Chapter 3

Affordable access –assessing cost effectiveness

3.1 As noted in Chapter 1, the Australian Government, like most governments in developed countries, provides subsidised patient access to medicines. For medicines listed on the Pharmaceutical Benefits Scheme (PBS), patients pay a contribution depending on their status as a general or concessional patient. The PBS provides safety nets to protect high medicine users from excessive medicine costs.[1] The Department of Health (DOH) explained that the PBS ensures that although the cost of most new cancer therapies can run to many thousands of dollars, Australian patients pay no more than the co-payment.[2]

3.2 Funding new cancer medicines is a challenging policy issue for all governments. The Australian Government uses a range of Health Technology Assessment (HTA) processes and mechanisms to determine which medicines will receive subsidy through the PBS. HTA seeks to provide a basis for providing subsidised access to new medicines while at the same time ensuring the sustainability of the PBS.

3.3 The National Medicines Policy (NMP) provides the overarching framework for the operation of the PBS. The NMP seeks to balance the following key factors: timely access to the medicines Australians need, at a cost individuals and the community can afford while maintaining a responsible and viable medicines industry.[3]

3.4 This chapter examines two key factors that influence affordable access to cancer drugs, the Pharmaceutical Benefits Advisory Committee (PBAC) assessment of the cost and the effectiveness of new cancer medicines as a prerequisite for listing on the PBS. The committee particularly considers concerns regarding the appropriateness of this approach to the assessment of cancer medicines. The methods used by PBAC to evaluate the cost effectiveness of cancer medicines are a source of some concern to many submitters. While recognising the value of a rigorous evidence based assessment process, many submitters expressed concern that the current PBAC assessment processes are unable to effectively respond to the volume and complexity of applications for listing of new and innovative cancer drugs on the PBS. A number of submitters expressed the view that PBAC's evaluation methodologies are limiting access to life-saving new therapies, variously describing the current assessment methodology as 'antiquated', inflexible, 'one-size-fits-all' approach and a key factor in limiting access to new cancer medicines.[4]

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1 Department of Health (DOH), *Submission 197*, p. 11.

2 DOH, *Submission 197*, p. 1.

3 DOH, *Submission 197*, p. 11.

4 Medicines Australia (MA), *Submission 142*, p. 3; Roche Products, *Submission 114*, p. 3; Merck, Sharp and Dohme (MSD), *Submission 120a*, p. 3;

The PBAC assessment framework

3.5 The *National Health Act 1953*, requires the PBAC to consider both the cost and clinical effectiveness of a proposed PBS listing relative to existing therapies.

> Section 101 (3) (A) specifies that the *'Committee shall give consideration to the effectiveness and cost of therapy involving the use of the drug, preparation or class, including by comparing the effectiveness and cost of that therapy with that of alternative therapies, whether or not involving the use of other drugs or preparations.'*
>
> Section 101 (3) (B) states that *'where therapy involving the use of a particular drug or medicinal preparation, or a class of drugs and medicinal preparations, is substantially more costly than an alternative therapy or alternative therapies, whether or not involving the use of other drugs or preparations, the Committee:*
>
> *(a) shall not recommend to the Minister that the drug, preparation or class be made available as pharmaceutical benefits under this Part unless the Committee is satisfied that the first mentioned therapy, for some patients, provides a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies.'*[5]

3.6 In recommending a listing to the Minister, PBAC also provides advice about how the new listing compares with alternative medicines and/or the current standard of care in terms of cost effectiveness ('value for money').[6]

3.7 Major submissions to the PBAC are required to include an economic evaluation to enable the PBAC to consider how much it would cost to achieve additional health outcomes with the proposed medicine compared with existing therapies that would be replaced.[7] The PBAC explained that consideration of 'cost' includes 'both the cost per patient treated and the total cost to the PBS, taking into account the number of patients likely to be given the drug'.[8]

3.8 The principles and methodologies used by the PBAC are set out in the PBAC Guidelines (Guidelines).

> The primary focus of an economic evaluation for PBAC decision making is on how much it would cost to achieve additional health outcomes with the new therapy ('proposed medicine') compared to existing therapies that would be replaced ('incremental cost-effectiveness'). Therefore, in the first instance, the costs associated with altered uses of medicines, medical and other related health care resources all need to be taken into account and outcomes valued in terms of overall quality and length of life; for example,

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5 Pharmaceutical Benefits Advisory Committee (PBAC), *Submission 196*, p. 5.

6 DOH, PBAC Guidelines, Version 4.4, Rationale and basis for economic evaluation, http://www.pbac.pbs.gov.au (accessed 15 September 2015)

7 DOH, PBAC Guidelines, Version 4.4, Rationale and basis for economic evaluation, http://www.pbac.pbs.gov.au (accessed 15 September 2015)

8 *Submission 196*, p. 5.

> 'quality-adjusted life years gained' (cost-utility analysis). This evaluation is referred to as the base case.[9]

3.9 The PBAC told the committee that the approach used 'enables drugs to be compared directly to existing best treatments, and the additional benefits and costs weighed across all types of diseases and treatments. This means that two drugs can be equitably assessed even if one treats a rare but serious disease and another relieves the symptoms of a common but less serious chronic condition, or if one is very expensive but will be used for very few patients and another is low cost but will be used by very large numbers of Australians.[10]

3.10 DOH provided the following summary of the PBAC approach to cost effectiveness:

> The PBAC essentially asks the question 'Is it worth spending an additional $x to achieve the additional benefit offered by the new drug compared to existing therapy?'. In answering this question, the PBAC takes into account a range of factors including the availability and cost of alternative treatments and the total cost and probable demand for the proposed medicine.[11]

3.11 The committee notes that the PBAC Guidelines are currently being reviewed. The review will identify significant new developments for methods since 2008 and will consider 'the relevance to PBAC practice of existing guidance documents on relevant methodologies contained within guidelines published by comparable international health technology assessment agencies, regulators and internationally recognised authorities in the assessment of evidence'.[12]

Evaluation of cost

3.12 The PBAC noted that one of the major challenges in the evaluation of the cost effectiveness of cancer drugs is that cancer drugs cost significantly more than other drugs.

> Cancer drugs that have been assessed by the Committee in the recent past have nearly all been, by any standards, "substantially more costly" than 'alternate therapies', as has recently been reported in the media and medical literature.[13]

3.13 The committee notes that the potential total cost of the 11 major submissions for cancer medicines considered at the PBAC's March 2015 meeting was $589

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9 DOH, PBAC Guidelines, Version 4.4, Rationale and basis for the economic evaluation, www.pbac.pbs.gov.au (accessed 15 September 2015)

10 *Submission 196*, pp 5-6.

11 *Submission 197*, p.7.

12 DOH, Pharmaceutical Benefits Advisory Committee Guidelines Review, www.pbs.gov.au (accessed 15 September 2015)

13 *Submission 196*, p. 6.

million. These submissions represent 23 per cent of the total number of submissions considered at the March meeting.[14]

3.14 As noted in chapter 1, cancer medicines are among the most expensive medicines on the PBS. Figure 3.1 indicates that new cancer medicines make up an increasing proportion of total PBS spending on cancer medicines. DOH advised that PBS benefits paid for new cancer medicines have increased at a rate of 33 per cent per year over the last five financial year, compared to a growth rate of only five per cent per year in benefits paid for established cancer medicines. In addition, DOH noted that:

> The PBS ensures that although the cost of most new cancer therapies can run to many thousands of dollars, Australian patients pay no more than the co-payment. On average over the last five financial years, the patient co-payment funded between 2-3% of the total cost of cancer medicines, compared to 15% for non-cancer medicines. The taxpayer funds the remainder.[15]

Figure 3.1: Patient numbers and expenditure for cancer medicine versus non-cancer medicine.

Financial Year	Cancer Medicine			
	Patient Count	Scripts	Benefit	Patient co-payment contribution as percentage of total cost
2009-10	270,510	1,957,274	$993,745,236	3%
2010-11	287,127	2,066,655	$1,086,669,622	3%
2011-12	295,470	2,234,906	$1,135,299,000	3%
2012-13	314,056	2,434,837	$1,230,201,528	2%
2013-14	337,289	2,607,167	$1,485,961,705	2%

Financial Year	Non Cancer Medicine			
	Patient Count	Scripts	Benefit	Patient co-payment contribution as percentage of total cost
2009-10	9,323,301	196,783,171	$6,998,721,883	17%
2010-11	9,493,086	202,950,640	$7,359,173,190	17%
2011-12	9,521,127	207,170,478	$7,646,269,254	17%
2012-13	9,450,295	208,178,027	$7,562,826,568	17%
2013-14	9,437,378	211,113,143	$7,709,455,066	16%

Source: Department of Health, Submission 197, p. 31.

3.15 The committee notes that the increasingly high cost of cancer medicines poses a significant challenge for the PBAC in assessing cost-effectiveness.

3.16 DOH stated that while the cost of new cancer medicines are substantially higher than other new non-cancer medicines, many new cancer medicines offer only a small incremental survival benefit to patients. DOH stated that '[e]ven where the

14 DOH, *Submission 197*, p. 17.

15 *Submission 197*, p. 5.

health benefits may be considered large, the prohibitive cost can act to restrict access, even after a reasonable timeframe to recoup development costs'.[16]

Comparative cost-effectiveness

3.17 The calculation of value for money is based on a health economic equation: the Incremental Cost Effectiveness Ratio (ICER), which is a cost/benefit ratio, quantifying the additional cost incurred for an additional health benefit derived.[17]

3.18 Unlike a number of other countries, the PBAC does not use a definitive threshold when assessing the cost effectiveness of medicines. Instead, it references the prices of new medicines against existing listed treatments for the same or similar indications.[18] Where there is no listed alternative treatment the PBAC considers the 'clinical place, overall effectiveness, cost and cost-effectiveness of the proposed medicine compare with standard medical care'.[19]

3.19 DOH told the committee that the comparative cost-effectiveness method is able to achieve better price outcomes as medicines which offer the same health benefits and have the same safety profiles will generally attract similar prices.[20]

3.20 Ms Felicity McNeill, First Assistant Secretary, Pharmaceutical Benefits Division, DOH, told the committee that the fact that the PBAC does not have fixed thresholds, is one of the advantages that the PBAC has over assessment models used in other countries:

> The PBAC has the flexibility, where something is of a particularly high cost, or there is a high cost of the quality of life you gain, to take other factors into account, such as the high clinical need or the severity of the disease, to make that drug suitable for recommendation. I think the drug … Soliris, is a very good example of where the health outcome that was delivered, which was well beyond the expected quality of life year gained in a traditional model, was considered by the PBAC. They have extraordinary flexibility, and they use it where they think they can. Whereas [under the United Kingdom's National Institute for Health and Care Excellence (NICE) system] you will have a fixed threshold, they do not have those thresholds.[21]

3.21 However, some submitters questioned the claim that the PBAC does not apply a fixed cost-effectiveness threshold in determining value for money. Novo Nordisk (NN) argued that while there is no explicit cost-effectiveness threshold for reimbursement of medicines in Australia, over the past four years, more than half of

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16 *Submission 197*, p. 16.

17 MA, *Submission 142*, p. 17.

18 DOH, *Submission 197*, p.7.

19 DOH, PBAC Guidelines, role of the Pharmaceutical Benefits Advisory Committee, 1.2.2 General guidelines followed by PBAC, www.pbac.pbs.gov.au (accessed15 September 2015)

20 *Submission 197*, p. 13.

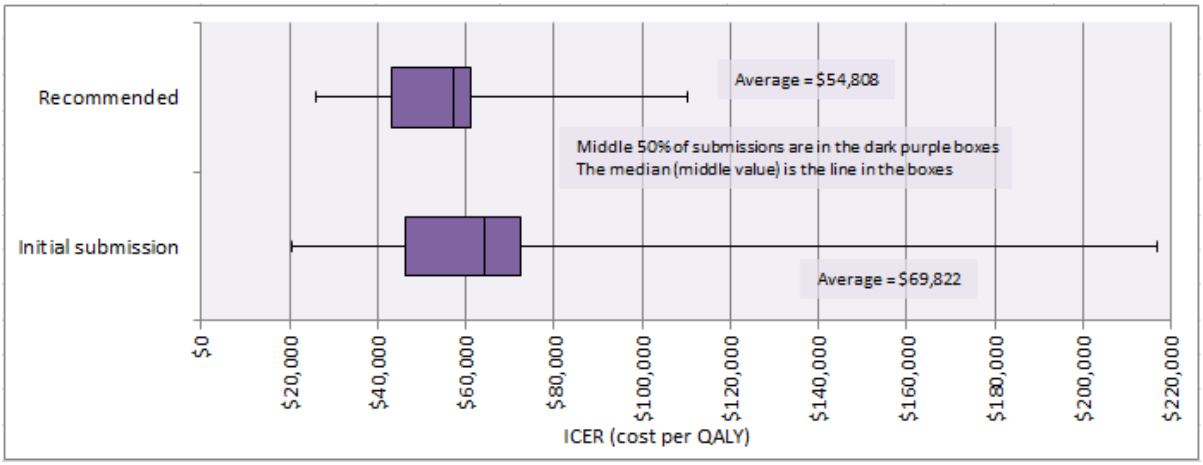
21 *Committee Hansard*, p. 87.

the major cost effectiveness submissions rejected by the PBAC have had an ICER below $45,000. NN states that this is 'despite Australia's economic capacity to pay for innovative and advanced treatments'. NN argued that the current PBAC policy and process significantly restricts the ability of pharmaceutical companies to achieve a reasonable premium for new medicines.[22]

3.22 Medicines Australia (MA) submitted that the experiences of sponsors of new medicines 'reveal that the PBAC's acceptable ICER is in the range of $45 000-$75 000. MA further stated that the implicit acceptable threshold is lowered when any form of clinical, economic and financial uncertainty exists in the economic evaluation, claiming that this contention is supported by ICER ranges captured in Public Summary Documents for recommended medicines.

3.23 DOH provided the following table to illustrate ICERs for first cancer submissions compared to recommended submissions. This indicates that the ICERs of the middle 50 per cent of recommended applications are in the range of $42 000-$61 000.

Figure 3.2: ICERs for first cancer submissions vs. recommended cancer submissions



Source: Department of Health, Submission 197, p. 31.

3.24 Pharmaceutical companies expressed concern that the PBAC comparative costing model poses a challenge to establishing cost effectiveness for cancer medicines. For example, Merck Sharp and Dohme (MSD) expressed concern that the PBAC practice of referencing the prices of new medicines against older existing treatments does not recognise the true value of new cancer medicines and cited examples of submissions that had proved unsuccessful on the basis of an 'unacceptably high incremental cost-effectiveness ratio'.[23] Submitters argued that price reductions as a result of post PBAC reviews have led to an erosion of the prices of comparator medicines, 'even recently listed on-patent medicines'.[24]

22 Ms McNeill, *Submission 147*, p. 2.

23 MSD, *Submission 120*, p. 6

24 Novo Nordisk, *Submission 147*, p. 2.

3.25 Submitters also questioned the relevance of cost-effectiveness to the assessment of new innovative treatments for cancer, noting that a number of factors mean that development costs for cancer medicines are invariably higher than for non-cancer medicines.[25] Submitters noted that advances in understanding of the formation and characteristics of the 'myriad diseases we refer to under the "catch all" banner that is cancer' has led to a focus on smaller disease populations.[26] This in turn has led to increased costs associated with the development of clinical trials. For example, trials in small populations must be run in many sites and over long periods of time in order to recruit sufficient patients, with patient identification itself requiring costly and elaborate testing.[27]

3.26 Rare Cancers Australia noted that there are real challenges in establishing the evidence to support the high cost of many cancer medicines, especially when the benefits are incremental and apply only to a small population.[28]

3.27 Pharmaceutical companies agreed that the current approach significantly restricts the ability of the industry to achieve a reasonable premium for new medicines. MSD explained the high prices associated with cancer drugs reflect the significant investment required in research and development to bring medicines to market. MSD noted that over time, the cost of individual medicines becomes comparatively lower, 'because drugs are not subject to price increases, unlike all other health care costs, and once generic they will be available at a significantly reduced price'.[29]

3.28 On a related issue, Amgen submitted that it may be difficult to demonstrate favourable cost effectiveness when a high cost new medicine is compared to a low priced off-patent medicine.[30] Eli Lilly Australia (Lilly) illustrated this by reference to its application for listing of the drug Alimta, used in the treatment of non-small cell lung cancer:

> At the time of PBAC's consideration of Alimta for first-line use the patent on Gemzar, the existing standard of care, had expired. Gemzar became subject to a very significant price fall (the price of the comparator 'eroded'). This price fall did not reflect any change to the therapeutic value of Gemzar but did significantly impact on the consideration by the PBAC of the comparative value of the benefits of Alimta for first-line use. As a consequence, Alimta was recommended under the PBS but the price recommended by the PBAC process for Alimta was significantly lower than if the patent on Gemzar had not expired. That price fell substantially below

25 See for example, MA, *Submission 142*, pp 11-12.

26 Rare Cancers Australia, *Submission 92*, p. 16.

27 Amgen, *Submission 119*, p. 7.

28 *Submission 92*, p. 1..

29 *Submission 120*, p. 6.

30 *Submission 119*, p. 4.

> what Lilly considered to be the fair value of Alimta. As a consequence, Lilly chose not to pursue the reimbursement of Alimta for first-line use.[31]

3.29 MSD submitted that the application of a 'shadow price' mechanism would better reflect the fair value of innovative medicines. A shadow price would be a Consumer Price Index adjusted price of the reference medicine when it was launched. Cost effectiveness analyses would then be undertaken using the shadow price.[32]

3.30 However, evidence from DOH indicated that the continual review of the cost of PBS medicines contributes to the ongoing cost effectiveness of listed medicines and the sustainability of the PBS. Post-PBAC reviews, together with mechanisms such as price disclosure, which monitors the discounting behaviour of pharmaceutical companies, helps to ensure that any discounts offered in the private market are reflected in the price paid by government. As a result, a number of cancer medicines have taken significant price reductions:

> For example, the ex-manufacturer price of an 80 mg vial of docetaxel was $1,420 when it was first subsidised in August 1996. As a result of competition, the price is estimated to be reduced to $17.43 following the next round of price disclosure, scheduled for 1 April 2015.[33]

3.31 DOH noted that while price reductions achieved through price disclosure achieve a better price for the government and therefore for taxpayers, they can also directly benefit patients.

> For example, the price of ondansetron 8mg tablets (used to treat nausea from cancer treatment) has decreased from $57.50 to $22.70. For general patients, this means they now pay $22.70 per script, rather than the co-payment of $37.70.[34]

3.32 The committee also heard that the high cost of new cancer medicines is not simply related to the cost of development and manufacture. The PBAC submitted it considers a major barrier to rapid PBS listing for new cancer drugs is the expectation of pharmaceutical companies with respect to pricing.

> The reason new cancer drugs are so expensive has been the subject of considerable debate but it is not simply related to the cost of development and manufacture. The pharmaceutical industry's expectations in relation to price and profit at international and national levels are also relevant.[35]

3.33 PBAC noted that for many new cancer drugs the price being requested, relative to the benefit of the medicine, is much higher than for other serious life-threatening diseases, or for the evidence of health outcomes provided.[36]

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31 *Submission 191*, pp 2-3.

32 Merck, Sharp and Dohme, *Submission 120*, p. 6.

33 DOH, *Submission 197*, p. 13.

34 DOH, *Submission 197*, p. 13.

35 *Submission 196*, p. 6.

36 *Submission 196*, p. 6.

3.34 Dr Agnes Vitry also submitted that several studies have demonstrated that the higher prices set for new cancer medicines are neither explained by their therapeutic value nor the cost of development. Dr Vitry noted evidence that prices remain high despite the marketing of competitive products.[37]

3.35 DOH summarised the competing tension inherent in the assessment of the cost effectiveness of cancer drugs.

> Cancer medicine pricing is an international issue, for an international industry, but access and subsidy responses are necessarily national. Funding decisions will be based on a range of local factors – clinical need, fiscal constraints, and opportunity costs to fund other forms of cancer care and prevention, as well as other diseases. Public funders look to maximise societal benefit, and thus must use different criteria to individuals making personal treatment choices that address their own needs and preferences.[38]

Evidentiary requirements

3.36 As noted previously, the assessment of cancer drugs is undertaken on the same basis as drugs for other illnesses. It includes assessment of clinical evidence regarding benefits and harms, relative to the cost and other factors such as the severity of the illness, the extent of unmet need and the views of consumers.[39]

3.37 The Act requires the PBAC to determine that a drug provides a 'significant improvement in efficacy or reduction in toxicity' compared to alternative therapies. In its submission, the PBAC advised the committee that the benefits of cancer drugs are assessed in terms of effects of overall survival, progression-free survival (PFS), response to treatment, quality of life and toxicity.[40]

3.38 Dr Suzanne Hill, the former Chair of the PBAC, explained that for all medicines submitted to the PBAC, the committee assesses the effects of the medicine based on the impact of the medicine on patient relevant outcomes:

> So for cancer, we think of that in terms of the likelihood of the new medicines producing improved survival compared to what we already have or temporarily slowing progression of disease, which is the term used for progression-free survival or, when we have it, the effects of [the medicine] on the quality of life of the patient. In all cases, we need to consider the risk of side effects or harm.[41]

3.39 The committee heard that the 'gold standard' for clinical evidence comes from randomised and controlled trials[42] and would ideally include final outcomes data. In its July 2013 report, *Access to cancer medicines in Australia*, Deloitte Access

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37 *Submission 128*, p. 6.

38 *Submission 197*, p. 22.

39 *Submission 196*, p. 3.

40 *Submission 196*, p. 3.

41 *Committee Hansard*, p. 71.

42 MA, *Submission 147*, p.35

Economics noted that overall survival is considered to be a clinically relevant and meaningful endpoint as it is relatively easy to measure, record and define and is free of bias.[43] However, as a number of submitters noted, this is not always a realistic or achievable expectation for cancer medicines.[44]

3.40 An endpoint of overall survival substantially prolongs the duration of clinical trials and increases both the number of patients that need to be recruited and the cost of the trial. The longer a trial, the higher the range of factors that may impact on the interpretation of the findings and the greater the chance of encountering ethical challenges, such as denying patients access to experimental treatments that have potential benefits.[45]

3.41 Roche Products submitted that one of the key challenges in gaining PBAC approval is the PBAC has 'a low tolerance for uncertainty', which frequently results in rejection and re-submission of applications and delays for cancer patients. Mr David Pullar, Manager, Government Affairs and Public Policy at Roche Products, noted:

> If you want to have absolute confidence that a medicine can be used at a very specific dose in a very specific patient population and deliver X months of additional survival and quality of life, that is very challenging to do and may just not be possible. We would be very happy to collaborate in that type of research. There are always benefits. But we need this system to be able to recognise that value and take a pragmatic approach to interpreting it.[46]

3.42 NN expressed concern that the current base case evaluation of the benefits of a new medicine is too narrow and does not include the broader patient perspective or the economic view of the benefits of a healthy and productive population.[47]

> Despite the economic evaluation (i.e., the cost effectiveness analysis) being mandated to take a 'societal perspective', only direct health care costs can be included as the base case for the majority of submissions. That is, no account can be made of 'indirect costs', including loss of productivity, impact of time/wages lost by carers, increase in welfare / disability payments, etc. This is unlike some of the other HTA systems in other jurisdictions, e.g., the Nordic countries in Europe, who do account for indirect costs.[48]

43 *Submission 142a*, p. vii.

44 See for example: Amgen, Submission 119, pp 2-3.

45 Roche Products, *Submission 114*, p. 13.

46 *Committee Hansard*, p. 26.

47 NN, *Submission 147*, p. 2.

48 *Submission 147*, p. 7.

Reliance on evidence related to progression free survival versus overall survival

3.43 DOH noted that, one of the main difficulties in assessing cancer medicines is that survival improvements are difficult to determine and are generally not the main outcome measured in clinical cancer trials:

> Many trials use response rates or Progression Free Survival [PFS] as the main outcome measure. PFS refers to the length of time, from either the date of diagnosis or the start of treatment, that patients diagnosed with the disease survive without their disease advancing.
>
> While this is considered an improvement in the quality of a cancer patient's life, many new cancer medicines improve Progression Free Survival but do not lengthen the patient's life. Further, Progression Free Survival outcomes do not readily translate to improvements in Overall Survival or Quality of Life, but sponsors often use Progression Free Survival clinical trial data to make assumptions about Overall Survival. This can make Overall Survival estimates overly optimistic. However, even with optimistic estimates, the Overall Survival benefits for cancer medicines submitted to PBAC are generally quite low. Combined with high medicine costs, these small improvements means some cancer medicines are found not to be cost-effective.[49]

3.44 MA responded to this evidence from DOH:

> Any rigorous method of calculating the cost-effectiveness of a medicine, as referenced by the DOH submission, still requires one or more assumptions to be made. There are some examples where PBAC have imposed an 'assumption' in the extrapolation methodology for survival data that they consider reasonable, yet it produces a long-term survival curve that is clinically unrealistic or implausible, and unfavourable to the new drug. At the same time, another country using the same rigorous methodology of Health Technology Assessment, makes a more balance assumption (an assumption based on highly informed specialist clinical input), which generates a much higher long-term survival benefit for the same drug.[50]

3.45 Roche Products noted that cancer medicines are typically registered with the TGA on the basis of PFS, ie the medicine significantly extends the time for the cancer to recur following treatment response. Roche Products described PFS as a relatively straight forward measure that usually compares the new medicine and the prior 'standard of care'.[51] However, the PBAC Guidelines state that clinical studies undertaken to support a general marketing application to the TGA often have not collected the array of information necessary for an economic evaluation by the PBAC.[52]

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49 DOH, *Submission 197*, pp 11-12.

50 Answer to question on notice, 20 April 2015 (received 25 May 2015), p. 2.

51 *Submission 114*, p. 13.

52 DOH, PBAC Guidelines, Version 4.4, *Rationale and basis for the economic evaluation*, pbac.pbs.gov.au

3.46 MA told the committee that, while the current PBAC guidelines do not mandate the provision of overall survival (OS) data, and provide advice on translating surrogate outcomes for use in evaluations where OS data is not available, the PBAC has a clear preference for OS data. MA cited positive PBAC recommendations based on PFS outcomes but clarified that these are usually associated with strict conditions, such as price reductions and/or the requirement for further data collections.[53]

3.47 Submitters expressed concern that reliance on 'gold standard' evidence often results in high rejection rates, requiring the sponsor to lodge several submissions before a listing recommendation is achieved.[54] As noted earlier, delays may also result where the conditions of approval are not acceptable from a sponsor company's perspective.

3.48 However, a number of submitters to the inquiry expressed concern that the PBACs evidentiary requirements pose a significant barrier to early access to new and innovative cancer drugs. Cancer Council Australia and Clinical Oncology Society of Australia (CCA/COSA) told the committee that the evidential requirements for PBS listing are probably one of the most prominent points of contention. CCA/COSA expressed concern that an endpoint of overall survival requires too long a time line for most cancer patients:

> Based on the experience of our health professional colleagues—people who are at the front line, who actually see patients—who have seen significant numbers of patients over a number of years who have had a benefit, we have made the point that it may take too long for that benefit to translate into the type of survival benefit that must then be applied to making a judgement about PBS listing.[55]

3.49 Janssen-Cilag (Janssen) expressed the view that delaying funding for an endpoint of overall survival is economically perverse:

> [T]he better a product is at providing survival the longer it must wait before the benefit can be assessed. Traditional assessment for funding broadens this gap. There is a need to look beyond the traditional hierarchy of evidence and develop new ways to incorporate growing evidence bases to support funding.[56]

3.50 Leukaemia Foundation of Australia (LFA) submitted that these challenges are exacerbated in the case of orphan drugs for rare cancers, such as blood cancers, due to the small patient population size and the associated difficulty and cost of obtaining the required data. Noting the significant delays experienced in the listing of these drugs,

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53 MA, answer to question on notice, received 25 May 2015, p. 1.

54 *Submission 147*, p. 2, MA, answer to question on notice, 20 April 2015 (received 25 May 2015), p. 1.

55 CCA/COSA, *Committee Hansard*, p. 55.

56 *Submission 140*, p. 10.

LFA argued that an alternate mechanism is required to ensure access to drugs for rare conditions for which there is no commercial incentive.[57]

3.51 Submitters to the inquiry indicated they would like to see greater acceptance of a broader set of clinical outcomes. CCA/COSA submitted that overall survival is only one critical endpoint that can be used to indicate the efficacy of a cancer drug.[58] CCA/COSA expressed strong support for earlier reportable endpoints, such as objective tumour response rates and PFS, to be given greater weight in PBAC assessment processes.[59]

3.52 The Haematology Society of Australia and New Zealand (HSANZ) told the committee that, while it understood overall survival is usually considered to be the most appropriate endpoint for demonstrating the efficacy of a medicine, 'in terms of a patient's well-being and clinical status, an improved PFS is a highly meaningful entity which is more appropriate for the assessment of the benefit of a cancer drug'.

> Moreover, with increasing utilisation of targeted therapy, surrogate endpoints in trials, such as biomarker levels and functional imaging may be used instead of survival barometers, because the results of the trial can be measured sooner. Importantly, with the availability of more lines of treatment, many clinical trials have to rely on assessment by PFS, since OS can be confounded by subsequent treatment. For ethical reasons, many trials have also allowed patients to 'cross-over' to the arm of the novel therapy, making demonstration of OS even more difficult. Such trials, even though the 'gold-standard' randomised Phase III trials, may not be the ideal vehicle to demonstrate an improvement in OS in an effective drug. [60]

3.53 MA told the committee that the PBAC is responding to some of these challenges. MA noted that the PBAC recently accepted the 'two-stage Webull approach (Latimer 2014) to be the most reliable correction method to adjust for trial cross-over for the drug pomalidomide'. MA commented that this is a positive communication to the industry, albeit delivered indirectly. MA said that this example highlights the need for all sponsors to be provided with direct advice well in advance of lodging a submission.[61]

3.54 Roche Products argued that the totality of available evidence needs to be considered in the evaluation of cancer drugs and that subsequent evidence collection must be fit-for-purpose. Roche Products noted that the current Access to Medicines Working Group, that comprises DOH and the medicines industry, is working on initiatives to address this.[62]

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57 *Submission 123*, p. 6.

58 *Submission 145*, p. 6.

59 *Submission 145*, p. 1.

60 *Submission 16*, p. 2.

61 Answer to question on notice, 20 April 2015 (received 25 May 2015), p. 2.

62 *Submission 114*, pp 13-14.

3.55 DOH told the committee that the PBAC does give weight to PFS where quality of life improvements can be demonstrated, but that this then needs to be considered in terms of the cost of the new medicine.

> Medicines that offer Progression Free Survival benefits but not Overall Survival benefits may be able to be valued as 'life enhancing', but the evidence does not support them as being 'life saving'. This distinction is often not reflected in the prices requested by sponsors.

3.56 CCA/COSA told the committee advances in cancer research have generated a greater understanding of molecular biology, resulting in the identification of smaller subsets of cancer and, along with rare cancers, naturally produces small patient sizes. CCA/COSA argues that greater use of surrogate endpoints which still demonstrate major outcomes in benefit, 'would support the generation of clinically meaningful data in cancers with long survival, or generally present at a later stage'.[63]

3.57 the Australian and New Zealand Society of Palliative Care (ANZSPC) told the committee that 'the requirement for stringent evidence-based efficacy, while a good fundamental principle, has its limitations in the palliative care population'.[64] In its submission, PCA noted that medications commonly used in palliative care, including Midazolam and glycopyrrolate, are not listed on the PBS, even though they are found to be quite cost effective. Dr Chapman of ANZSPC told the committee:

> … these medicines are routinely used as part of palliative care practice, though one of the complexities of the clinical practice of palliative care is the evidence base for some routinely used mediations that show efficacy in the patient in front of you may not be as broad as is required for PBS listing. So, many of these medications have not been submitted by those companies for those indications for that reason.[65]

3.58 MA told the committee that there is a need to acknowledge both the complexity of cancer and the limitations of current regulatory and reimbursement systems in responding to this. MA submitted that, rather than denying access to cancer medicines on the basis of uncertainty, more flexible evidentiary requirements should be adopted that are capable of dealing with issues such as crossover in clinical trials and which properly reflect the value of cancer medicines to patients, careers and the community.[66]

Measuring quality of life - assessing the value of cancer medicines

3.59 Many submissions to the inquiry expressed concern that the current assessment methodology does not adequately capture quality of life considerations. Cancer Drugs Alliance (CDA) described the cost effectiveness model as out-dated and

63 *Submission 145*, p. 7.

64 *Committee Hansard*, p. 55.

65 *Committee Hansard*, p. 54.

66 MA, *Submission 142*, p. 4.

recommended shifting from what it described as a static assessment of cost-effectiveness to an assessment of value and quality.[67]

3.60 As noted previously, the PBAC seeks to apply a consistent assessment methodology across all medicines. Mr Andrew Stuart, Deputy Secretary, DOH explained that use of the quality-adjusted life year (QALY) creates a level playing field for all medicines for all patient groups:

> The QALY is a quality-adjusted life year—that is, for each medicine, how much improvement do we get from that medicine in a quality-adjusted year of life for a patient for a given dollar? That is a very good way and a pretty simple way of trying to put medicines on a level playing field so that you can compare the cost-benefit of medicines across cancer and multiple sclerosis and Alzheimer's disease and so on.[68]

3.61 The cost per QALY is used as a guide to the cost of the medicine necessary to extend a person's life one year in a good state of health, or for a longer period in a reduced state of health.[69] DOH further explained:

> A QALY is a value used to measure changes in life expectancy and changes in quality of life from health interventions such as medicines. A QALY of 1 is a year of perfect health, whereas death is considered to be zero. This measure is used because it can give some comparability between varying health conditions, such as those that cause death very quickly to those that cause significant disability but do not shorten life span.[70]

3.62 The PBAC Guidelines indicate that, in considering the suitability of a medicine for PBS listing, the PBAC focuses on health outcomes. While the PBAC may consider nonhealth outcomes and the costs and cost offsets of nonhealth care resources, these may not be as influential in decision making as health care outcomes and resources:

> PBAC may also consider nonhealth outcomes, including aspects of the delivery of a health care intervention beyond the health gain obtained; for example, greater convenience or production gains to society beyond those valued by the population benefiting with improved health. However, the valuation of nonhealth outcomes is not straightforward and those outcomes might not be as influential in decision making as health outcomes.
>
> Similarly, PBAC mainly considers the costs of providing health care resources. These extend beyond the costs of the medicine to include possible cost offsets of reduced provision of health care resources as a result of listing a medicine. PBAC may also consider costs and cost offsets

67 *Submission 53*, pp 5-6.

68 *Committee Hansard*, p. 87.

69 Department of Parliamentary Services, Parliamentary Library, *Growth in expenditure on high cost drugs in Australia*, Research Paper Series, 2014-15, 7 January 2015, p. 10.

70 DOH, *Submission 197*, p.7

> of nonhealth care resources, but these might not be as influential in decision making as health care resources.[71]

3.63 Submitters expressed concern that considerations of quality of life are not given more weight in the assessment of cancer drugs[72] and that the current PBAC assessment process is limited in its ability to properly reflect the value of the health gains deemed important by cancer patients themselves.[73] Submitters also called for greater transparency in how such considerations are incorporated into final PBAC decisions.[74]

3.64 Professor Zalcberg of CDA expressed concern that as a measure, the QALY is not sufficiently sensitive to the value that an individual places on quality of life.

> You can use a QALY to equate people having a hip replacement to someone with cancer diagnosed and who has got a year to live. You can simply say: A QALY is a QALY. But I would ask the committee: is a quality-adjusted life-year the same for someone who is having a hip replacement and can now walk to their post box and get their letters without being in pain—and I am not trying to belittle that as an unimportant problem; it is an important problem. Is that quality the same as the quality for someone who has advanced cancer, has a year to live and has an extension of a year? I do not have the answer to that. I would say it is a community issue for discussion and to think about. But patients with cancer do not have time to wait the two or three years that we are talking about. Yes, this is an important problem across all serious diseases and the reform process that we have talked about is equally applicable to all serious conditions. But we need to be cognisant of the time frames and what is happening in cancer.[75]

3.65 LFA also argued that more importance needs to be placed on assessment of quality of life outcomes. 'If a new drug allows a person to get well and return to work or to normal roles in family or community, should not the economic benefits to society be taken into account?' LFA argued that the HTA tools used by the PBAC should be extended to include wider quality of life measures when assessing the cost benefits of targeted drugs for rare/subtype cancers.[76]

3.66 Dr Katherine Nielsen, Director of Research and Advocacy, Ovarian Cancer Australia, told the committee that consideration of the value of a cancer drug should incorporate facts such as a clear extension of remission, improvement of symptoms and quality of life.

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71 DOH, PBAC Guidelines, Version 4.4, Rationale and basis for the economic evaluation, 1.3 Assessing suitability for listing, www.pbac.pbs.gov.au

72 Cancer Voices Australia, *Submission 49*, p. 5.

73 Amgen, *Submission 119*, p. 6; MA, *Submission 142*, p. 4.

74 Roche Products, *Submission 114*, p. 15.

75 *Committee Hansard*, p. 67.

76 *Submission 123*, p. [9]

> These aspects are rated highly important by women with ovarian cancer. Our research showed that greater than 90 per cent of women rated the value of a treatment highly if it extended the period of remission or made them feel better. We need a formal mechanism to evaluate and score quality of life and progression-free survival in healthy technology assessments of benefit and value.[77]

3.67 Novartis drew the committee's attention to a 2014 analysis of five countries, including Australia, that use cost per QALY versus those countries that do not, which found that access to novel cancer medicines was lower in countries using QALY than in the countries not using QALY. Novartis noted that this analysis also found, based on recent survival data, the countries which use fewer novel medicines may achieve less favourable outcomes for patients.[78]

3.68 Roche Products noted that several countries are investigating multi-criteria decision making, 'which incorporates numerous decision criteria and also allows for weighted consideration for the criteria'. Roche Products proposed that a review of the PBAC process could usefully draw on the experience of countries such as the Netherlands, Sweden and the Canadian province of Quebec in considering indirect costs and benefits such as patient and carer work productivity.[79]

3.69 Mr Richard Vines, Executive Chair, Rare Cancers Australia, summed up the general tenor of many submissions.

> This issue is not just about money; it is about compassion. It is about hope. It is about quality of life. It is about quantity of life. It is about time with children. It is about time with family. And it is about dignity and grace at the end of life. It is about how we as a community care for those amongst us who are most vulnerable. Perhaps, most critically, it is also about how we empower our cancer physicians to care for us. They are the ones we trust with our lives, no-one else.[80]

Facilitating input from clinicians and the community

3.70 Many submitters argued that a key step in balancing economic considerations with greater recognition of broader quality of life considerations in the assessment of cancer medicines is for there to be greater emphasis placed on expert oncology and consumer input into the decision making process.[81]

3.71 Current PBAC processes include provision for expert oncology and consumer comments to be considered as part of the evaluation of applications for PBS subsidy. Patients, carers, members of the public and health professionals and members of

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77 *Committee Hansard*, p. 11.

78 *Impact of cost-per-QALY reimbursement criteria on access to cancer drugs*. IMS Institute for Healthcare Informatics report, December 2014, cited in *Submission 87*, p. 28.

79 *Submission 114*, p. 15.

80 *Committee Hansard*, p. 40.

81 See for example: Melanoma Patients Australia, *Submission 116*, p. [3]; MSD, *Submission 120*, p. [5]; Ovarian Cancer Australia, *Submission 137*; MA, *Submission 142*, p. 4;

consumer interest groups are able to provide comments on applications under consideration at particular meetings via an online submission process.[82]

3.72 The committee heard that consumers and consumer organisations can experience difficulties in participating in the PBAC process.[83]

3.73 The PBAC Guidelines also state that the PBAC may:

- seek expert opinion from relevant professional bodies and/or appropriate specialists;
- meet with relevant medical professional organisations; and
- seek input from appropriate consumer bodies.[84]

3.74 However, the committee heard that such stakeholders should have a stronger voice in work of the PBAC, as well as providing input to decision makers about the reimbursement of individual cancer medicines.[85]

3.75 Dr Christopher Steer, President, Private Cancer Physicians of Australia and Member of the Medical Oncology Group of Australia told the committee of the key role that clinicians can play in informing the assessment of cancer drugs. Dr Steer described clinicians as gatekeepers of the process caught between the population based thinking of the PBAC and government and the need to advocate for the individual patient:

> We cancer clinicians understand the relative benefits and limitations of new treatments according to clinical trial evidence. We feel we can advise decision makers from a position of some authority based on science.[86]

3.76 Ms Nicola Richards, Head of Public Affairs at MSD noted that the PBAC system needs to capitalise on the fact that Australia has some of the world's leading oncologists:

> We are often involved in the cutting-edge clinical trials so who better than them to give the PBAC advice on: if we do not have overall survival for this drug for five years, what do they think this offers their patients and what do the patients think it offers them? Because two to three months for patients and clinicians is often the bridge between one treatment and the next treatment and extends their life.
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> Every advance in a cancer like breast cancer is a combination of incremental benefit over time. It is not usually one massive jump. We are

82 DOH, PBS, PBAC Meeting Agenda and Consumer Comments, http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-consumer-comments (accessed 15 September 2015)

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84 DOH, *PBAC Guidelines*, Version 4.4, Role of the Pharmaceutical Benefits Advisory Committee, www.pbac.pbs.gov.au.

85 MA, *Submission 142*, p. 4.

86 *Committee Hansard*, p. 51.

> always looking for the massive jump in outcome survival for any drug but that does not happen overnight and it does not happen easily. So that input you will see in a lot of the submissions is around formalising the way consumers can say what is the value of this drug to them outside of the actual clinical evidence that the companies are well positioned to place and from doctors who have used the drug? What do they see the value to patients as? In Canada they have a way that that is taken into formal consideration through the process.[87]

3.77 Cancer Action Victoria told the committee:

> Cancer patients are important stakeholders who should have a greater involvement. While the Australian system provides for consumer representation on the PBAC, and allows for consumer input in relation to individual products, the opportunity for the consumer voice is limited.[88]

3.78 Cancer Voices Australia emphasised the importance of greater involvement of consumer organisations:

> This is a compelling reason for greater input from consumer organisations when PBAC is making approval decisions, especially as Australia has little post-marketing surveillance of disease-control effectiveness or the maintenance of good quality of life. We recommend that cancer consumer groups, such as Cancer Voices and the Australian Cancer Consumer Network (a new network of 30 cancer consumer groups), be consulted to obtain the broad view of the many.[89]

3.79 In its White Paper, CDA noted the need for more meaningful engagement with consumer groups by the PBAC, together with greater visibility and transparency of PBAC processes.[90] CDA recommended that the PBAC improve and increase its communication with consumers and consumer groups, including through social media, and provide improved guidance on how to make submissions, how submissions are used and how decisions are made.[91]

3.80 CDA also noted that cancer patients and consumer organisations feel significantly underrepresented, detached and disenfranchised from the PBAC assessment process, 'despite being the actual end-users of the medicines and being best placed to make judgements on the impacts of medicines'. To address this, CDA recommended the establishment of a consumer sub-committee the PBAC could call on for information regarding specific conditions and the inclusion of at least one consumer representative on the PBAC with a cancer background.[92]

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87 *Committee Hansard*, pp 28-29.

88 *Submission 151*, p. 2.

89 Cancer Voices Australia, *Submission 49*, p. 5.

90 Cancer Drugs Alliance, *Improving Access to Cancer Medicines*, White Paper, March 2015 (CDA White Paper), pp 12-13.

91 CDA White Paper, p. 12.

92 CDA White Paper, p. 13.

3.81 In its evidence to the inquiry the PBAC outlined the steps it is currently taking to enhance the ability of clinicians and consumers to participate in its work. The PBAC described some of the initiatives it considers could enhance the participation of consumers and clinicians, including increased transparency throughout the system and improving the level of information available to consumers and patient groups. The PBAC noted that consumers and patient groups are currently hampered in their ability to find out what is on the agenda for PBAC meetings and to access important detail in relation to products under consideration and acknowledged that there is no systematic communication strategy with respect to committee recommendations. The PBAC told the committee that it recognises the need for a more systematic approach to communicating committee recommendations, appropriately tailored to consumers, while still maintaining the integrity of the scientific and clinical research that underpins them. The PBAC has been working with DOH to address this.[93]

3.82 The PBAC submitted that the current emphasis on protecting commercial-in-confidence information does not encourage an effective discussion in the community of the real benefits, harms and cost of new medicines that come before the PBAC. The PBAC noted that cost and price information is systematically redacted from published documents and consumers and clinicians do not have access to the data provided to the PBAC. The committee heard that this can lead to a mismatch between the information upon which the PBAC has based a decision and the information provided in the public domain regarding a drug. Dr Hill, told the committee:

> I guess the other part of it is that there has been a lot of literature on what happens when you look at what is reported in the public domain in medical journals about clinical trials, compared to what was done in the protocols or what was planned to be done in the trial protocols. So sometimes, for example, one outcome—maybe it is response rate, maybe it is quality of life, maybe it is something else—will be reported in the first paper that is publicly presented on a drug. And then what the committee might see is the complete set of outcomes, so we might see not just response rate; we might see some survival data; we might see some harms; we might see more detailed side effects. We might see a whole lot of stuff that is in the regulatory dossier and that becomes part of the PBAC submission that gives us a different perspective to that which is presented in the public domain at public meetings and in journal papers.[94]

3.83 Dr Hill further stated:

> I think it is very important that a committee such as the PBAC that is making recommendations to the minister on potential expenditure of public money should be able to provide all of the data that it sees in the public domain and if necessary say that we see an effect on X that looks like a 20 per cent effect, whereas what is being reported is an 80 per cent effect. I

93 *Submission 196*, p. 13.

94 *Committee Hansard*, p. 74.

> think it is incumbent upon good quality decision-making to be able to present that information.[95]

3.84 At its March 2015 meeting, the PBAC piloted a new process of consumer and patient hearings on selected applications, prior to the meeting. The PBAC heard presentations from consumer groups for Hepatitis C, melanoma, chronic lymphoma and inflammatory bowel disease.[96] In July 2015 the PBAC convened a second consumer hearing on biosimilar medicines in the context of its consideration of applications at its March and July meetings.

3.85 The PBAC told the committee:

> For the first time, these hearings allowed a direct conversation between the PBAC and patient groups about the benefits and harms and costs of some of the medicines on the Committee agenda. Both the PBAC and patient groups found these discussions extremely informative. Equally, the PBAC members were concerned to hear directly that the perceived benefits from some of these new drugs were completely at odds with the evidence that was in company submissions.[97]

A role for formal consultation mechanisms

3.86 Submitters noted that more formal mechanisms for capturing stakeholder input could play a significant role in evaluating questions of quality of life and value in the assessment of cancer medicines and could help to ensure that the assessment of a new medicine for subsidisation incorporates the views of the patients, their clinicians and the broader society.[98] MA submitted:

> The community has little voice in the system that it relies upon to measure the value of life and the additional value new cancer medicines provide to the public. … This contrasts with the UK where there was widespread debate following the approval of sunitinib in the UK in 2008/9 which resulted in NICE's review of their current process in regard to assessing the value of cancer medicines and adoption of new criteria, which included an increase in ICER threshold deemed acceptable by NICE. (Rafferty, 2009) Australia has not yet had a meaningful debate about the value of life, including 'end of life care', and what the community considers acceptable.[99]

3.87 The PBAC also identified a need for more formal discussion around community values and opportunity costs associated with health expenditure:

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95 *Committee Hansard*, p. 75.

96 Minister for Health, the Hon Sussan Ley MP, *More consumer consultation in PBS process*, Media Release 13 March 2015.

97 *Submission, 196*, p. 13.

98 See for example, MA, *Submission 142*, p. 4; Pharmaceutical Society of Australia, *Submission 176*, p. 6; Dr Katherine Nielsen, Ovarian Cancer Australia, *Committee Hansard*, p. 10; Mr David Pullar, Roche Products, *Committee Hansard*, p. 22; CVA, *Submission 49*, p. 4.

99 *Submission 142*, p. 21.

> There needs to be a frank and complete discussion between the community and pharmaceutical manufacturers about what the Australian community expects in terms of benefits and harms of new medicines, balancing early access uncertainty, and understanding opportunity cost compared to other use of the same health care resources and the community's willingness to pay. The PBAC could then reflect these values and preferences accurately in its assessment and recommendations.[100]

3.88 Evidence to the committee noted the benefit of various models of formal community engagement used overseas as part of HTA and suggested that Australia could draw on this experience. Takeda submitted that formal mechanisms such as these offer the ability to account for attributes associated with a medicine that are beyond the narrow terms of 'survival' and 'cost'.[101] Mr David Pullar, representing Roche Products, told the committee that citizen's councils offer a means of balancing the academic rigour of the PBAC process with consideration of social and ethical questions:

> What we see is: the PBAC are technical experts in health economics, medicine and related fields; they are not necessarily representative of the broader community when it comes to making social and ethical judgements. So what we have seen has worked well, particularly in Ontario in Canada, and in the UK, with these citizens' juries, is: they are asked those social and ethical questions. The PBAC will look at the data and they will then have to translate that into a prioritisation: 'This works this well; it delivers these benefits; here is what we are willing to pay for that, and here is how we trade that off against other medicines we could spend money on.' So what a citizens council could look at is: end-of-life care versus early intervention; treating a rare condition that may be disadvantaged at the expense of maybe a large population. So it is those social and ethical judgements, where it really is up to the community to have a voice, where we think they would play in, and that would complement the economic and clinical analysis.

3.89 MA outlined measures adopted in the United Kingdom (UK) to facilitate greater stakeholder involvement:

> The UK has also invested heavily in processes to place the public and patients at the heart of decision-making through stakeholder involvement in order to better capture the community's experiences and needs. Members of the public now sit on the NICE Board; patient representatives provide input to technology assessments and are involved in guideline development in addition to the establishment of a Citizen's Council.[102]

100 *Submission 196*, p. 15.

101 *Submission 122*, p. 6

102 *Submission 142*, p. 22.

3.90 The UK Citizen's Council (Council) is a panel of 30 members of the public, chosen to reflect the demographic characteristics of the UK.[103] The council meets annually to consider issues requiring value judgements identified through the activities of NICE's advisory bodies.[104] The Council is intended to provide NICE with a public perspective on overarching moral and ethical issues. The Council's recommendations and conclusions are incorporated into social value judgements and, where appropriate, into NICE's methodology.[105]

3.91 Council members meet annually for two days at a time. The Council's discussions are arranged and run by independent facilitators and are open to public observers. During the meetings, Council members listen to different views from experts on a topic and undertake exercises which allow them to examine the issues in detail and thoroughly discuss their own views. The members' views and conclusions are captured by an independent rapporteur and the report is circulated to members for comment and amendment before finalising. After a meeting, the report is made available for public comment. A summary of these comments along with the report are then presented to NICE's board for discussion.

3.92 MA also noted the success of the pan-Canadian Oncology Drug Review (pCODR) process in capturing the input of all stakeholders:

> The pCODR process was considered successful, partly because of the inclusion and meaningful involvement of all stakeholders; transparency and rigour of HTA process and decision making criteria; together with incoproation of broad-based considerations of societal and patient value. The pCODR model reflected a deliberate decision to adopt a stakeholder focussed approach with cancer and to overcome challenges faced in HTA. pCODR delivered high quality, practical, scientific advice that squarely addressed the issues raised by patients, clinicians and cancer agencies that were unable to be addressed under conventional HTA approaches.[106]

3.93 The committee notes that pCODR has been integrated into the Canadian Agency for Drug Technologies and Health (CADTH), but understands that it has retained its emphasis on incorporating stakeholder input throughout the assessment process.

3.94 pCODR takes account of evidence from patient groups, drug manufacturers, clinician-based tumour groups, and the pCODR Provincial Advisory Group. CADTH notifies patient groups at the outset of a pCODR review and invites them to provide input. This step is intended to capture patients' experiences and perspectives of living

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103 The members of the Citizens Council reflect the age, gender, socioeconomic status and ethnicity of the people of England and Wales. Councillors are recruited by an independent organisation and for a period of three years, with one third retiring each year.

104 National Institute for Health and Care Excellence, Citizens Council, https://www.nice.org.uk/get-involved/citizens-council (accessed 6 June 2015).

105 National Institute for Health and Care Excellence, Citizens Council, https://www.nice.org.uk/get-involved/citizens-council (accessed 6 June 2015).

106 *Submission, 142*, pp 22-23.

with a medical condition for which a drug under review is indicated, their experiences with currently available treatments, and their expectations for the drug under review.[107]

3.95 Patient values are also considered in the deliberations of the pCODR Expert Review Committee (pERC) which includes patient representatives alongside clinicians and economists. An interview with patient representatives of the pERC suggests that patient perspectives are genuinely considered alongside economic, clinical and implementation considerations and illustrates the capacity of a forum such as the pERC to balance competing perspectives in funding decisions:

> **JSH:** I want to go back to the patient values quadrant. Some people might cynically say, "They spend time on it, but do you really think it matters?" Can you think of an example [in which] you feel that that quadrant made an important contribution to a recommendation that the entire committee made?
>
> **Response:** One example for me was when I could see the sense of the table shifting as we focused on the patient reports about their experience with the disease, their experience with the drug and the difference that the drug was making to their quality of life. The difference, in the presentation from the economic guidance report, was a small difference, but I think it became clear to the table, looking at the patient input that, in fact, it was a substantial difference to patients. We were looking at a small increase in progression-free survival, but in the eyes of the committee, the benefit of reducing a very unpleasant side effect was recognized to be more significant in terms of the difference it made in quality of life: more than just applying that small difference in progression-free survival would usually suggest in the decision matrix that we're faced with. It made a real difference to the final recommendation.
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> **Response:** I can remember a time talking about a certain drug and a side effect. The side effect profile wasn't drawing too much attention, and a patient member spoke up and said, "Whoa, I've had that. That's really nasty. And, if there's a drug that has a similar cost and a similar benefit and can avoid that side effect, we should be thinking about that."
>
> **JSH:** Do you think it's worthwhile considering the economic evidence, or do you find [that] it's not really that useful?
>
> **Response:** In the system we have, many treatments we're providing are going to be paid for, by and large, by the public purse.
>
> **Response:** And, every time you pay for x, you can't pay for y. I value the general practitioner's perspective on perc because of the reminders that there's a world out there besides cancer, and if we spend x amount of money on oncology drugs, it may come out of mental health or heart

107 CADTH pan-Canadian Oncology Drug Review, https://www.cadth.ca/pcodr/about-pcodr

> disease or something else, and we need to be reminded of that, because we're in the cancer bubble.[108]

Committee view

3.96 The committee notes the significant challenges associated with assessing the cost-effectiveness of cancer medicines. The increasingly targeted nature of cancer treatments, often delivering significant but incremental improvements in patient outcomes, combined with the fact that cancer medicines are generally more expensive than non-cancer medicines is a significant test for the PBS.

3.97 Funding decisions must also be equitable and robust. The committee recognises that the methodologies employed by PBAC seek to establish a level playing field. Cancer patients and non-cancer patients alike, must have confidence that decisions are based on a rigorous examination of appropriately robust clinical data. At the same time, the committee recognises that such an approach can, in itself be inherently time consuming.

3.98 The committee notes calls for the adoption of a more flexible approach to the evidential requirements of the system to address the challenges associated with assembling clinical data in relation to cancer medicines. The committee considers that greater formal emphasis should be placed on quality of life considerations within the PBAC process and understands the challenges this presents. The current review of the PBAC Guidelines offers an opportunity to examine the issues raised regarding the PBAC's cost effectiveness methodology in closer detail in consultation with all relevant stakeholders. At the same time, consideration should be given to avenues for facilitating more formal discussion regarding community values and health expenditure.

3.99 The committee also notes calls for consumers and clinicians to play a more central and substantial role in the evaluation of new medicines. The committee recognises the PBAC's commitment to improving the effectiveness of its engagement with clinicians and consumers and the steps it is taking, together with DOH, to improve the transparency and accessibility of the process.

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108 Current Oncology, Meaningful patient representation informing Canada's cancer drug funding decisions: views of patient representatives on the Pan-Canadian Oncology Drug Review, October 2014, 21(5) 263-266, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4189566/