with its incremental consequences. The number of cost benefit analyses undertaken in health care has increased considerably over recent years even though attempting to assign monetary values to health outcomes is still considered controversial.

Cost-benefit analysis is potentially the most powerful of techniques for economic evaluation because it can address questions of allocative efficiency that other techniques cannot. For this reason, we would like to see it explored for potential use in future reviews.

## **2.2 Recommendation 2 - Perspective**

PHARMAC proposes use of a health care system perspective but also to include direct patient co-payments for treatment. This perspective is justified on the basis that it is that of "the funder". This perspective is appropriate for most interventions being analysed.

However, in some cases it may be important to consider a wider perspective because the costs under consideration maybe largely in the non-health sector. We would contend that the funder is actually the government (not PHARMAC or the Ministry of Health) and therefore if there are significant costs (or cost savings) to government associated with the interventions being analysed, these should be included in the analysis.

It also needs to be noted that a societal perspective (which includes everyone affected by the intervention and counts all significant health outcomes and costs that flow from it, regardless of who experiences the outcomes or costs<sup>2</sup>) is an important consideration. There are instances where indirect costs to society (such as reduced productivity) should be included in decision-making because of the relevance to the disease being studied. The friction cost method can be used to minimise overestimation of the impact of indirect costs.

At the very least, the impact of the pharmaceutical on indirect costs borne by society needs to be one of the factors included within PHARMAC's decision criteria.

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<sup>2</sup> Definition from Gold et al. 1996

### **2.3 Recommendation 4 - Choice of Comparator**

We suggest that the definition of comparator being “treatment(s) used in current clinical practice” be amended such that the treatment “most likely to be replaced in practice” is used to define the most appropriate comparator.

“Current practice” may not be appropriate in areas where practice is changing rapidly. Another issue that may be of relevance is the availability of evidence available on particular comparisons. For example, there may be a substantial body of evidence against comparators that are considered a gold standard for treatment elsewhere and this may need to be taken into account in selection of a comparator for the economic analysis.

We support the use of properly constituted expert panels being used to select the appropriate comparator for an economic analysis.

### **2.4 Recommendation 5 -Preferred Data Sources / Level of Evidence**

The PHARMAC guidelines propose a modified version of the SIGN guidelines for classifying clinical evidence. It is not understood why PHARMAC has chosen to amend the original classifications and it appears to be onerous for PHARMAC to insist on a different and unique scoring system. (Perhaps more explanation of this is required).

PHARMAC’s guidelines recommend only use of evidence graded 1+ or above according to the modified SIGN classification. This is not a practical recommendation and is considered inappropriate.

Various grades of evidence may be needed in deriving inputs to the economic analysis. For example, appropriately solicited expert opinion becomes necessary where no other evidence is available, especially when deriving estimates of resource use. It is entirely appropriate for the economic analysis to source inputs from various sources as rarely will there be sufficient evidence of grade 1+ and above to provide all the inputs to any analysis. The pragmatic approach that should be followed is that the highest level of evidence available should be used.

This recommendation to use only Grade 1+ evidence and above is also contradictory with other parts of the PHARMAC document. For example, Recommendation 15 considers it appropriate for EQ-5D scores to be “mapped” using PHARMAC’s “opinion”. This is clearly advocating the use of evidence for the primary outcome that is well outside of the modified SIGN classification.

The PHARMAC document also states that cost data from overseas or clinical trials should not be used. This also contradicts Recommendation 6. The use of resource use measured in naturalistic clinical trials (rather than protocol

driven costs) conducted in countries with similar patterns of resource use to New Zealand (or in New Zealand for that matter), with New Zealand unit costs applied is surely more valid than expert opinion.

## **2.5 Recommendation 7 - Inclusion of Statistically Significant Events**

It is necessary to consider clinical, statistical and economic significance of any differences between treatments when deciding what should be included in the analysis. As clinical trials are powered based on the primary outcome measure only, there may be insufficient power to demonstrate statistically significant differences between two treatments on other parameters such as secondary outcomes, safety and economic parameters. However, these differences may be clinically and/or economically significant and should therefore be included in the analysis. The impact of a decision to include or exclude certain parameters can be tested in the sensitivity analysis.

## **2.6 Recommendation 9 - Time Horizon for Analyses**

In general, the use of a lifetime time horizon for analyses is supported for interventions that are used long term or impact on survival. However, the guidelines need to state clearly that the time horizon should be appropriate to intervention being studied and the population being analysed. It is not necessary to use a lifetime horizon in many cases.

## **2.7 Recommendation 14 - Use of NZ EQ-5D Tariff 2 and GBD Weights**

PHARMAC propose the EQ-5D as the preferred instrument for deriving QOL weights. A literature review to June 2004 published recently on the use of QALYs for estimation of effectiveness in health care found that the most frequently used instrument was the EQ-5D, used in 47.5% of studies. Therefore, in opting for the EQ-5D, PHARMAC has chosen an instrument that is widely used.

The EQ-5D has 5 attributes: mobility, self-care, usual activity, pain discomfort and anxiety/depression. Each attribute has three levels: no problem, some problems and major problems, thus defining 243 possible health states, to which has been added unconscious and dead for a total of 245 in all.

Preferences for the EQ-5D scoring function were measured using the time trade off technique. The original weights were developed using a random sample of 3,000 members of the adult population in the UK. NZ weights were obtained using TTO on a sample of 919 individuals in New Zealand. The results of this sample were recalculated with a final sample size of 396. The latter weights are recommended for use by PHARMAC. We have some concerns about whether using the weights from such a small sample is appropriate. It is suggested that the EUROQOL group be consulted on this issue and asked to endorse the preferred approach.

Disability adjusted life years (DALYs) were developed by WHO initially for their Global Burden of Disease and Injury study. Subsequently they have been recommended by WHO for use in generalised cost-effectiveness analysis. The scoring of health conditions is based on 3 factors: the number of life-years lost compared to Japanese women, weights applied to each healthy life-year to reflect productivity at work and home and weights for each unhealthy life year are applied to capture degree of functional limitation imposed on a person. PHARMAC appear to be proposing to use the latter weights (for unhealthy life years) as their second method of obtaining quality of life weights for use in cost utility analysis. This is discussed in the next section.

## 2.8 Recommendation 15 - Mapping of Health States

The process that PHARMAC uses in mapping health states is unacceptable even by their own guidelines and inconsistent with Recommendation 7 on standards of evidence. There is considerable concern over the way in which PHARMAC currently carries out such mapping.

If patients have valued quality of life in a clinical trial, then this should be the preferred source of weights for the analysis. Opinion of health professionals is considered less preferable because although health professionals may be aware of the clinical nature of disease and the burden it can cause for their patients, it is unlikely that they - having never experienced the disease themselves- would really be able to judge the patients' HR-QoL properly. The unlikelihood is evidenced by studies that show a low correlation between patient and clinician utilities. Therefore, if patient-derived weights are not available, the next preferred source for mapping health states would be properly constituted expert panels of relevant health professionals.

The following table presents a possible hierarchy for health related quality of life weights to be used in economic analyses (with 1 being preferred and 8 being least preferred).

1	Weights obtained in a clinical trial with adequate sample size using EQ-5D.
2	Weights obtained in a clinical trial with adequate sample size using another MAU, TTO, SG or rating scale.
3	Weights obtained from a sample of patients using the EQ-5D.
4	Weights obtained from a sample of patients using another MAU, TTO, SG or rating scale.
5	Weights obtained from an appropriately conducted expert panel using EQ-5D.
6	Weights obtained from an appropriately conducted expert panel using another MAU, TTO, SG or rating scale.
7	Informal mapping of weights using EQ-5D.
8	Informal mapping of weights using GBD, another MAU, TTO, SG or rating scale.

The current practice of mapping being carried out by 1 or more PHARMAC staff is not acceptable and should therefore only be used as a last resort.

## **2.9 Recommendation 17 - Pharmaceutical Costs**

PHARMAC proposes to include manufacturers' rebates as well as reduction in drug costs at patent expiry and a 2% annual decrease in pharmaceutical costs. The rationale for the latter is to make an allowance for an annual 2% increase in other health care costs.

We have no objection to the inclusion of rebates.

As for the proposal to reduce product cost at patent expiry, it is not clear how PHARMAC propose to assign a cost after patent expiry. In the absence of a commercial arrangement, assumptions about price reductions at patent expiry are speculative. This is particularly the case for biologicals and products where no generic is anticipated. Also, it is not clear what assumptions would be made about the magnitude of reduction in price at patent expiry. Therefore, such reduction should not be included unless an agreement is already in place with a supplier for such a price reduction and therefore the reduction is certain and the magnitude of the reduction is known.

We do not agree with the proposal to decrease pharmaceutical costs by 2% annually. It is more appropriate to increase other individual health care costs by their expected rate of inflation.

## **2.10 Recommendation 18 - Hospital Inpatient Costs**

In the absence of better information, it is appropriate that DRG-based costing be used for hospital inpatient costs. However, it needs to be recognised that DRGs provide an estimate only and may either underestimate or overestimate actual cost of treatment. Therefore it may be necessary to adjust these provided this can be justified with available evidence.

It is suggested that the high outlier per diem be used to estimate marginal cost of hospitalisation where the duration of hospitalisation is reduced by an intervention.

## **2.11 Recommendation 20 - Range of Costs for Inclusion**

We support provision of better advice on standard costs to be used in economic analyses. This is particularly useful for suppliers who are not familiar with the New Zealand health care system. We would propose that a more comprehensive document providing guidance on a standard list of costs be provided on a regular basis. This could follow a format similar to the PBAC (Australian) "Manual of Costs".

### **2.12 Recommendation 21 - Range of Costs for Exclusion**

We propose that costs to other government departments are included in analyses because government is the “funder”. We also propose that indirect costs to patients be included where appropriate so at the very least, that these are considered in decision-making. (See also comments on Recommendation 3).

As earlier stated, the rejection of clinical trials as a source of resource use data is inconsistent with recommendations on clinical data. If appropriately gathered evidence on resource use is available, then surely this is preferable to expert opinion.

### **2.13 Recommendation 22 - Discount Rate**

We support the proposal to discount costs and benefits at 3.5%. This is consistent with recommended rates elsewhere and New Zealand has long been out of step with other jurisdictions.

9 October 2006