

The Senate

Community Affairs
References Committee

Availability of new, innovative and specialist
cancer drugs in Australia

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44th Parliament

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ABBREVIATIONS

| | |
|-----------|-----------------------------------------------------------------|
| ACD | Australian Cancer Database |
| Act | <i>National Health Act 1953</i> |
| AIHW | Australian Institute of Health and Welfare |
| ALK | anaplastic lymphoma kinase |
| ALLG | Australasian Leukaemia and Lymphoma Group |
| AMWG | Access to Medicines Working Group |
| ANZCHOG | Australian New Zealand Children's Haematology/Oncology Group |
| ARTG | Australian Register of Therapeutic Goods |
| AusPAR | Australian Public Assessment Report |
| AYAs | adolescents and young adults |
| BCNA | Breast Cancer Network Australia |
| CADTH | Canadian Agency for Drug Technologies and Health |
| CAV | Cancer Action Victoria |
| CBCF | Cure Brain Cancer Foundation |
| CCA/COSA | Cancer Council Australia/Clinical Oncology Society of Australia |
| CDA | Cancer Drugs Alliance |
| CDF | Cancer Drugs Fund |
| CDR | Common Drug Review |
| CLL | Chronic Lymphocytic Leukaemia |
| committee | Senate Community Affairs Reference Committee |
| Council | United Kingdom Citizen's Council |
| CVA | Cancer Voices Australia |
| DAE | Deloitte Access Economics |

| | |
|------------|-------------------------------------------------------|
| DOH | Department of Health |
| EFC | Efficient Funding of Chemotherapy |
| EMA | European Medicines Agency |
| F1 | Formulary 1 medicines |
| F2 | Formulary 2 medicines |
| FDA | Food and Drug Administration |
| Guidelines | Pharmaceutical Benefits Advisory Committee Guidelines |
| HSANZ | Haematology Society of Australia and New Zealand |
| HTA | Health Technology Assessment |
| HSDP | Highly Specialised Drugs Program |
| IARC | International Agency for Research on Cancer |
| ICER | Incremental Cost Effectiveness Ratio |
| IPU | Individual Patient Use |
| Janssen | Janssen-Cilag Pty Ltd |
| LFA | Leukaemia Foundation of Australia |
| Lilly | Eli Lilly Australia |
| LSDP | Life Saving Drugs Programme |
| MA | Medicines Australia |
| MAP | Managed Access Programme |
| MBS | Medical Benefits Schedule |
| MES | Managed Entry Scheme |
| Minister | Minister for Health |
| MOGA | Medical Oncology Group of Australia |
| MSAC | Medical Services Advisory Committee |
| MSD | Merck Sharp and Dohme |
| NCR | national chemotherapy registry |

| | |
|-----------------|-----------------------------------------------------------------------------|
| NICE | National Institute for Health and Care Excellence |
| NHPA | National Health Priority Areas |
| NHS | National Health Service |
| NMP | National Medicines Policy |
| NN | Novo Nordisk |
| Novartis | Novartis Oncology Australia New Zealand |
| OCA | Ovarian Cancer Australia |
| OS | overall survival |
| Panel | Expert Panel, Review of Medicines and Medical Devices |
| PAG | Provincial Advisory Group |
| PATS | Patient Assisted Travel Schemes |
| PBAC | Pharmaceutical Benefits Advisory Committee |
| PBS | Pharmaceutical Benefits Scheme |
| pCODR | pan-Canadian Oncology Drug Review |
| PCPA | Private Cancer Physicians of Australia |
| pERC | pCODR Expert Review Committee |
| PFS | Progression Free Survival |
| Price Agreement | An agreement made under section 85AD of the <i>National Health Act 1953</i> |
| RCA | Rare Cancers Australia |
| SAS | Special Access Scheme |
| SHPA | Society of Hospital Pharmacists of Australia |
| SIBs | social impact bonds |
| TGA | Therapeutic Goods Administration |
| UK | United Kingdom |
| US | United States |
| WISH | World Innovation Summit for Health |

| | |
|----|---------------------------------|
| WM | Waldenstrom's Macroglobulinemia |
|----|---------------------------------|

LIST OF RECOMMENDATIONS

Recommendation 1

6.40 The committee recommends that the Australian Government initiate a comprehensive review of the system for the registration and subsidisation of medicines. The review should examine:

- all available pathways for the registration and listing of new medicines, or new indications for medicines already registered on the ARTG and listed on the Pharmaceutical Benefits Scheme, including making provision for utilisation of assessments conducted by comparable overseas regulators; provision for clinicians and/or patient groups to apply for an extension of existing registrations to additional indications, managed access programs and risk-sharing, and the adoption of more flexible evidential requirements;
- options for improving the operation of assessment processes including:
 - enhancing engagement with sponsors and other stakeholders to better tailor their applications to the requirements of the PBAC, including consideration of pre-application planning meetings;
 - applying tiered assessment processes as a means of matching resources to the complexity of applications;
 - encouraging greater cooperation between the PBAC, the TGA and the Medical Services Advisory Committee, including examination of options for enhancing the operation of parallel processing arrangements; and
 - ensuring greater transparency throughout the assessment process;
- options for expanding the post-market review of medicines;
- enhancing and formalising mechanisms for consumers and clinicians to play a more central and substantial role in the evaluation of new medicines and new indications for already listed medicines, including:
 - consideration of options for expanding consumer and clinician representation on the PBAC;
 - enhancing existing avenues for stakeholder input, including the use of consumer and patient hearings; and
 - avenues for incorporating public perspectives on overarching moral, ethical and opportunity cost considerations into PBAC decision making processes, including consideration of models employed by comparable overseas regulators; and
- options for ensuring that the necessary administrative and technical resources are available to support the implementation of an enhanced PBAC system.

Recommendation 2

6.41 The committee recommends that the Australian Government commission a review of current data collection mechanisms for cancer medicines, including identification of:

- obstacles to the integration of existing databases and potential avenues for addressing these;
- opportunities to incorporate data from post-market evaluations; and
- avenues for capturing data relating to the off-label use of cancer medicines.

Recommendation 3

6.42 The committee recommends that the Australian Government establish a Steering Committee to examine the feasibility of establishing a national register of cancer medicines.

Chapter 1

Introduction

Access to cancer drugs in Australia

1.1 Australia is often described as the cancer capital of the world with the highest age-standardised incidence of cancer. Half of all Australians will develop cancer in their lifetime and one in five will die from it.¹ Australia also has cancer survival outcomes that are equivalent to the best in the world. Australia's one year survival rate for all cancers combined is 81 per cent and overall five year relative cancer survival rates are more than 66 per cent.² Together with investment in cancer detection and screening, investments in medical research have led to dramatic advances in the way cancer is treated and will be treated in the future.³

1.2 At the same time, there is widespread concern that Australian cancer patients continue to face significant delays and expense in accessing new cancer drugs, or existing drugs that are not available under the Pharmaceutical Benefits Scheme (PBS) for their form of cancer.⁴

The inquiry

1.3 On 3 December 2014, on the motion of Senator Nick Xenophon, the Senate referred the following matter to the Senate Community Affairs References Committee (committee) for inquiry and report by 26 March 2015:

The availability of new, innovative and specialist cancer drugs in Australia, with particular reference to:

- (a) the timing and affordability of access for patients;
- (b) the operation of the Pharmaceutical Benefits Advisory Committee and the Pharmaceutical Benefits Scheme in relation to such drugs, including the impact of delays in the approvals process for Australian patients;
- (c) the impact on the quality of care available to cancer patients; and
- (d) any related matters.⁵

1 Medicines Australia (MA), *Committee Hansard*, 20 April, p. 1.

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

3 Cancer Drugs Alliance (CDA), *Submission 53*, p. 1.

4 See: Herald Sun, *Melbourne woman pays \$5k for drug PBS doesn't cover for her type of cancer*, 14 December 2014, <http://www.heraldsun.com.au/news/victoria/melbourne-woman-pays-5k-for-drug-pbs-doesnt-cover-for-her-type-of-cancer/story-fni0fit3-1227155867412> (accessed 8 June 2015); News.com.au, Lifestyle, *Cancer sufferer Chris Brugger's family spend \$16,000 every three weeks just to keep him alive*, 20 April 2015, <http://www.news.com.au/lifestyle/health/cancer-sufferer-chris-bruggers-family-spend-16000-every-three-weeks-just-to-keep-him-alive/story-fneuzlbd-1227312367195> (accessed 8 June 2015)

5 *Journals of the Senate*, No. 73-3 December 2014, p. 1966.

1.4 On 9 February 2015, the Senate extended the reporting date to 22 May 2015.⁶ The reporting date was subsequently extended to 17 September 2015.⁷

Conduct of the inquiry

1.5 The committee advertised the inquiry in *The Australian* on 15 January 2015. Details of the inquiry were placed on the committee's website and the committee wrote to 54 organisations, inviting submissions by 27 February 2015. Submissions continued to be accepted after that date. The committee received 205 submissions. A list of the individuals and organisations who made submissions to the inquiry is provided at Appendix 1.

1.6 A public hearing was held in Canberra on 20 April 2015. A transcript of the hearing is available on the committee's website,⁸ and a list of the witnesses who gave evidence at the hearing is provided at Appendix 2. The committee thanks those individuals and organisations who contributed to the inquiry.

The structure of the report

1.7 Chapter 1 sets out the context of the inquiry. It provides an overview of the incidence of cancer in Australia and describes the regulatory pathway for the approval of medicines for marketing in Australia and reimbursement of the cost of some of those medicines through the PBS.

1.8 Chapter 2 examines the factors that affect the timing and affordability of access to new cancer medicines. It considers the operation of the TGA, the PBAC and the PBS.

1.9 Chapter 3 considers the PBAC's approach to the assessment of the cost and effectiveness of new cancer medicines as a prerequisite for listing on the PBS. It also considers the role that consumers and clinicians can play in this process.

1.10 Chapter 4 considers the impact of delays in the approvals process for Australian cancer patients. It examines the available pathways for access to cancer drugs not available through the PBS together with the need for timely and accurate information about new cancer medicines.

1.11 Chapter 5 examines some alternate models for facilitating access to new and innovative cancer drugs together with the need for improved data collection to support such models.

1.12 Chapter 6 presents the committee's conclusions and recommendations.

6 *Journals of the Senate*, No. 75-9 February 2015, p. 2054.

7 On 25 March 2015, the reporting date was extended to 17 June 2015, *Journals of the Senate*, No. 89—25 March 2015, p. 2399; on 17 June 2015, the reporting date was extended to 4 August 2015, *Journals of the Senate*, No. 97—17 June 2015, p. 2686; on 4 August 2015 the reporting date was extended to 9 September 2015, *Journals of the Senate*, No.103—10 August 2015, p. 2856; on 9 September 2015 the reporting date was extended to 15 September 2015, *Journals of the Senate*, No. 113—p. 3070; and on 15 September 2015 the reporting date was extended to 17 September 2015, *Journals of the Senate*, No. 116—p. 3120.

8 See: http://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs.

The incidence of cancer in Australia

1.13 It is estimated that 45 780 people will die from cancer in 2015, an average of 125 deaths every day.⁹ This figure represents approximately three out of every 10 deaths registered in Australia¹⁰ and is 84 per cent higher than the number of deaths reported in 1982 (24 922 cases).¹¹

1.14 The Australian Institute of Health and Welfare (AIHW) has estimated the risk of being diagnosed with cancer before the age of 85 is 1 in 2 for males and 1 in 3 for females.¹²

1.15 The number of expected diagnoses has increased 2.6 times compared to the number of new cancer cases reported in 1982 (47 417 cases). This corresponds to 467 cases per 100 000 people, compared to 383 cases per 100 000 people in 1982 (an increase of 22 per cent).¹³

1.16 The most common diagnoses for new cancer cases in 2014 was estimated to be:

- prostate cancer (17 050 cases);
- colorectal cancer (16 640 cases);
- breast cancer (15 410 cases);
- melanoma of the skin (12 640 cases); and
- lung cancer (11 580 cases).

1.17 Together, these forms of cancer comprise approximately 60 per cent of all expected diagnosed cancers.¹⁴

9 CDA, *Submission 53*, p. 1.

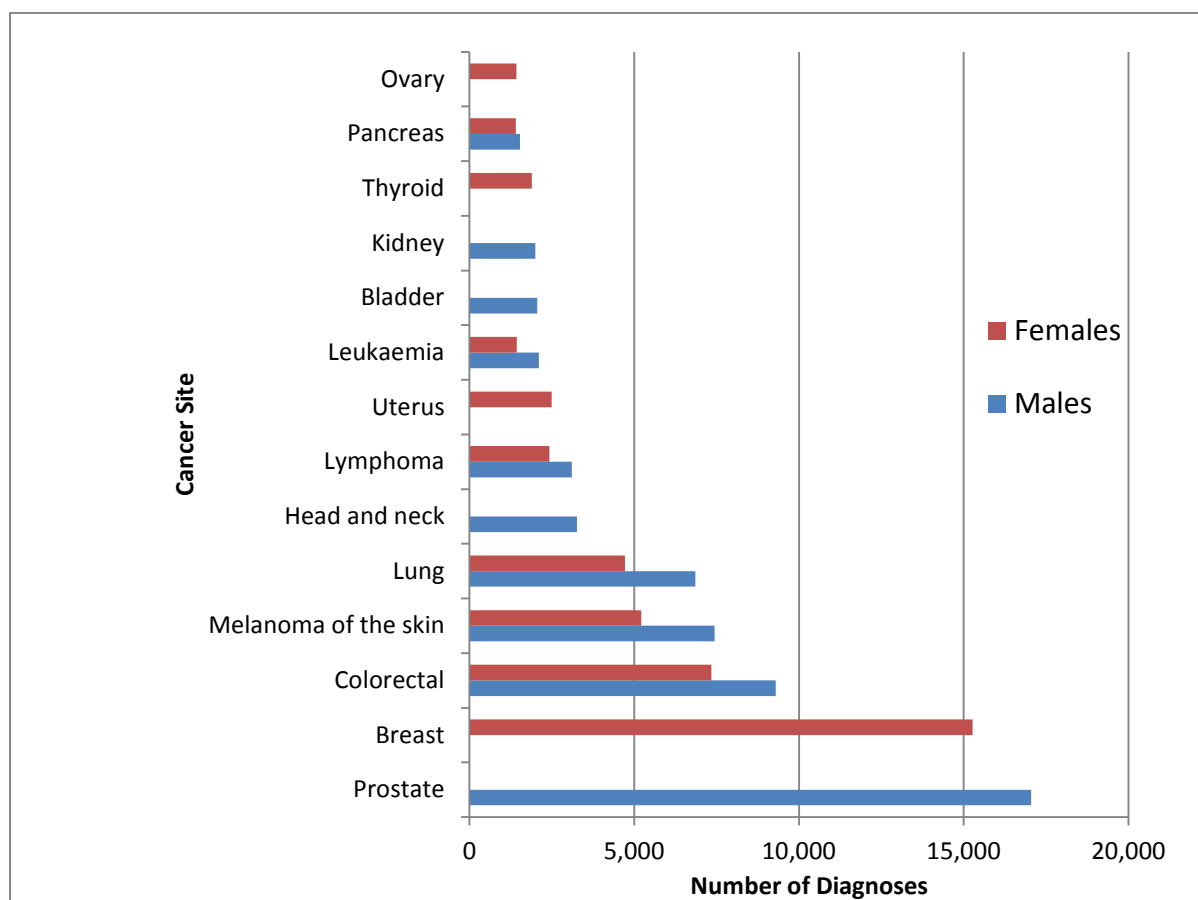
10 Australian Institute of Health and Welfare (AIHW) (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, p. 48.

11 AIHW (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, p. 51. The increased number of deaths does not correspond to the number of deaths per 100,000 people: 168 in 2014 to 209 in 1982 (a decrease of 20 per cent).

12 AIHW (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, pp 15 and 17. These estimates do not include certain carcinomas which are not required to be notified to public health authorities.

13 AIHW (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, p. 19.

14 AIHW (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, p. 16.

Figure 1.1: Estimated 10 most common diagnoses of cancer, Australia, 2014

Australian Institute of Health and Welfare, *Cancer in Australia, An overview 2014*, Cancer Series No.90, Cat. No. CAN 88, Canberra: AIHW, p. 17.C

1.18 The AIHW predicted the diagnosis of 150 000 new cases by 2020, an increase of almost 40 per cent from 2007. The AIHW attributes this increase primarily to an ageing and increasing population, and has reported:

Which cancers will present the biggest burden in 2020?

For males, prostate cancer is expected to remain the most common cancer diagnosed in 2020 (25,300 cases), followed by bowel cancer and melanoma of the skin (about 10,800 cases each) and lung cancer (7,500 cases). For females, breast cancer is projected to continue to be the most common cancer diagnosed in 2020 (17,200 cases), followed by bowel cancer (9,200), melanoma (6,800) and lung cancer (6,100).

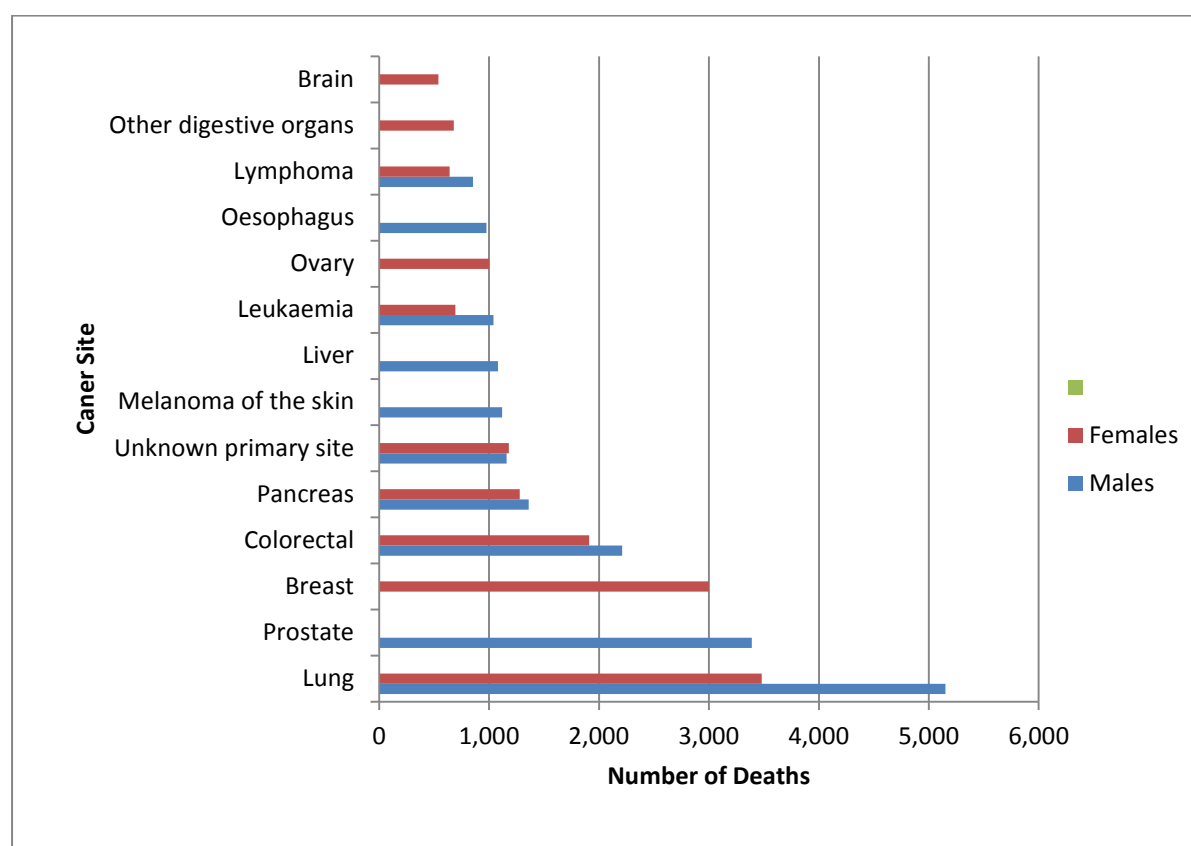
Which cancers are on the rise?

Age-standardised rates for liver cancer are projected to increase by 38% from 2007 to 2020 in males and 78% in females, while thyroid cancer rates are projected to increase by 33% in males and 62% in females.

Increases are also expected in rates for melanoma (30% males; 18% females), testicular cancer (25%) and lung cancer in females (16%).¹⁵

1.19 The most common causes of death resulting from cancer do not precisely correlate with the top five cancer diagnoses. Instead, lung cancer will be the most common cause of death (8 630 people), followed by colorectal cancer (4 120 people), prostate cancer (3 390 people), breast cancer (3 030 people) and pancreatic cancer (2 640 people). These five cancers represent just under half (48 per cent) of the total mortality from cancer, with lung cancer alone accounting for nearly one in five deaths (19 per cent).¹⁶

Figure 1.2: Estimated 10 most common causes of death from cancer, Australia, 2014



Australian Institute of Health and Welfare (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, p. 49.

15 AIHW (2012), *Cancer incidence projections, Australia 2011 to 2020*, Cancer Series No. 66, Cat. no. CAN 62, Canberra: AIHW, p. viii.

16 AIHW (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, p. 49.

1.20 The AIHW estimated that the risk of dying from cancer before the age of 75 years is one in nine for males and one in 13 for females. By the age of 85 years the risk increases to one in four for males and one in six for females.¹⁷

International comparison

1.21 The International Agency for Research on Cancer (IARC) (part of the World Health Organisation) maintains the GLOBOCAN database, which provides contemporary estimates on the incidence, mortality and prevalence of major cancer types at a national level for 184 countries.¹⁸

1.22 According to the most recent GLOBOCAN estimates, the number of new cancer cases diagnosed worldwide in 2012 was 14.1 million.¹⁹ In that same year, 122,031 new cases were diagnosed in Australia, representing less than one per cent (0.87) of the global diagnoses. However, the incidence rate for cancer in Australia (323 per 100,000) was higher than the rate for other regions.²⁰

1.23 In terms of mortality, the IARC estimated the number of deaths from cancer worldwide was 8.2 million in 2012. For Australia, 43,400 people were expected to die from cancer, a mortality rate of 96 per 100 000 people.²¹

Cancer as a national health priority

1.24 Cancer poses a complex challenge for the Australian healthcare system. Cancer is not one disease. It is many hundreds of diseases, each of which can manifest differently in each cancer patient. As the prevalence of cancer trends upwards, the health and economic impacts on individuals and the health system can be expected to continue to increase. At the same time, the costs of new cancer medicines are increasing at a faster rate than other new medicines.

1.25 Cancer is one of nine National Health Priority Areas (NHPA) and accounts for 19 per cent of the total disease-related burden, making it the highest disease-related burden on society.²²

17 AIHW (2014), *Cancer in Australia, An overview 2014*, Cancer Series No. 90, Cat. no. CAN 88, Canberra: AIHW, p. 50.

18 See: International Agency for Research on Cancer, World Health Organisation, *The GLOBOCAN Project*, <http://globocan.iarc.fr/Default.aspx> (accessed 23 January 2015).

19 See: International Agency for Research on Cancer, World Health Organisation, *All Cancers (excluding non-melanoma skin cancer): Estimated Incidence, Mortality and Prevalence Worldwide in 2012*, http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx (accessed 23 January 2015). This estimate did not include non-melanoma skin cancer.

20 See: International Agency for Research on Cancer, World Health Organisation, *Australia*, http://globocan.iarc.fr/Pages/fact_sheets_population.aspx?country=36 (accessed 23 January 2015).

21 See: International Agency for Research on Cancer, World Health Organisation, *Australia*, http://globocan.iarc.fr/Pages/fact_sheets_population.aspx (accessed 23 January 2015). The average world rate for 2012 was 102 per 100,000 people.

22 CDA, *Submission 53*, p. 2.

1.26 The annual cost of cancer to government has been placed between \$4 billion and \$5 billion per annum. This funding supports a range of measures along a continuum of care including: research, prevention programs and national screening programs as well as 'timely access to cost-effective, clinically indicated treatments through the Medicare Benefits Schedule (MBS) and the Pharmaceutical Benefits Scheme (PBS).' The Department of Health (DOH) states that the mix of funding must be balanced to deliver the best health outcome for the most cancer patients.²³

1.27 Expenditure on cancer medicines accounts for one third of current cancer funding. As Figure 1.3 illustrates, in 2013-14, \$1.5 billion was spent on subsidising the cost of PBS-listed cancer medicines.²⁴ This represents 16 per cent of the total PBS expenditure of \$9.2 billion.²⁵

Figure 1.3: Cost of PBS cancer medicines

| PBS expenditure for cancer medicines | Benefits paid (\$ billions) | | | | |
|-----------------------------------------|-----------------------------|---------|---------|---------|---------|
| | 2009-10 | 2010-11 | 2011-12 | 2012-13 | 2013-14 |
| PBS and RPBS benefits paid - cancer | \$0.994 | \$1.087 | \$1.135 | \$1.230 | \$1.486 |
| Total PBS benefits paid – all medicines | \$8.392 | \$8.873 | \$9.194 | \$8.996 | \$9.149 |

Department of Health, *Submission 197*, p. 22.

1.28 An additional \$50 million is used to fund the Herceptin Program each year.²⁶

Figure 1.4: Cost of Herceptin Program

| Expenditure for Herceptin Program (non-PBS) | Benefits paid (\$ millions) | | | | |
|---------------------------------------------|-----------------------------|---------|---------|---------|---------|
| | 2009-10 | 2010-11 | 2011-12 | 2012-13 | 2013-14 |
| Total benefits paid | \$48.9 | \$53.3 | \$54.1 | \$57.2 | \$53.3 |

Department of Health, *Submission 197*, p. 22.

1.29 DOH advised that cancer medicines are some of the most expensive medicines on the PBS:

Despite reaching one sixth of total expenditure, cancer-related scripts (2.6 million) supplied in 2013-14 represent only around 1% of all PBS scripts (213.7 million). The funding benefited approximately 3% (over 337,250 patients) of the total 9.8 million patients supported through the PBS in that year.²⁷

1.30 Cancer medicines are generally more expensive than non-cancer medicines and, as Figure 1.5 below illustrates, new cancer medicines make up an increasing proportion of total PBS expenditure on cancer medicines. DOH advised that:

23 DOH, *Submission 197*, p. 5.

24 *Submission 197*, p. 5

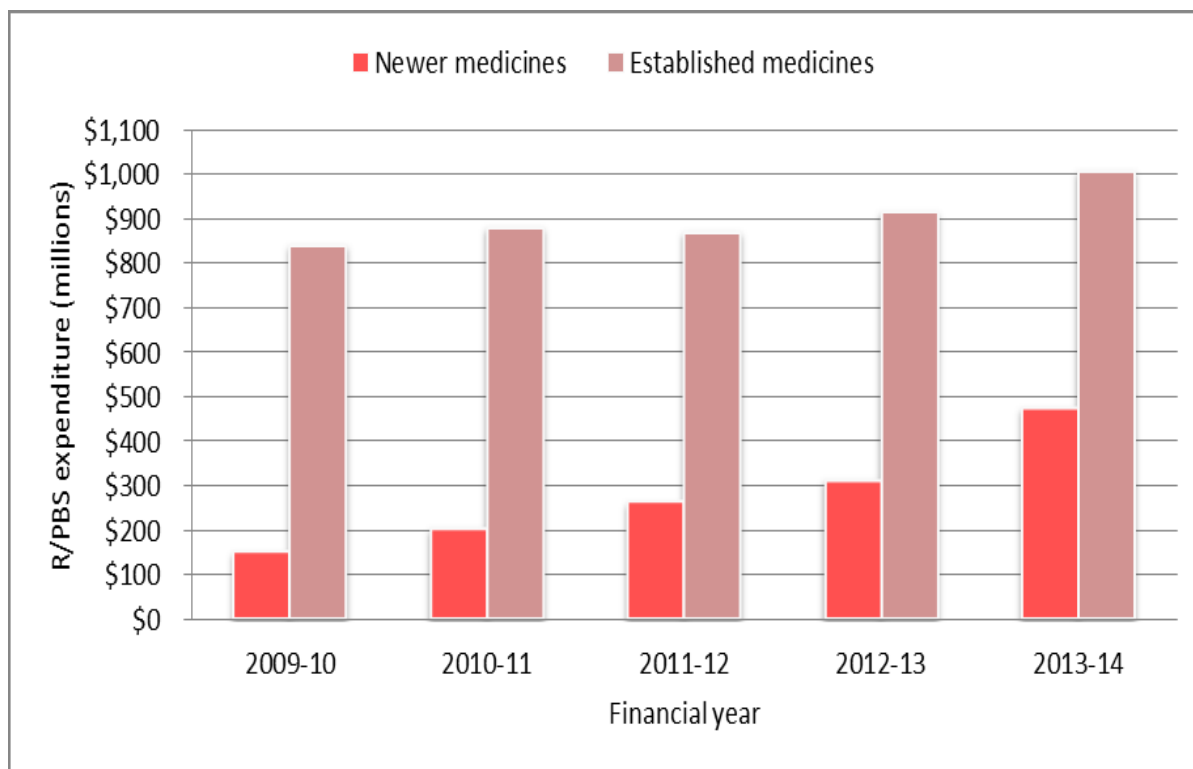
25 *Submission, 197*, p. 8.

26 *Submission 197*, p. 22. Herceptin is a treatment for breast cancer.

27 *Submission 197*, p. 8.

PBS benefits paid for newer cancer medicines increased at a rate of 33% per year over the last five financial years, compared to a growth rate of only 5% per year in benefits paid for established cancer medicines.²⁸

Figure 1.5: Cost of established versus newer PBS cancer medicines



Department of Health, *Submission 197*, p. 23.

Assessment of cancer medicines in Australia

1.31 The Australian Government employs a range of processes and mechanisms to assess the quality, safety, efficacy, effectiveness and cost effectiveness of health technologies and procedures. Collectively, these processes and mechanisms are referred to as Health Technology Assessment (HTA).

The DOH advises that '[a] well-performing HTA system will:

- facilitate patient access to cost-effective health technologies that improve health outcomes;
- minimise the use of technologies that are ineffective or harmful;
- contribute to value for money investments in health technology in the context of limited health care resources;
- keep pace with evolving technologies, clinical practices and HTA methodologies;
- provide clear information on processes, rules and outcomes to stakeholders; and

-
- ensure the system is designed to achieve these outcomes in the most timely, effective, efficient and targeted way'.²⁹

1.32 Concerns have been raised at the ability of the system to meet the above criteria and the vast majority of submissions have called for a fundamental review of the system.

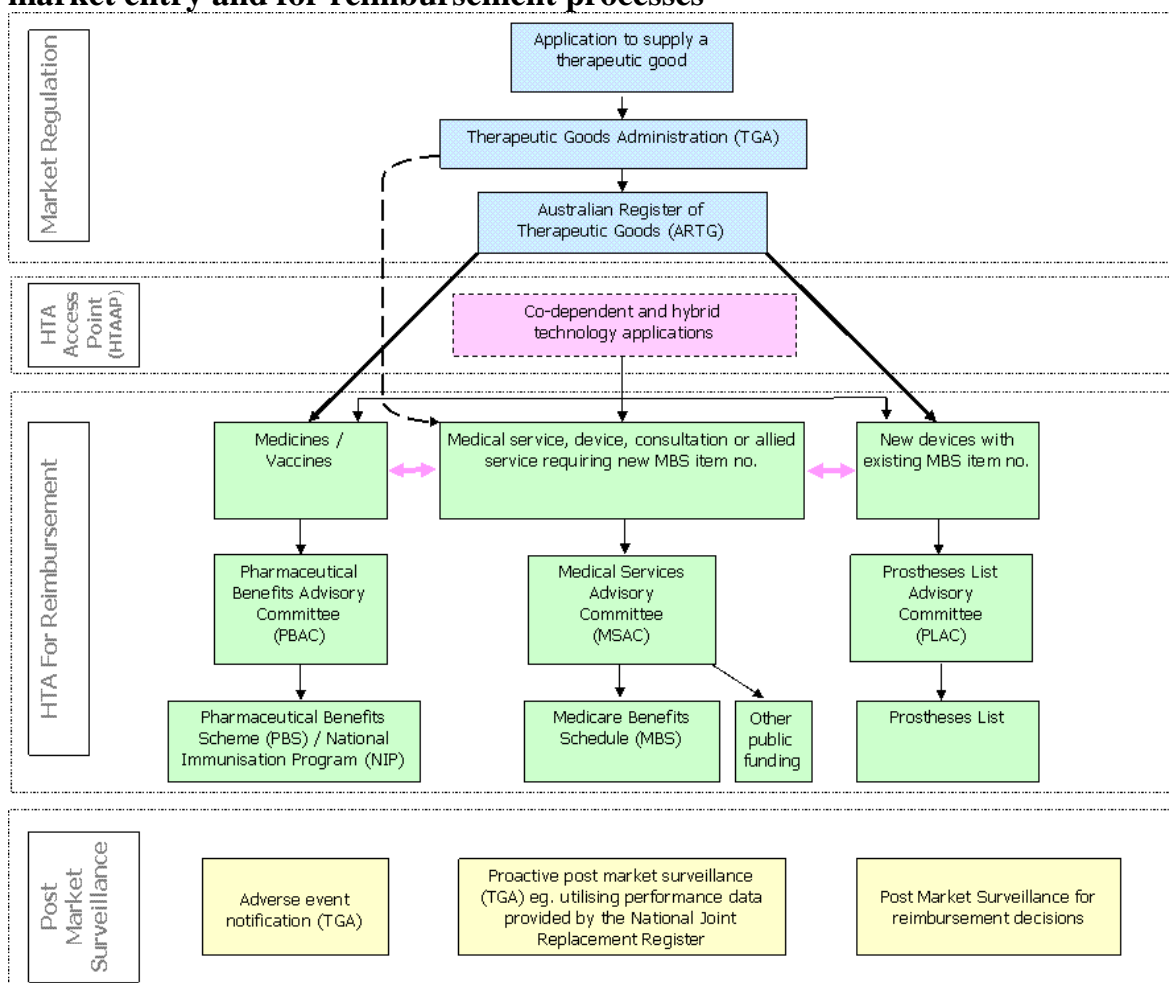
1.33 Through its HTA system, the Australian Government seeks to ensure the sustainability of the Australian Government's health financing arrangements. As Figure 1.6 illustrates, in order to gain approval and reimbursement of medicines in Australia sponsors are required to demonstrate the merit of the medicine against five critical requirements:

- quality, safety and efficacy, as assessed by the TGA;
- clinical and cost effectiveness, as assessed by the PBAC; and
- financial feasibility/acceptability as assessed by the Minister for Health and the Cabinet.³⁰

29 DOH, Health Technology Assessment, What is Health Technology Assessment (HTA), <http://www.health.gov.au/internet/hta/publishing.nsf/Content/about-1> (accessed 14 June 2015).

30 Deloitte Access Economics, Medicines Australia Oncology Industry Taskforce, 'Access to cancer medicines in Australia', July 2013, *Submission 142a*, p. v.

Figure 1.6: Map of current Australian Government HTA processes for market entry and for reimbursement processes



Department of Health, *Australian Government HTA Process*, Health Technology Assessment website.³¹

1.34 The following section provides an overview of the pathways through which cancer medicines are assessed, approved and reimbursed for use in Australia.

Therapeutic Goods Administration

1.35 Before a medicine can be made available to patients in Australia, it must first receive regulatory approval from the TGA. The TGA administers a uniform, national system of regulatory controls to ensure the quality, safety, efficacy and timely availability of therapeutic goods for human use. The TGA regulates therapeutic goods through:

- pre-market assessment;
- post-market monitoring and enforcement of standards; and

31 <http://www.health.gov.au/internet/hta/publishing.nsf/Content/commonwealth-1> (accessed 14 June 2015)

-
- licensing of Australian manufacturers and verifying overseas manufacturers' compliance with the same standards as their Australian counterparts.³²

1.36 The TGA approves and regulates products based on an assessment of risks against benefits, considering factors such as side effects, potential harm through prolonged use, toxicity and the seriousness of the medical condition for which the product is intended to be used.³³ While most therapeutic goods are required to undergo an evaluation by the TGA before they can be supplied in Australia, there are a number of ways that patients can gain access to products that have not been approved for use in Australia:

- Authorised prescribers: a medical practitioner may be granted authority to become an authorised prescriber of a specified unapproved therapeutic good to specific patients with a particular medical condition.
- Special access scheme: arrangements which provide for the import and/or supply of an unapproved therapeutic good for a single patient, on a case by case basis.
- Medicines that have not received TGA approval may be accessed only under specific circumstances.

1.37 Only medicines registered on the Australian Register of Therapeutic Goods can be included on the Schedule of Pharmaceutical Benefits (PBS Schedule).

The Pharmaceutical Benefits Scheme

1.38 Under the PBS the Commonwealth subsidises the cost of a wide range of prescription medications to all Australian residents who hold a medicare card.³⁴ Patients pay a contribution depending on their status as a general or concessional patient and the PBS provides safety nets, primarily through reimbursements paid to community or hospital pharmacies, to protect high medicine users from excessive medicine costs.³⁵

1.39 The overarching framework for the operation of the PBS is provided in the National Medicines Policy (NMP). Among other things, the NMP provides for 'timely access to the medicines that Australians need, at a cost individuals and the community can afford'.³⁶ The PBS Schedule lists all medicines available to be dispensed to patients at a Government-subsidised price.

32 DOH, Therapeutic Goods Administration, How the TGA regulates, <https://www.tga.gov.au/how-tga-regulates> (accessed 7 June 2015).

33 DOH, Therapeutic Goods Administration, How the TGA regulates, <https://www.tga.gov.au/how-tga-regulates> (accessed 7 June 2015).

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

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

36 DOH, *National Medicines Policy Document*, 2000, p. 1.

1.40 On 27 May 2015, the Minister for Health, the Hon Sussan Ley MP, announced a package of reforms to the PBS. In introducing the Pharmaceutical Benefits Scheme Access and Sustainability Package (reforms), the Minister stated:

This reform package is designed to be a sensible start that focuses on longer-term structural reform to enable ongoing investment in new medicines while ensuring they remain affordable for patients and taxpayers.³⁷

1.41 The reforms include:

...a five per cent reduction in the price taxpayers pay for on-patent medicines that have been listed for five years or more on the PBS. This is expected to deliver efficiencies of about \$1 billion to ensure new F1 medicines can be listed for patients as well.³⁸

1.42 The committee notes that the potential for this measure to impact on research and development of new medicines was raised during consideration of the National Health Amendment (Pharmaceutical Benefits) Bill 2015.³⁹

The Pharmaceutical Benefits Advisory Committee

1.43 The PBAC is an independent expert body comprised of doctors, health professionals and consumer representatives appointed by the Australian Government. The PBAC meets three times a year to consider new medicines for listing on the PBS. No new medicine can be listed unless the PBAC makes a positive recommendation.

1.44 When recommending a medicine for listing, the PBAC takes into account the medical conditions for which the medicine was registered for use in Australia, its clinical effectiveness, safety and cost-effectiveness. The PBAC is assisted in its analysis and advice by the Drug Utilisation Sub Committee and the Economics Sub Committee.⁴⁰

1.45 Following a positive recommendation from the PBAC, the sponsor of the medicine is required to negotiate pricing and any applicable prescribing restrictions with the DOH.⁴¹ If the cost is more than \$20 million in any one year of the Forward

37 The Hon Sussan Ley MP, 'Pharmaceutical Benefits Scheme to be reformed', 27 May 2015, <https://www.health.gov.au/internet/ministers/publishing.nsf/Content/health-mediarel-yr2015-ley063.htm> (accessed 16 September 2015).

38 The Hon Sussan Ley MP, 'Pharmaceutical Benefits Scheme to be reformed', 27 May 2015, <https://www.health.gov.au/internet/ministers/publishing.nsf/Content/health-mediarel-yr2015-ley063.htm> (accessed 16 September 2015).

39 Senator Hon Jan McLucas, *Senate Hansard*, 23 June 2015, p. 4159.

40 DOH, *Pharmaceutical Benefits Advisory Committee (PBAC)*, <http://www.pbs.gov.au/info/industry/listing/participants/pbac> (accessed 30 May 2015).

41 Prior to the 2014-15 Budget, pricing of pharmaceuticals was managed by the Pharmaceutical Benefits Pricing Authority (PBPA). The abolition of the PBPA was expected to help streamline the PBS listing process.

Estimates, the recommendation must then be approved by the Minister for Health or Cabinet.⁴²

Medical Services Advisory Committee (MSAC)

1.46 A separate but similar process applies for the assessment of medical services or technology. The MSAC is an independent expert committee that provides advice to the Minister for Health on the strength of evidence relating to the comparative safety, clinical effectiveness and cost-effectiveness of any new or existing medical service or technology, and the circumstances under which public funding should be supported through listing the service and technology on the MBS. The MSAC meets up to four times a year.

1.47 Co-dependent and hybrid pharmaceuticals are currently considered separately by the PBAC and the MSAC using different approaches to assessing evidence against the HTA criteria. This is because listing needs to occur under two separate funding programs.

Alternate access schemes

Life Saving Drugs Programme (LSDP)

1.48 The Australian Government provides subsidies for a limited range of medicines not eligible for funding under the PBS through the LSDP.⁴³ Through the LSDP, eligible patients are able to gain access to expensive lifesaving drugs for very rare life-threatening conditions. The LSDP currently subsidises ten medicines for eligible patients with one of seven rare and life threatening diseases.

1.49 Submissions for a drug to be considered for inclusion in the LSDP must be lodged in conjunction with submissions to the PBAC for PBS listing. Submissions are received in March, July and November each year by DOH. If the PBAC accepts that a drug is clinically effective for the proposed indication but rejects it for listing on the PBS on the grounds that it is not cost effective, the sponsor of the drug may request the application be considered for inclusion in the LSDP.⁴⁴

1.50 In April 2014, the then Minister for Health, the Hon Peter Dutton MP, announced a post-market review of the LSDP to examine issues such as access and equity, value for money and the future administration of the program.⁴⁵

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

43 Subsidised access is provided to eligible patients under section 32B of the *Financial Framework (Supplementary Powers) Act 1997* and schedule 1AA of the Financial Framework (Supplementary Powers) Regulations 1997, item number 415.009 (Targeted Assistance – Pharmaceuticals). See DOH, *Life Saving Drugs Programme, Post Market Review, Issues Paper*, April 2015, p. 7.

44 DOH, *Life Saving Drugs Programme (LSDP), Post Market Review, Issues Paper*, April 2015, p. 7.

45 DOH, *LSDP, Post Market Review, Issues Paper*, April 2015.

Orphan Drugs Program (ODP)

1.51 The ODP, administered by the TGA, was established to encourage drug manufacturers to develop and market medicines affecting small populations. An orphan drug is a medicine that is intended to treat, prevent or diagnose a rare disease, or is not commercially viable to supply to treat, prevent or diagnose another disease or condition.

1.52 Before an application to register an orphan drug is made, a sponsor must seek orphan drug designation. The quality, efficacy and safety of orphan drugs are assessed at the same standard as other registered medicines. Orphan drug designation by the TGA does not mean that the drug will be automatically considered for inclusion in the LSDP.⁴⁶

Comparable international models

1.53 A number of submissions highlighted models introduced overseas to improve access to new cancer drugs, and involve patients in the evaluation process.

United Kingdom

1.54 In 2010, the United Kingdom established the Cancer Drugs Fund to assist patients to access certain drugs before they receive National Institute for Health and Care Excellence (NICE) approval.⁴⁷ According to a 2013 report by Deloitte Access Economics, the fund subsidises drug treatments, including radiopharmaceuticals, for patients who have been unable to access a drug recommended by their oncologist.⁴⁸ The Cancer Drugs Alliance noted in its submission that the fund:

continues to cover approximately 59 cancer drugs and during the 5 years it has been in existence has allowed more than 60 000 cancer patients to receive treatment they would have not have otherwise had access to.⁴⁹

1.55 Patients in the UK can also be involved in setting decision-making criteria for the approval of new drugs and can participate in the Health Technology Assessment (HTA) committee.⁵⁰

Canada

1.56 In Canada, the pan-Canadian Oncology Drug Review (pCODR) was established in 2007 separate to the Common Drug Review (CDR) to assess cancer drugs and make recommendations to provincial cancer agencies/governments to guide

46 DOH, Orphan drugs, <https://www.tga.gov.au/orphan-drugs>, (accessed 1 June 2015)

47 Medicines Australia (MA), *Submission 142*, p. 22.

48 Deloitte Access Economics, Medicines Australia Oncology Industry Taskforce, 'Access to cancer medicines in Australia', July 2013, *Submission 142a*, p. 49.

49 Cancer Drugs Alliance, *Submission 53*, p. 4.

50 MA, *Supplementary Submission 142*, p. 8.

drug funding decisions. In April 2014, pCODR was integrated into the Canadian Agency for Drug Technologies and Health (CADTH).⁵¹

1.57 As part of the pCODR, patients can provide input at the beginning of and throughout the process for evaluating new cancer drugs.⁵² Medicines Australia noted that the pCODR model 'reflected a deliberate decision to adopt a stakeholder focussed approach with cancer and to overcome challenges faced in HTA'.⁵³

United States of America

1.58 The United States (US) Food and Drug Administration (FDA) regulates the use of prescription medications in the US. The FDA provides pharmaceutical companies with four pathways that 'get important new drugs to the patient earlier' to 'treat serious conditions and fill an unmet medical need'.⁵⁴ These are aimed at:

- Expediting Product Development through:
 - Fast Track Designation
 - Breakthrough Therapy Designation
- Expediting Registration through:
 - Accelerated Approval
 - Priority Review.⁵⁵

1.59 Fast Track Designation works by facilitating the development and expediting the review of medications. A pharmaceutical company applies for fast track consideration when there is no therapy available or if 'a therapy may be potentially better than available therapy'.⁵⁶

1.60 Merck Sharp and Dohme describe the Breakthrough Therapy Designation as 'unique in that the FDA invests significant resources and time in numerous discussions with the sponsor and close co-operation in the development of the clinical program'.⁵⁷ Depending on the type of application and the stage of development, an application to one of the four pathways can result in a range of different assistance options including

51 Medicines Australia (MA), *Submission 142*, p. 22–23.

52 MA, *Submission 142, Attachment 2*, p. 9.

53 MA, *Submission 142*, p. 22.

54 United States Food and Drug Administration, *Fast Track*, September 2015, <http://www.fda.gov/forpatients/approvals/fast/ucm405399.htm> (accessed 16 September 2015).

55 Merck Sharp and Dohme (MSD), *Submission 120a*, p. 4.

56 United States Food and Drug Administration, *Fast Track*, September 2015, <http://www.fda.gov/forpatients/approvals/fast/ucm405399.htm> (accessed 16 September 2015).

57 MSD, *Submission 120a*, p. 2.

access to rolling review, access between pathways and increased access to FDA advice during the approvals process.⁵⁸

58 United States Food and Drug Administration, *Breakthrough Therapy*, September 2015, <http://www.fda.gov/ForPatients/Approvals/Fast/ucm405397.htm> (accessed 16 September 2015).

Chapter 2

Timely access to new cancer medicines

2.1 A key theme throughout the inquiry has been the need for a fundamental review of the regulatory and reimbursement processes for cancer drugs. Some submitters told the committee that the current process has served Australia well, but expressed concern that without 'modernisation' it would not be able to keep pace with the growing trend in applications for new medicines.¹ Some submitters described the current process as complex and time-consuming and considered that it delivered suboptimal outcomes for Australian patients.²

2.2 Chapters 2 and 3 of this report examine the regulatory pathway for subsidised access to new cancer medicines in Australia and consider some aspects of that pathway that may be contributing to delays in access. Broadly speaking, evidence to the inquiry identified four key areas of concern: timeliness of decision making; assessment of cost-effectiveness; the need for greater consumer input and improved access to information. This chapter will focus on the first of these factors, while Chapter 3 will consider the assessment of cost-effectiveness, the impact of delayed access on cancer patients and the role for greater consumer input.

Timelines for access to new medicines in Australia

2.3 As noted in chapter 1, the committee heard that one of the key factors affecting access to medicines is the timing of applications by pharmaceutical companies to the TGA seeking registration of medicines and to the PBAC seeking reimbursement. The Department of Health (DOH) noted that for cancer medicines submitted for TGA approval between 2009-2014, submissions were made an average of 38 weeks after the lodgement of a submission to the United States (US) Food and Drug Administration (FDA) and an average of 38 weeks after the lodgement of a submission to the European Medicines Agency (EMA). DOH told the committee that this approach is often a function of the size of the Australian market:

This kind of business approach seeks to establish, as early as possible, a positive response in the regions offering the most potential for profit, due to their large population size. This avoids the situation where a deferral or rejection from a country with a small population, like Australia, could influence other authorities, thereby jeopardising the profit margins that could be achieved in larger countries/regions.³

2.4 The committee notes that this factor is outside the control of the TGA and PBAC.⁴ DOH told the committee:

1 Cancer Drugs Alliance (CDA), *Submission 53*, p. 5.

2 Medicines Australia (MA), *Submission 142*, p. 18; Cancer Council Australia/Clinical Oncology Society of Australia (CCA/COCSA), *Submission 145*, p. 18.

3 *Submission 197*, p.18.

4 Clinical Oncology Society of Australia, *Answers to Questions on Notice*, p. 2.

The ability to deliver timely access to medicines is also affected by the timing of the applications which, in Australia, is at the discretion of pharmaceutical companies. It is acknowledged that these companies operate in a global industry and this can affect their decisions. Sponsors often choose to apply first in the US or Europe, delaying consideration of the medicine in Australia.⁵

2.5 The PBAC said that comparisons of dates of regulatory submissions show that new products are submitted to the TGA 'a median of 105 days after they are submitted to the EMA, although the TGA accepts the same evidence package as the EMA'.⁶

2.6 In contrast, pharmaceutical companies provided some positive examples of the introduction of new medicines into the Australian market. For example, Bristol-Myers Squibb submitted:

... Australia was the second country in the world to approve ipilimumab (known as YERVOY) for the treatment of patients with advanced or metastatic melanoma in June 2011, just three months after its approval by the Food and Drug Administration (FDA) in the United States.⁷

2.7 The committee notes that this timely approval of ipilimumab may reflect the fact that Australia has the highest incidence of melanoma in the world.⁸

TGA registration process

2.8 The TGA registration process consists of eight phases with established timeframes specified under the *Therapeutic Goods Act 1989*.⁹ The committee received evidence suggesting that there is merit in reviewing the registration process to identify circumstances in which a more flexible approach might be supported. In particular, submitters identified options through which Australia might leverage off overseas regulators or learn from their experience.

2.9 As noted earlier, the committee heard that it is rare for international sponsors to seek registration in the Australian market ahead of applications to the FDA or the EMA. Submitters noted that the TGA accepts the same evidence package as the EMA and proposed that the TGA registration process could be streamlined by taking account of circumstances where a medicine had been assessed and approved by a recognised regulatory body.¹⁰

2.10 Some submitters suggested automatic conditional approval for drugs approved by the FDA or EMA.

5 *Submission 197*, p.18.

6 *Submission 196*, p. 11.

7 *Submission 138*, p. 2.

8 Melanoma Institute Australia, *Understanding Melanoma*, www.melanoma.org.au

9 DOH, *Submission 197*, p. 9.

10 Merck Sharp and Dohme, *Submission 120b*, p. 2.

2.11 Cancer Action Victoria noted the recommendation of the National Commission of Audit that recognising approvals made by overseas authorities would provide better outcomes for consumers by cutting delays caused by the approval process and reducing the estimated administrative costs incurred by pharmaceutical companies.¹¹

2.12 Similarly, Merck Sharp and Dohme (MSD) proposed that the TGA could adopt the evaluation reports from an overseas regulatory authority as the basis of an Australian approval:

Evaluation reports from an approved regulatory authority would be assessed before an independent sovereign decision was made by the TGA. Through leveraging international experiences and resources, patients in Australia could secure timelier access to medicines, whilst the TGA would make significant efficiency gains by reducing duplication of effort.

2.13 MSD suggested that by adopting this approach, new medicines could be made available to Australian cancer patients in as little as three months after overseas approval.¹²

2.14 Leukaemia Foundation of Australia told the committee:

We would support for rare cancers in particular where drugs are approved in the United States and Europe that there be an automatic conditional acceptance through the TGA of those drugs and bringing a much shorter time for those drugs to be available. We also support a managed access scheme through the PBS to bring those drugs in for those rare cancers.¹³

2.15 However Cancer Voice SA cautioned against adoption of overseas approvals without first undertaking an evaluation of past data to demonstrate that such an approach would produce better, different or faster decisions.¹⁴

2.16 Submitters also noted that Australia has no process in place to expedite the review of critical or breakthrough medicines.¹⁵ Cancer Council Australia and Clinical Oncology Society of Australia (CCA/COSA) told the committee:

The [EMA] in the United Kingdom and the [FDA] in the United States provide the opportunity for expedited approval in a shorter timeframe and in some cases based on earlier indicators of effectiveness, for breakthrough therapies. The EMA and FDA regulators allow companies to test cancer drugs using surrogate measures instead of overall survival and other patient

11 *Submission 151*, p. 4.

12 *Submission 120b*, p. 2.

13 Mr Anthony Steele, Head of Blood Cancer Support, Leukaemia Foundation of Australia, *Committee Hansard*, p. 12.

14 *Submission 150*, p. 2.

15 Mr Christian Sellars, Director, Market Access, Merck Sharp and Dohme, *Committee Hansard*, p. 23,

centred measures such as tumour size and progression depending on the medicines fit for purpose.¹⁶

2.17 In its submission, MSD provided an overview of the FDA's Fast Track Designation and Breakthrough Therapy Designation. Key features of both designations are the level of interaction between the FDA and the sponsor and the degree of flexibility with respect to the submission of the marketing application. In both models early and frequent interaction ensures marketing applications and compressed development programs still meet the FDA's rigorous standards for safety and effectiveness while facilitating earlier access to important medicines for cancer patients.¹⁷

2.18 DOH told the committee that, while there is currently no formal expedited evaluation system, if the TGA considers an application to be a significant therapeutic advance or of critical importance, it will, 'wherever possible, work with the relevant applicant with a view to facilitate an early decision, provided the product meets the TGA's quality, safety and efficacy requirements.'¹⁸

2.19 Mr Christian Sellars, Merck Sharp and Dohme, outlined a case study for the committee to illustrate the difficulties MSD perceives in the TGA registration process:

I thought I might, if you will indulge me, tell the brief story of one research area that was mentioned ... by the Australian Melanoma Research Foundation, some of your earlier witnesses. This is the type of product that Ron Walker, the Melbourne businessman, was treated with. The area is called immunotherapy and it is a very promising new area of research.

MSD was very fortunate over the weekend to publish our first head-to-head trial in the New England Journal of Medicine on melanoma for this cancer area. What we are seeing is that about a third of patients are seeing a visible reduction in their tumours. That reduction is sustained over a year, which is a fantastic outcome in a cancer type that has resisted effective treatment for many years. What is probably most exciting about this area—and it is not just MSD; there are four or five companies that are investing substantial amounts in trials. Our organisation alone has 150 trials in this space on 30 different tumour types. It is probably taking up the biggest chunk of our \$7 billion research budget at the moment. But it is showing substantial value across many of the cancer types that we have tried it in so far.

So, when we still had phase 1 data only, which was last year, we put a submission in to the TGA. The TGA has no formal fast-track approval, but we felt that the importance of this therapy in an area of very severe need justified a not-normal approach, so we put in based on phase 1 data and we were very fortunate that the TGA processed us and the approval came

16 Cancer Council Australia and Clinical Oncology Society of Australia, *Answer to Questions on Notice*, p. 2.

17 *Submission 120a*, p. 5.

18 *Submission 197*, p. 38.

through within eight months from submission. The normal approval time is 12. That was approved on Friday.¹⁹

2.20 Mr Sellars told the committee that, rather than an example of the system working, the process of submitting this product illustrated the uncertainty that companies face when deciding to seek early approval for a treatment:

The process of submitting this product has actually been extraordinarily disruptive and ad hoc. We have had no certainty about how data would have been considered, when decisions would have been made, how the TGA process would line up to the PBAC process and whether we would find ourselves in a situation where these cogs did not quite line up perfectly and, effectively, we would lose our slot.²⁰

2.21 The committee heard that a further impediment to timely access to cancer medicines is the requirement for an application for the registration of a new indication for a medicine already listed in the ARTG, to be made by the sponsor of medicine.²¹ Medical Oncology Group of Australia (MOGA) told the committee that the PBS currently has inadequate coverage of new indications that are outside the TGA-approved indications, despite the availability of evidence to support the new indication. The committee heard that there are a number of reasons the registration of indications with the TGA does not keep pace with evidence development including:

- the complexity of the approval process;
- only drug sponsors are permitted to lodge an application for a new indication;
- a lack of commercial incentives for the sponsor to seek further approval; and
- data ownership issues in circumstances where evidence may be developed by research institutions without the involvement of the original sponsor.²²

2.22 The committee heard that addressing these issues, to allow clinicians and/or patient groups to lodge an application for a new indication for an already registered medicine, could improve the responsiveness of the registration process to changes in the clinical setting.²³

2.23 The committee notes the independent Review of Medicines and Medical Devices Regulation, announced in October 2014, has examined the regulatory framework administered by the TGA. The review has sought to identify:

19 *Committee Hansard*, pp 22-23.

20 *Committee Hansard*, p. 23.

21 See for example: Deloitte Access Economics, MA Oncology Industry Taskforce, 'Access to cancer medicines in Australia', July 2013, *Submission 142a*, p. ix.

22 MA, *Submission 142a*, p. ix; Medical Oncology Group of Australia (MOGA), *Submission 108*, p. 2.

23 MOGA, *Submission, 108*, p. 2; Rare Cancers Australia, *Additional information* (received 16 September 2015).

- areas of unnecessary, duplicative, or ineffective regulation that could be removed or streamlined without undermining the safety or quality of therapeutic goods available in Australia; and
- opportunities to enhance the regulatory framework so that Australia continues to be well positioned to respond effectively to global trends in the development, manufacture, marketing and regulation of therapeutic goods.

2.24 The independent Expert Panel (Panel) provided the Government with its first report on 31 March 2015 and the committee notes that the Panel's report includes recommendations to:

- expand the pathways by which sponsors can seek marketing approval for a medicine or medical device, including making provision for utilisation of assessments conducted by comparable overseas regulators, and for expedited assessments in defined circumstances; and
- enhance transparency and predictability of processes and decisions to build trust and confidence in the TGA's ability to ensure Australians have timely access to high quality, safe and efficacious products.²⁴

Time to PBS listing

2.25 The committee heard that, from a cancer patient's perspective, the critical timeline is that between regulatory approval of a cancer medicine by the TGA and its listing on the PBS. Submitters spoke of a significant time lag between these two regulatory decision points.²⁵ The committee heard varying estimates of the average time of this lag.

2.26 Medicines Australia (MA) submitted that the average time from registration of a medicine by the TGA to reimbursed access on the PBS is in excess of 18 months:

- new listings take on average 589 days (over 1 ½ years), compared to 456 days in Canada, 584 in England and 256 in France; and
- subsequent listings take on average 700 days (nearly 2 years), compared to 189 days in Canada, 474 in England and 365 in France.²⁶

2.27 MA said that 'disturbingly, some medicines took up to 1,600 days (4½ years) for a new listing and 2,400 days (more than 6½ years) for a subsequent listing'.²⁷ At the committee's hearing, MA stated that new cancer medicines can take six months longer than other types of medicines—on average 1.6 years from TGA registration to PBS listing.²⁸

24 Review of Medicines and Medical Devices Regulation, Report on the regulatory framework for medicines and medical devices, March 2015, www.health.gov.au

25 See for example: MA, *Submission 142*, p. 3; CDA, *Submission 53*, p. 4.

26 *Submission 142*, p. 14.

27 *Submission 142*, p. 14.

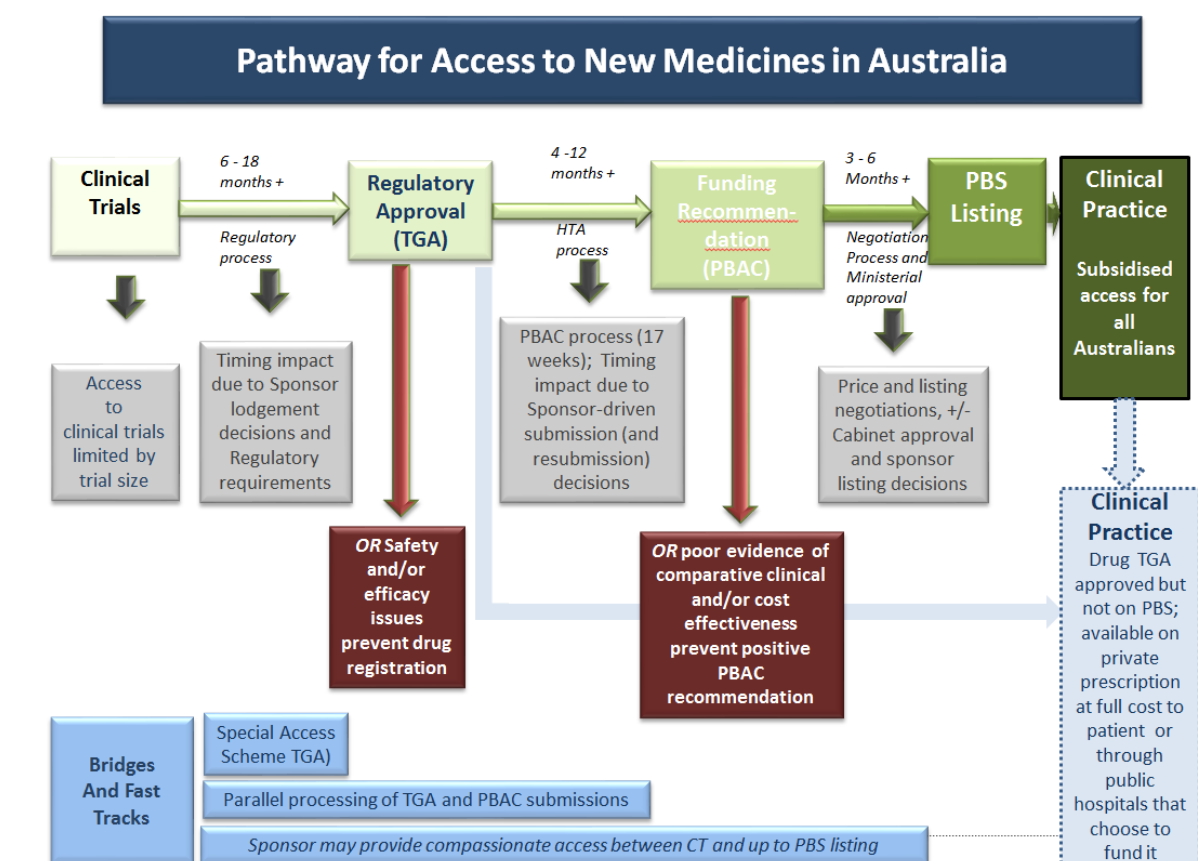
28 MA, *Committee Hansard*, 20 April 2015, p. 2.

2.28 Novartis Oncology Australia New Zealand (Novartis) told the committee:

In research specifically conducted for our submission, we found when reviewing listings for all medicines since 2011 that it takes an average of almost 2½ years—890 days—for a cancer medicine to be listed on the PBS from when it was approved by the TGA. During the same time period non-cancer medicines are taking less than half as many days—391 days.²⁹

2.29 DOH provided indicative timelines for each phase of the regulatory and reimbursement process. Figure 2.1 below indicates that the expected time between regulatory approval by the TGA and PBS listing can range from between seven to 18 months.

Figure 2.1: Pathway for Access to New medicines in Australia



Department of Health, *Submission 197*, p. 10.

The PBAC assessment process

2.30 The time for the PBAC review of an application for a medicine is currently 17 weeks from submission of the application to recommendation to the Minister.³⁰ DOH

²⁹ *Committee Hansard*, p. 21.

³⁰ PBAC, *Submission 196*, p. 3.

told the committee that the PBAC has one of the fastest reimbursement processes in the world.³¹

2.31 DOH provided an overview of the PBAC process, highlighting the rigorous and formal nature of the process and the volume and complexity of the analysis undertaken during the 17 week timeframe.

There are two aspects to the process. First of all, the process is rigorous and it is formal. There is a substantive amount of evidence to go through. There is complex work, and there is a large volume of work that is all written. That is the purpose of the application. It is a written application. That application is then assessed. The department contacts six academic institutions around the country. Those groups are specialist health technology assessors. They produce a written and comprehensive evaluation report. That evaluation report is provided to the company. The company has the opportunity to respond. That report, together with the comments and feedback from the company, goes in front of two of the subcommittees of the PBAC: the economics subcommittee and the drug utilisation subcommittee. After the subcommittee meetings, those subcommittees issue their advice to the PBAC. That advice is also provided to the company, and once again the company has the opportunity to respond to that. All that material is provided to the PBAC within the 17-week cycle.³²

2.32 However, MA submitted that very few applications receive a positive recommendation in 17 weeks from the lodgement of the first submission and identified this as a key factor in the time lag from TGA approval to PBS listing.

Most medicines and applications for new indications require more than one submission to achieve a positive PBAC recommendation and subsequent PBS listing. To prepare and resubmit, following an initial rejection, takes at least one and sometimes more cycle(s) such that it commonly takes 12-18 months for a positive decision, and can take several years.³³

2.33 MA told the committee that the average number of submissions required to obtain a positive recommendation from the PBAC for cancer medicines is 2.3 for new listings, equating to approximately three years, and 2.5 for subsequent listing (equating to approximately 3.5 years).³⁴

2.34 Submitters argued that the fixed, cyclical nature of the PBAC's assessment process means that if an application for listing is unsuccessful and the sponsor needs to resubmit, this can add substantially to the timeline. Novartis told the committee:

It is often the case for cancer medicines that the submission may be rejected or deferred by the PBAC leaving the sponsor to wait until the next available

31 *Committee Hansard*, p. 80.

32 Ms Adriana Platona, *Committee Hansard*, p. 82.

33 *Submission 142*, p. 16.

34 *Submission 142*, p. 16.

PBAC cycle to resubmit. This is leading to sponsors and the PBAC playing out a long drawn out negotiation using multiple submissions and multiple PBAC meetings. This often takes years and uses significant resources on both sides.³⁵

2.35 Submitters also noted that preparation for a major submission to the PBAC takes, on average four to six months and is costly and resource intensive.³⁶ As noted above, the tendency for applications to require resubmission to address new issues, to provide more complete data or to change the type of analysis can add significantly to the timeline for PBS listing.

2.36 Witnesses suggested that alternative processes should be explored to expedite the resubmission process. Some witnesses suggested that a designated fast-track approval process should be implemented, while others suggested adopting a tiered submission process has the potential to allocate resources according to need, by freeing up resources from less complex applications to allow greater focus on more complex, high-risk medicines, or those with a higher clinical need.³⁷ Submitters noted that similar approaches have been implemented in the US and in the Netherlands.³⁸

2.37 DOH stressed that the TGA and the PBAC 'are very keen to be adaptive and flexible where there is a need to'. Ms Felicity McNeill, First Assistant Secretary, noted:

We had some cancer drugs at the July meeting that were not initially given positive recommendations. We were then able to bring together stakeholder groups such as consumers and clinicians to do some work and bring it back to the November PBAC meeting, where it got a positive recommendation.³⁹

2.38 The committee heard that a significant factor in delays in securing listing approval stems from difficulties associated with assembling trial data that is sufficiently robust to satisfy PBAC requirements early in the assessment process.

2.39 Both DOH and PBAC submitted a key factor influencing both the timing of PBAC decisions and the likelihood of a successful application for listing is the quality of evidence provided to support the application.⁴⁰

There is an increasing trend for the clinical evidence documenting the effectiveness and cost-effectiveness of new cancer medicines to be of such poor quality that it does not allow confident assessment of benefit. For example, studies without proper comparison groups are increasingly being

35 *Submission 87*, p. 23.

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

37 CDA, White Paper, p. 18; Mr Timothy James, Chief Executive Officer, MA, *Committee Hansard*, p. 2; Ms Nicola Richards, Head of Public Affairs, Merck Sharp and Dohme, *Committee Hansard*, p. 27.

38 Mr David Pullar, Roche Products, *Committee Hansard*, p. 22.

39 *Committee Hansard*, p. 38.

40 *Submission 197*, p. 12; *Submission 196*, p. 8.

used as the basis of proposals for listing. Even when well-designed comparative trials are conducted the data presented are often from early analyses. Decades of research have consistently shown this type of data will over-estimate the benefits of a new medicine or other intervention.⁴¹

2.40 Novartis suggested that consideration could be given to elements of the assessment approach adopted in the US, which accepts earlier data and employs a system of rolling submissions which allows sponsors to submit additional data as trials progress and data emerges.⁴²

2.41 The committee heard that, while the PBAC undertakes its evaluation largely on the basis of the information provided in the applications, there is some flexibility in the current system to enable a sponsor to provide additional information during the assessment period in certain circumstances. The former Chair of the PBAC stated:

The PBAC works with the evidence that is presented in the sponsored submission. We do not invent new data or go and find new data. The evaluation process, at least, provides the sponsor along the course of the 17-week pathway at the moment the opportunity to see the evaluation and the appraisal, and any additional analyses are done. That is very much based on what the sponsor actually submits. Should the sponsor, for example, submit to us as part of the parallel process with an unspecified patient population, because TGA has not yet finalised the patient population that is most suitable for the drug, and we along the way get the TGA's proposed patient population, then the evaluation process can provide the sponsor the opportunity to resubmit some limited data in the 17 weeks that exists currently to, shall we say, revise the analysis or refine the analysis to match what is coming through TGA.⁴³

Pre-submission planning meetings

2.42 Submitters suggested that one means of addressing the 'churn' in the application process and improving the likelihood of successful applications would be to provide for pre-submission planning meetings. MA told the committee that sponsors would welcome the opportunity to meet with evaluators early in the application process 'to provide clarity around the evidence, the form of submission, the data required, [and] the appropriate pathway':

We would welcome a more open and more engaging, a more, if you like, user-friendly process in which a sponsor and the government and perhaps, ideally, the evaluator, can come together early, understand issues, challenges and opportunities and see the way clear to provide as much appropriate certainty and clarity as can be.⁴⁴

41 *Submission 196*, p. 8.

42 Mr Christoph Lorez, *Committee Hansard*, p. 25.

43 Dr Suzanne Hill, *Committee Hansard*, p. 75.

44 Mr James, MA, *Committee Hansard*, 20 April 2015, p. 6.

2.43 The committee heard that, while such meetings may be arranged at the request of a stakeholder, submitters see value in formally incorporating such meetings into the assessment process.⁴⁵

2.44 The committee notes that the assessment system applied by the National Institute for Health and Care Excellence (NICE) in the United Kingdom, includes early scoping meetings to discuss the 'decision problem', secure agreement on the comparator and on the appropriate endpoint for determination of cost-effectiveness prior to the sponsor making a submission.⁴⁶ Similarly, pre-submission planning meetings are a feature of the system administered by the pan-Canadian Oncology Drug Review (pCODR). The pCODR pre-submission process takes place between six to 12 months prior to the lodgement of the submission and aims to assist the submitter and other stakeholders through the process.⁴⁷

2.45 In its White Paper, *Improving Access to Cancer Medicines*, the Cancer Drugs Alliance notes that there is significant value in improving early multi-stakeholder engagement, including: improved understanding of the drug and disease area in advance of initiating the submission and evaluation, improvements in the relevance and consistency of the assessment process and identifying important factors for inclusion in the application.⁴⁸

2.46 By contrast, while acknowledging that there is always room for improvement, DOH told the committee that the existing process is 'fundamentally based on constant engagement with pharmaceutical companies'. DOH illustrated this by describing the process applied to the assessment of the drug pembrolizumab. Ms Adrian Platona, Assistant Secretary, Pharmaceutical Evaluation Branch said:

For that particular drug, which has received a lot of attention today and in the media recently, we, the department had a least three meetings with the company to discuss the nature of the application and the evidence in the application.⁴⁹

Parallel processing

2.47 A number of submitters told the committee that a key factor in delays in listing of medicines on the PBS is that application to the key regulatory bodies, the

45 MSD, *Submission 120ss*, p. 3.

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

47 Dr Nigel Rawson, *Has pCODR Improved Access to Oncology Drugs? Timeliness and provincial acceptance of pan-Canadian Oncology Drug Review recommendations*, June 2014, p. 3, <http://www.fraserinstitute.org/uploadedFiles/fraser-ca/Content/research-news/research/publications/has-pCODR-improved-access-to-oncology-drugs.pdf> (accessed 6 June 2015).

48 CDA, *Improving Access to Cancer Medicines*, White Paper, March 2015, p. 16.

49 *Committee Hansard*, p. 82.

TGA, PBS and Medical Services Advisory Committee (MSAC)⁵⁰ is sequential and dependent on fixed meeting dates.⁵¹

2.48 Since January 2011 sponsors have had the option of progressing applications through the TGA and PBAC processes simultaneously.⁵² Theoretically, submissions assessed via the parallel process will have compressed timeframes.

2.49 However, the committee heard that while assessment by the TGA and PBAC happens in parallel, the process does not necessarily result in faster listing of medicines.⁵³ DOH advised the committee that to date 20 per cent of major applications for cancer medicines have used this option.⁵⁴ MA told the committee that between 2011 and 2014, 27 per cent of major submissions to the PBAC had used the parallel TGA-PBAC process and indicated an expectation that the figure will grow.⁵⁵ MA subsequently noted that the time to listing 'varies greatly' regardless of whether drugs are assessed via the parallel process.⁵⁶ Novartis indicated that the average time from TGA approval to PBS listing has increased since 2011 when the parallel process was introduced. Data commissioned by Novartis showed that for oncological drugs, the mean time for approval to listing was 637 days prior to July 2011, and increased to 890 days after July 2011.⁵⁷

2.50 Submitters noted that parallel processing is a relatively new process and suggested that there is some scope for fine tuning. MA told the committee that there has been a lower recommendation rate for cancer medicine submissions using parallel processing, and noted that there is no guarantee that parallel processing will result in a faster listing.⁵⁸

50 The Medical Services Advisory Committee (MSAC) is an independent expert committee that provides advice to the Minister for Health relating to the comparative safety, clinical effectiveness and cost effectiveness of any new or existing medical service or technology, and the circumstances under which public funding should be supported through listing on the Medicare Benefits Schedule (MBS). Co-dependent and hybrid pharmaceuticals are currently considered separately by PBAC and MSAC using difference approaches to assessing evidence against the HTA criteria because listing needs to occur under two separate funding programs. See DOH, *Co-dependent and Hybrid Technologies*, <http://www.health.gov.au/internet/hta/publishing.nsf/Content/co-1> (accessed 14 June 2015).

51 Cancer Council Australia and Clinical Oncology Society of Australia and (CCA/COSA) *Submission 145*, p. 4.

52 DOH, *Submission 197*, p. 12.

53 Mr James, MA, *Committee Hansard*, p. 4.

54 *Submission 197*, p. 12.

55 *Committee Hansard*, p. 4.

56 MA, *Supplementary Submission 142*, p. 4.

57 It is not clear how many oncological drugs in the sample size cited by Novartis utilised the parallel process. Novartis Oncology Australia New Zealand (Novartis), *Submission 87*, p. 10.

58 Mr James, *Committee Hansard*, p. 4.

2.51 Ms McNeill, First Assistant Secretary, Pharmaceutical Benefits Division, DOH, expressed disappointment at the concerns raised regarding parallel processing.

We have seen some really fantastic outcomes in that space and, yes, we have seen some that have not been successful at all. There is a bit of risk management there and we do accept that. When you are going to the TGA and you are not quite sure what the final registration may be and you are looking at the subsidy for that particular indication, we appreciate there is a risk with that. But there also becomes an opportunity with that too, and that is why we have engaged in this process with industry to try and further that. We always learn from these things; systems evolve. But if 30-plus percent of submissions are coming through this, there must be something in there that is going reasonably well.⁵⁹

2.52 In its submission the PBAC stated that the decision of some sponsors to submit applications well in advance of TGA approval may be distorting the time to approval:

Provided the data package is adequate and the price requested by the sponsor is reasonable and found to be cost effective, the PBAC may be of a mind to recommend approval before the final approval by TGA (e.g. dabrafenib for melanoma). However, some sponsors are now choosing to submit applications to the PBAC so far in advance of TGA approval that the PBAC has no option but to reject or defer them, as the TGA-approved indication is critical to determining a PBAC listing. This practice may be distorting the reported time to approval.⁶⁰

2.53 Roche Products's evidence confirmed that, in deciding whether to submit an early application for parallel processing, sponsors consider the likelihood of satisfying PBAC data requirements on the basis of the data available.

[W]e certainly aim to submit our applications under parallel process or at the earliest opportunity. Where there have been delays or decisions not to submit at that earliest opportunity or through parallel processes, because of the PBAC's need for data certainty, our company may decide to delay that application until additional data become available to minimise that uncertainty or to conduct additional assessments to identify the population where the drug is most cost-effective.⁶¹

2.54 Submitters told the committee that greater collaboration is needed between each of the regulatory and reimbursement agencies with regard to the assessment of clinical evidence to enhance the efficiency of parallel processing.⁶² The committee notes that the Review of Medicines and Medical Devices Regulation recognised the synergies between the TGA, the PBAC and the MSAC and considered that there

59 *Committee Hansard*, p. 83.

60 *Submission 196*, p. 11.

61 *Committee Hansard*, p. 26.

62 MA, *Answers to Questions on Notice*, p. 5; *Submission 145*, p. 4, MSD, *Submission 120*, p. [2].

would be benefits in considering organisational structures to facilitate improved integration of these functions across the lifecycle of medicines and medical devices.⁶³

2.55 The committee notes that additional timing complexities are associated with the assessment of co-dependent technologies, and that there is a view that systems improvements have failed to address these:

It is common for cancer medicines, particularly targeted medicines, to have an associated diagnostic test or treatment-associated device to ensure the medicine is used where most effective.

Submissions for targeted medicines partnered with a diagnostic test are complex in terms of content and process. They currently require a separate recommendation from two separate committees with differing meeting schedules; the Medical Services Advisory Committee (MSAC) for the test and the PBAC for the drug. There appears inadequate interaction between the two committees, and the submission processes vary greatly between the two.⁶⁴

Timely and transparent price negotiations

2.56 The committee heard that another source of delay in the listing of cancer medicines is the post-PBAC negotiations between the sponsor and government over price. The PBAC submitted that:

Delays following a positive recommendation by PBAC may be due to inability of the sponsor and Government to agree on the price and other details of financial agreements. For example, there was an 18-month delay between the Committee's recommendation for the listing of abiraterone for metastatic prostate cancer and the sponsor agreeing to supply the drug on the PBS under the recommended circumstances. During this period, there were multiple additional applications for the same product and listing that had to be reviewed by the PBAC.⁶⁵

2.57 DOH clarified that while a decision not to proceed with listing may reflect the sponsor's dissatisfaction with the PBS subsidy, it may also reflect a desire to seek changes in the approved indication for the drug. Ms McNeill, said:

It can sometimes be both, but more often than not it is about price, that is usually the vast majority of the concerns we have.

...

Often you are struggling as a pharmaceutical company to demonstrate the value of your drug in the order of when you may be used in a treatment cycle—whether you are first line, second line or third line.⁶⁶

63 Review of Medicines and Medical Devices Regulation, *Report on the regulatory framework for medicines and medical devices*, March 2015, p. 169.

64 *Submission 142*, p. 17. See also Amgen, *Submission 119*, pp. 5-6.

65 *Submission 196*, p. 12.

66 *Committee Hansard*, p. 85.

2.58 Ms McNeill further explained:

When you have a positive PBAC recommendation it is not like you can never come back and ask for that to be changed. But other drug companies will often put up their drug, take the recommendation and list on the PBS so that the patient has subsidised access from the word go; and then they put in resubmissions to the PBAC to seek changes in indication or changes in price thereafter. It is entirely up to a drug company which way they choose to do it. In [the case of abiraterone], they chose not to list and then continued to argue. They decided not to go for the PBS subsidy but to leave it in the private market until they got the recommendation they wanted.⁶⁷

2.59 Novartis recommended that a negotiation period should be established for all parties:

Once a cancer medicine has received a positive PBAC recommendation, and an opportunity exists to list the medicine, a negotiation framework and prescribed timeline (6 months) should be implemented to ensure all parties (i.e. DoH, PBAC and Sponsor) may reach a timely outcome.⁶⁸

2.60 CanTeen submitted that there is need for greater transparency in the pricing of cancer drugs with particular reference to utilising the clinical evidence to increase the alignment between the price of cancer medicines and their effectiveness.⁶⁹

2.61 PBAC also expressed concern that public discussion of new cancer medicines does not pay sufficient attention to the benefits and harms, as well as the cost of new medicines, stating that:

It is highly likely that earlier access to cancer drugs will *greatly* increase cost to the community if the mechanism by which earlier access is granted involves acceptance of prices that result in much higher estimates of cost-effectiveness.⁷⁰

Transparency

2.62 A number of submitters commented on the need for greater transparency throughout the TGA and PBAC process. Dr Katherine Nielsen, Director of Research and Advocacy, Leukaemia Foundation of Australia told the committee that greater transparency could lead to greater procedural efficiency and would help the public to understand the reasons for delays:

We have seen in many submissions that it averaged 31 months in 2012 for cancer drugs and generally required more than one submission. Whether this is due to price expectations or unrealistic requirements in

67 *Committee Hansard*, p. 84.

68 *Submission 87*, p. 23.

69 *Submission 146*, p. 4.

70 *Submission 196*, pp 7-8.

demonstrating clinical effectiveness is not clear because the processes are not actually transparent, so we do not really know.⁷¹

There is a lack of transparency about how decisions are made at the PBAC level and the MSAC level. It would be good to have better transparency for the public and also better expectations between the parties—the sponsor and the government—in terms of what is needed to demonstrate the value and cost-effectiveness of a drug and how to improve that. But we also need to have transparency around that so that people understand why there are delays. At the moment, we do not know why there are delays; there simply are.⁷²

2.63 The PBAC also recommended an increase in transparency around committee processes, particularly the evidence provide to the PBAC. Noting that some 'high value' commercial information may need to be withheld, PBAC stated that the majority of documents submitted to the PBAC can, and should be made publicly available.⁷³ Dr Suzanne Hill, Former Chair, PBAC, explained this position at the committee's hearing:

We believe that there should be an agreement between industry, the government, patients and physicians to have much more of the submitted documentation released to the public. Likewise, we believe that as much as possible of the documentation that is generated during the evaluation process should be made available. We are concerned that without such a change there will continue to be the fundamental misconceptions about the committee's decision making that have emerged in some of the submissions to this inquiry. More importantly, there will continue to be misinterpretation of data in and by the media, and patients will continue to be under pressure to obtain access to medicines that really may not offer them any value at their own sometimes considerable expense.⁷⁴

2.64 MA rejected these claims stating that the current transparency processes in Australia are among the best in the world and have resulted 'from extensive dialogue between industry and Government about the best way to implement the process,' while still respecting legitimate commercial in confidence considerations.⁷⁵

2.65 Submitters noted that greater transparency would assist sponsors and consumer groups to identify the reasons why applications have been unsuccessful and help to reduce submission 'churn'.

2.66 The Unicorn Foundation told the committee:

We put so much effort into these submissions but do not actually find out why it has been rejected or why not. I think that it is even just opening the

71 Dr Katherine Nielsen, *Committee Hansard*, p. 10.

72 *Committee Hansard*, p. 14.

73 *Submission 196*, p. 13.

74 *Committee Hansard*, pp 71-72.

75 MA, *Answer to Question on Notice*, 20 April 2015, p. 10 (received 25 May 2015).

lines of communication with consumers and consumer groups on how to make effective submissions but also on why a drug was passed or why not, based on the actual evidence put forward.⁷⁶

2.67 Witnesses noted that greater transparency would also assist patients and their oncologists to make informed choices about treatments.⁷⁷

Committee view

2.68 The committee notes that the processes for assessing applications for registration and listing are appropriately rigorous and are based on clear cyclical timelines. At the same time the committee notes the concerns raised by sponsors and other stakeholders regarding the potential for inefficiency and uncertainty in the system.

2.69 The committee considers that Australia should strive to achieve world's best practice in the approval of medicines and should therefore maintain a commitment to continuous improvement of its assessment processes. The committee also notes that the pharmaceutical industry has a significant role to play in achieving timely listing of cancer medicines.

2.70 The committee has received evidence pointing to fast track processes used by overseas regulators and notes that key features of such processes are early and frequent interactions between the regulator and the sponsor and a process of 'rolling review'. These mechanisms ensure collaboration in the design of trials to collect data that will support registration together with the flexibility to submit sections of the application for review as they are ready.⁷⁸

2.71 The committee considers that some of the suggested avenues for streamlining the assessment process, particularly in the case of resubmitted applications, merit further consideration, for example:

- pre-application planning meetings to assist sponsors and other stakeholders to better tailor their applications to the requirements of the PBAC;
- the scope for a tiered assessment process that matches resources to the complexity of applications; and
- a review of the parallel processing arrangements to identify opportunities to allow flexibility in the submission of data in order to achieve compressed timeframes in appropriate circumstances.

2.72 The committee notes concerns raised regarding the timeliness and transparency of pricing decisions and notes that the Review of Medicines and Medical Devices Regulation made similar findings. The Review has made recommendations to improve transparency and predictability of TGA processes. The committee considers

76 Ms Simone Leyden, *Committee Hansard*, p. 44.

77 Professor Brendon Coventry, Research Director, Australian Melanoma Research Foundation, *Committee Hansard*, p. 17.

78 Merck, Sharp and Dohme, *Submission 120a*, p. 5.

that greater transparency throughout the TGA and PBAC processes would aid understanding of the requirements of the assessment process and would support cancer patients and their oncologists to make informed choices with regard to their treatment. Greater transparency would also help to dispel any misconceptions regarding the assessment of particular medicines.

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

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,

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

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

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 (accessed 15 September 2015)

20 *Submission 197*, p. 13.

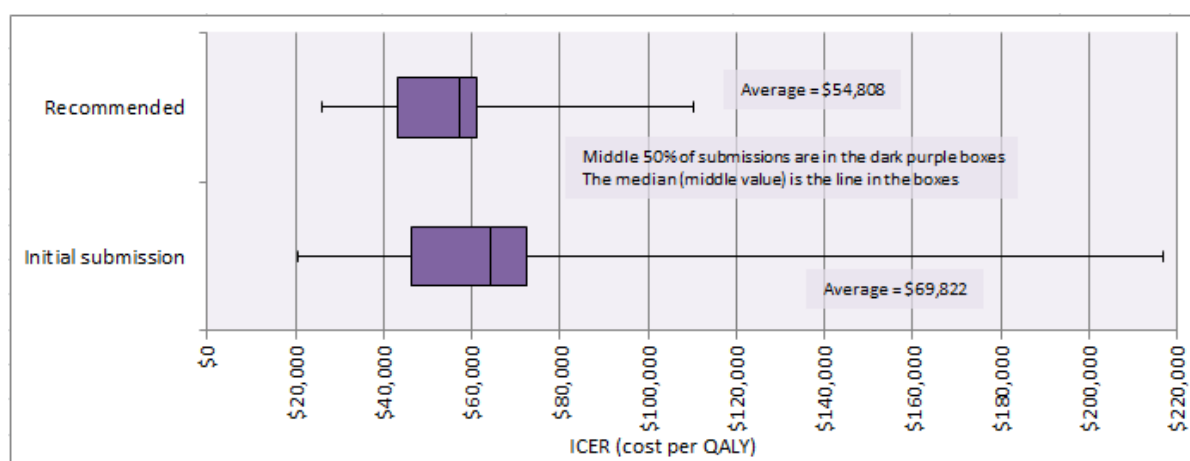
21 *Committee Hansard*, p. 87.

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

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 trials⁴² and would ideally include final outcomes data. In its July 2013 report, *Access to cancer medicines in Australia*, Deloitte Access

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

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,

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

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 drugs⁷² 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 Zalcborg 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.

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

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.

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)

83

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

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:

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 incorporation 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

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.

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

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.

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/>

Chapter 4

Impact of delayed access to cancer medicines on cancer patients

4.1 Throughout the inquiry the committee heard that timely, affordable access to treatments and quality care are inherently linked for cancer patients. A strong message in the submissions was that most cancer patients, particularly those with advanced disease, cannot afford to wait for effective treatment options to become available in a subsidised form in Australia.

4.2 The committee heard that the quality of cancer care is negatively impacted when the appropriate course of treatment for a patient's cancer profile is either not available in Australia or is not subsidised via the Pharmaceutical Benefits Scheme (PBS).¹

4.3 The committee received evidence that suggested underuse of potentially successful treatments has played a part in the low survival rates of patients with lung, colorectal and ovarian cancers in Denmark and the United Kingdom.²

4.4 This chapter examines the impact difficulties in accessing cancer medicines can have on the quality of care available to cancer patients. It considers the avenues available to individual cancer patients to access cancer medicines that have not been listed on the PBS before considering the particular challenges faced by rural and regional cancer patients, patients with rare and less common cancers and children, adolescents and young adults.

The impact of delayed access on cancer patients and their families

4.5 The committee received many submissions from individual cancer patients and their families urging the committee to support the expedited listing of specific cancer medicines. Personal accounts from cancer patients and their families highlighted the distress experienced by patients and their families when apparently superior treatment options are not available in Australia via the PBS. The committee heard that delays in the approval of cancer treatments, together with delays in the commencement of treatment due to the need to seek special approval or organise finance is a source of significant stress for cancer patients.³ The committee heard repeatedly that cancer patients with advanced disease cannot afford to wait and that the knowledge that a particular drug may enable them to gain more valuable time or

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

2 De Angelis R et al, Cancer survival in Europe 1999-2007 by country and age: results of EURO CARE 5—a population-based study. *Lancet Oncol* 2014; 15:23-34, cited by Novartis Oncology, *Submission 87*, p. 28.

3 Pharmaceutical Society of Australia, *Submission 176*, p. 6.

improve their quality of life, but at a price outside their ability to pay, is a source of great anguish.⁴

4.6 Ms Lorraine Hoskin's account of the plight of a young family friend is indicative of a great many submissions to the inquiry:

A young family friend has recently been diagnosed with a rare form of cancer. After the chemotherapy options have now been exhausted without a positive result his only option to gain more valuable time is a very expensive cancer drug. The decision whether to start this treatment is a major stress to him because of the financial cost which will affect the future of his young wife and family.

On top of the extreme suffering he has endured fighting this wretched disease, the added torment of knowing there is a drug which could help him, but at a huge cost is very unfair.⁵

4.7 Submitters described the significance to cancer patients and their families of maintaining a normal life. Many described the physical, emotional and mental toll associated with cancer treatments that disrupt everyday activities and separate cancer patients from family life. Cancer patients spoke of the importance of being able to return to the workforce and contribute to society, and emphasised the distress felt when this is not possible. Ms Lee McKerracher told the committee:

The cost of treatment may be expensive, but how can you put a price on giving a family member an extra 6 months, 12 months, 2 years with their family. Some may even be able to return to the workforce or their studies to contribute to society with whatever time they have left – we should give them the chance to do so.⁶

4.8 Evidence to the committee emphasised the potential of many new cancer medicines to improve the quality of life of many cancer patients by reducing the need for costly and invasive treatments such as surgery or hospitalisation. For example, Medicines Australia (MA) noted that consumer comments received by sponsors indicate that a simple and short outpatient administration of a single new targeted cancer drug has greater benefit compared to a treatment regimen involving multiple chemotherapies, long infusion times and the requirement to travel to the hospital several times per week or month.⁷

4.9 For Ms Karen Cowley, a breast cancer survivor, access to the drug Kadcyla has stabilised her disease and allowed her to feel a degree of control in her life:

Living with cancer affects a person physically, emotionally, and mentally. It can interfere with everyday activities. For many years I felt I was on a tightrope having many different regimes of drugs to manage my disease with many side effects. Kadcyla has been a revelation, since May 2014, I

4 See for example: Mr Paul Hobson, *Submission 6*, p. 2.

5 *Submission 30*, p. [1].

6 *Submission 25*, p. [1].

7 Medicines Australia, *Answer to question on notice*, 20 April 2015 (received 25 May 2015), p. 3.

feel that I have some control in my life as my disease is stable and I have less side effects. Administration of the drug is also less invasive, with only one infusion taking less than an hour whereas other medications took several hours.⁸

4.10 Such benefits extend beyond the patient to those supporting them who are spared months of worry and stress and caregiver time.⁹

4.11 The committee received many submissions from cancer patients and their families highlighting the significant physical, financial and psychological impacts of being unable to access new and innovative cancer drugs. Many patients are faced with the harsh dilemma of either paying a significant amount of money to access the latest, most effective treatments for their cancer or being unable to access the treatment at all.¹⁰ Ms Louise Marshall of the Australian Melanoma Consumer Alliance told the committee that many cancer patients are faced with the choice of selling their home, accessing their super or relying on the fundraising efforts of friends and family.¹¹

4.12 Bowel Cancer Australia told the committee:

The alternative for many is forgoing treatment and therefore the possibility of precious extra time with their loved ones.¹²

4.13 A number of submitters gave accounts of their frustration at finding the medicine needed to treat their cancer was not listed on the PBS for their cancer, or for their stage of the disease. Ms Bridget Whelan, who has ovarian cancer, told the committee that:

I finished chemotherapy in May 2014 and spent some time recovering and getting my health back. Chemo takes quite a toll on your body and your mind.

Since then I have been on what is called a "maintenance drug" – it's a drug to slow tumour growth and prolong your remission. I pay for this drug. When I started it, it wasn't on the PBS at all. It now is, but not for me. Only for women diagnosed for the first time. So I entered into a co-pay arrangement with the pharmaceutical company. It's expensive. It's more than another mortgage. I am so lucky I am in a position to do this. I imagine only a handful of women in Australia can and that disturbs me greatly. This is a drug which has shown good results in worldwide trials in prolonging the remission of women just like me. The alternative, the standard Australian Government funded approach, is that after my last chemo, I would do nothing and just wait for it to come back.¹³

8 Ms Karen Cowley, *Submission 11*, p. 1.

9 Medicines Australia, *Answer to question on notice*, 20 April 2015 (received 25 May 2015), p. 3.

10 Cancer Drugs Alliance (CDA), *Improving Access to Cancer Medicines*, White Paper, March 2015, p. 8.

11 *Committee Hansard*, p. 61.

12 Bowel Cancer Australia, *Submission 149*, p. 6.

13 Ovarian Cancer Australia, *Submission 137*, p. [11].

4.14 Mr Scott Beyer, who has non-Hodgkin lymphoma, told the committee of the disappointment of knowing the preferred treatment for his cancer is not listed on the PBS:

When we first met with the head oncologist at the Alfred hospital to discuss my options he said I would be better off to stay on Bentuximab for an extended period of time or until the drug possibly failed to keep the cancer under control. We alluded to the fact that it was going to be such financial burden on our family that this wasn't going to be possible. He was of the understanding that this drug was on the PBS, but what he didn't realise was that it didn't cover my type of cancer. The fact that he believed I would be better suited staying on Brentuximab for an extended period of time in lieu of going through an arduous and sometimes fatal procedure shows how important the access to these drugs is, but the fact of the matter is it is financially out of my reach.

In this day and age this is just unacceptable and truly disappointing.

4.15 With the support of family and friends, Mr Beyer has been able to raise funds to support his treatment, but expressed concern that 'this generosity can't last forever'.¹⁴

4.16 Submitters expressed concern that Australian patients appear to be missing out on new cancer treatments and are relying on older alternative treatments, with harsh side effects, compared with cancer patients in many other countries.¹⁵ Mr Janis Kinne told the committee of the constant stress of living with advanced prostate cancer and not being able to access best practice treatments available in other countries:

It is very tense and very stressful for anyone afflicted and their families. Hormone resistant cancer can appear at any time for no evident reason. When it does the prognosis is not good and life expectancy starts down the slippery slope. Men with prostate cancer in United States are able to be treated successfully with Zytiga or Xtandi before chemotherapy. It is frustrating that Zytiga and Xtandi are not available in Australia on the Pharmaceutical Benefits Scheme before chemotherapy. Instead of getting best practice treatment, I have to undergo chemotherapy with its harsh side effects before I can get access to Zytiga and Xtandi on the Pharmaceutical Benefits Scheme.¹⁶

Impact on medical advice

4.17 Delays in access to subsidised medicines also pose challenges for medical practitioners. The committee heard that cancer physicians often encounter the moral and ethical dilemma of raising the potential of treatment with particular cancer

14 Mr Scott Beyer, *Submission 104*, p. 1.

15 See for example: Mr Andrew Warden, *Submission 7*, p. 5; Mr David Prestridge, *Submission 5* [1]; Ms Natalie Cook,

16 *Submission 12*, p. [1].

medicine with a patient who may not be able to access that medicine in a subsidised form in Australia.¹⁷

4.18 Breast Cancer Network Australia (BCNA) told the committee that past research indicates that women have not always been told about expensive new treatments if the medical oncologist thought the patient could not afford it, for fear of distressing the patient and her family.¹⁸ Rare Cancers Australia (RCA) raised a similar concern:

... where a drug is not funded for the particular indication that afflicts the patient, the clinician is faced with less optimal choices, namely:

- Prescribe a "second choice" medication that is funded through the PBS.
- Seek compassionate or charitable access to the first choice medicine through a compassionate program or clinical trial. This option is not always available.
- Present the facts to the patient and let them decide if they can fund their own treatment.
- Deliberately misdiagnose the patient so that the patient can access the treatment through the PBS for a funded indication. **In these circumstances we are confronting clinicians with the choice of fraud or inadequate care.**¹⁹

4.19 Mr Anthony Steele, Head of Blood Cancer Support, Leukaemia Foundation of Australia (LFA) said:

Patients are not being told about all available therapies. We think there should be some sort of onus on health professionals to provide information on all available therapies. We get stories from patients who are told that to access a therapy they need to pay for it. They have been prepared to sell their house and been very devastated by it. In consultation with the Leukaemia Foundation we have put them through other means of getting access to the therapies, sometimes free of charge or highly discounted. It was at maybe a competing hospital or a different centre, across the river or in a different state. They are not advised of all available therapies. We think patients should be advised of all available therapies.²⁰

4.20 Submitters argued that a cancer patient should have the choice of trying new and innovative treatments, particularly if these have the potential to offer an improved quality of life. Ms Jolanda Visser told the committee that she would like to have the option of accessing drugs that may improve her quality of life or slow the progression of her disease:

I respect the system and also understand that the government does not want to make drugs available without [them] being thoroughly tested. However, I also think that we patients should be given a choice. It should be my choice

17 CDA White Paper, p. 8.

18 *Submission 90*, p. 6.

19 *Submission 92*, p. [8].

20 *Committee Hansard*, p. 9.

to try other drugs, as if I am forced to continue to take the medication I am currently taking, I will also have to face some realities of a diminished quality of life, progression in my disease which could introduce new risks and even a shorter life span.²¹

Alternative pathways for access to cancer drugs

4.21 Cancer patients have a limited number of options available to them to gain special or off- label access to cancer medicines that are not available through the PBS. Cancer patients may receive off-label access via:

- compassionate access programs, where a pharmaceutical company may provide patients with access to new medicines, often free of charge;
- hospital formularies, where the hospital agrees to pay for the treatment for that individual patient;
- clinical trials; or
- by meeting the associated costs out of private funds.

4.22 For cancer medicines that are not listed on the Australian Register of Therapeutic Goods, the Therapeutic Goods Administration (TGA) manages the Special Access Scheme (SAS). The SAS provides for the import and/or supply of an unapproved therapeutic good for a single patient, on a case-by case basis.²²

4.23 The term off-label refers to the use of a medicine in ways other than specified in the TGA approved product information. Off-label use includes when a medicine is prescribed or administered:

- for another indication;
- at a different dose;
- via an alternate route of administration; or
- for a patient or an age or gender outside the registered use.

4.24 The committee notes that off-label prescribing is an integral part of patient care for many cancer patients. The Council of Australian Therapeutic Advisory Groups has stated:

In some circumstances, off-label use of a medicine may represent the best available option for a patient or the standard of care. The off-label use of medicines allows patients to access innovative and potentially useful new medicines or older medicines for new indications, dose or routes based on recent evidence. In patient groups, such as paediatrics, oncology, psychiatry

21 *Submission 139*, p. 2.

22 Department of Health, *Therapeutic Goods Administration*, Special access scheme, www.tga.gov.au (accessed 15 September 2015)

and palliative care, off-label use of medicines is prevalent and may provide the only treatment option.²³

4.25 Off-label prescribing is common in paediatric oncology and is not limited to new medicines. The Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG) submitted:

A recent study at the Sydney Children's Hospital showed that 68% of standard chemotherapy agents were prescribed "off label". During the same time period over 80% of "new" anti-cancer therapies were prescribed "off label" (personal communication). The extent of "off label" prescribing reflects the fact that the levels of evidence required by regulatory authorities are not available for rare diseases such as paediatric cancer.²⁴

4.26 The committee notes that both patients and medical practitioners face a level of risk in the use of off-label medicines as there are clinical, safety, ethical, legal and financial issues associated with such use which require careful consideration.²⁵ Off-label medicines may have less supporting evidence and have undergone less scrutiny for efficacy, safety and cost-effectiveness than medicines registered by the TGA. Prescribers are therefore expected to exercise professional judgement in prescribing off-label use of medicines.²⁶

4.27 At the same time, the committee notes evidence that some cancer patients have a higher propensity for the risks associated with such use. Mr Barrie Littlefield, Head of Engagement, Cure Brain Cancer Foundation (CBCF) told the committee:

It is fair to say that it is something that is very often overlooked by the medical community and others. In the vast majority of cases, people living with brain cancer have a very short time to live. Therefore, their risk propensity is extremely high in many cases—far higher than their doctors sometimes realise. They are quite prepared to take extreme risks when they need to if they think they have hope of a cure. So I think there needs to be a resetting around the ethical boundaries that are currently being set around access as well. I think it is well worth considering that.²⁷

Compassionate or early access pathways

4.28 Compassionate and early access programs are initiated by the sponsors of a medicine and approved by the drugs or therapeutics committees of participating

23 Council of Australian Therapeutic Advisory Groups, Rethinking medicines decision-making in Australian Hospitals, Guiding Principles for the quality use of off-label medicines, November 2013, p. 6.

24 *Submission 152*, p. 7.

25 Council of Australian Therapeutic Advisory Groups, Rethinking medicines decision-making in Australian Hospitals, Guiding Principles for the quality use of off-label medicines, November 2013, p. 4; Department of Health, *Submission 197*, p. 20.

26 Council of Australian Therapeutic Advisory Groups, Rethinking medicines decision-making in Australian Hospitals, Guiding Principles for the quality use of off-label medicines, November 2013, p. 6.

27 *Committee Hansard*, p. 15.

hospitals.²⁸ Most compassionate access programs provide access for a limited time or to a pre-specified financial commitment. MA told the committee that in more than two thirds of cases this access is used to cover the gap between TGA registration and PBS reimbursement.²⁹ MA referred the committee to research undertaken by Deloitte Access Economics (DAE), which found that nearly 5000 patients were provided with compassionate access in Australia during 2011-12 from a sample of nine pharmaceutical companies. In most cases the access was provided free of charge.³⁰ The DAE report states that approximately \$10 million of cancer medicines are provided to patients prior to PBS listing, or even experimentally prior to TGA approval, through specialist cancer centres.³¹

4.29 However, MA noted that the sustainability of such programs is a significant issue for the pharmaceutical industry, particularly when there are delays in achieving PBS listing:

...companies are frequently criticised by clinicians, the Government and PBAC when unanticipated, lengthy delays in listing decisions mean that ongoing access cannot be commercially sustained indefinitely.³²

4.30 Mr Timothy James, Chief Executive Officer, MA, told the committee:

...we support our members in their efforts to provide access to new medicines to patients, but we point out that these are not themselves sustainable access models and should not be performing the role of the PBS.³³

4.31 Key concerns raised in relation to compassionate access programs are that cancer patients are reliant on their treating clinician to lobby for them to gain compassionate access to treatment and that such access is not assured.³⁴

4.32 Ovarian Cancer Australia (OCA) noted that access to compassionate access program is often subject to strict eligibility criteria, and that even if a patient is successful in gaining entry, many patients still face significant costs:

While compassionate access schemes do sometimes exist in the interim period between TGA approval and PBS listing, these are at the discretion of the drug sponsor and they do not necessarily cover all of the drug costs. We have seen many instances of patients facing considerable financial burden to meet the costs of non-PBS listed medicines.³⁵

28 MA, *Submission 142*, Appendix C, Deloitte Access Economics, Access to cancer medicines in Australia, Medicines Australia Oncology Industry Taskforce, July 2013, p. 51

29 *Submission 142*, p. 25.

30 *Submission 142*, p. 25.

31 *Submission 142*, p. 25.

32 *Submission 142*, p. 26.

33 *Committee Hansard*, p. 2.

34 Melanoma Patients Australia, *Submission 116*, p. [2].

35 *Submission 137*, p. 4.

4.33 The committee heard a number of personal accounts indicating the magnitude of the financial burden faced by cancer patients. Mrs Karen Cowley described for the committee the personal impact of making a significant contribution to receive the drug Kadcyła³⁶ through a pharmaceutical company's compassionate program:

I paid \$15,000. I am now on a disability pension and my husband has just turned 60 and working 6 days a week to make ends meet. It's too much for him. Going forward we are unable to fund another drug. Even though I am a skilled professional, I am trying to get part-time work to make ends meet but being in my late 50s with cancer, difficult to find work. The irony is that Kadcyła has made me well enough to feel I can work again. I live in hope, as it goes against my grain to be a pensioner which has been my last option as our savings are depleted due to my loss of income and 8 years of out of pocket medical costs.³⁷

4.34 In some cases, cancer patients must reach a threshold of treatments before they become eligible for a compassionate program. Mr Chris Brugger, who is currently taking the drug brentuximab vedotin to treat Hodgkin's lymphoma, told the committee that his treatment costs his family \$16 000 per dose every three weeks. In the event that Mr Brugger requires more than nine doses, the pharmaceutical company will supply the drug free of charge:

The drug company has a compassionate program where, once you get to nine doses, they will supply it after that. There is research on this drug, in America, that shows it used to be capped at 16 doses but now you can stay on it indefinitely, as maintenance. My oncology nurses have spoken to the drug reps and they have said the compassionate program will be fine for me. If I need to get over nine doses, they said I am a perfect candidate for it, because I am young and otherwise healthy. I am a perfect candidate for it. If I were in my 60s or something it probably would not be as good a prospect.³⁸

4.35 Mrs Lesley Royle's account of her access to the drug Agrylin on compassionate grounds prior to it being added to the PBS highlights the uncertainty surrounding a patient's ability to secure private health insurance coverage to defray out-of-pocket costs:

My Private Health Cover agreed to pay the difference between the private script price (which was \$75.00 at the time) and the actual cost of the drug. I was prescribed 3 months' supply and my health fund pulled their funding, leaving me and my husband to pay nearly \$2000.00 in pharmaceutical costs.³⁹

4.36 The committee heard that there has not been a systematic effort to gauge the ability and willingness of health funds to fund non-listed PBS items. The DAE report

36 Kadcyła is a treatment for HER2-positive metastatic breast cancer

37 Ms Karen Cowley, *Submission 11*, p. 1.

38 *Committee Hansard*, p. 19.

39 Mrs Lesley Royle, *Submission 113*, p. 2.

noted that health fund payments appear predominately to be *ex gratia* and legislative requirements surrounding the coverage of non-PBS listed medicines are unclear.⁴⁰

Public hospital formulary

4.37 The committee also notes concerns raised about the availability of cancer medicines through public hospital formularies. Access to subsidised medicines for admitted public patients in public hospitals is dependent on the formulary of individual hospitals and in Queensland, the state-based formulary. The decision to list pharmaceuticals on the formulary of Australian hospitals is a consideration for the drug committees of individual hospitals or states and territories.⁴¹

4.38 The committee heard that as there is no single streamlined process across institutions and jurisdictions to assess proposed formulary listing of a medicine, the timeframe of each listing process is variable.⁴² Requests to prescribe drugs outside a hospital's list of approved medications, such as new anti-cancer therapies, usually involves an application to the hospital executive or jurisdictional advisory body.⁴³ CanTeen told the committee that varying policies between hospitals and states can lead to inequities in access:

While clinicians can request that their hospital pay for such drugs via individual patient usage applications, most public hospitals also cannot afford such drugs. Moreover, while one hospital may approve an individual patient usage application for a specific agent, another hospital may not, thereby creating further inequity of access.⁴⁴

4.39 Link HealthCare submitted that funding of cancer medicines through the hospital system is limited for both in-patient and out-patient medicines and poses an additional burden on hospital budgets.⁴⁵ Link Health Care illustrated this with a case study of the drug Defibrotide, used in the treatment of a serious complication resulting from haematopoietic stem-cell transplantation, hepatic veno-occlusive disease:

Defibrotide is currently only available to patients under the [Special Access Scheme] and is prescribed throughout the transplantation centres across Australia. Funding is provided through the hospital budgets and a three week course of treatment can cost around \$40,000 to \$100,000 per patient based on the recommended daily dose of 25mg per kg.

The South Australia Medicines Evaluation Panel, at their meeting on 14 November 2012, recommended rejecting funding of defibrotide "due to the

40 *Submission 142a*, Deloitte Access Economics, *Access to cancer medicines in Australia*, July 2013, p. 48;

41 *Submission 142a*, Deloitte Access Economics, *Access to cancer medicines in Australia*, July 2013, p. 47; see also: Link Healthcare, *Submission 125*.

42 Deloitte Access Economics, p. 47.

43 *Submission 152*, p. 10.

44 *Submission 146*, p. 3.

45 *Submission 125*, pp 5-6.

number of Individual Patient Use (IPU) requests for this medicine exceeding the threshold for review as directed under SA Health policy".⁴⁶

4.40 ANZCHOG also told the committee that it is not realistic to expect new and innovative cancer medicines to be funded from hospital operational budgets and that some hospitals have had needed to fund the supply of such drugs from donated funds.⁴⁷

Clinical trials

4.41 Another important potential avenue for early access to new cancer medicines that have not yet received TGA approval or PBS listing is through participation in clinical trials. Clinical trials may be sponsored by pharmaceutical companies or may be initiated by researchers and health professionals.

4.42 However, as noted in chapter 3, the committee heard that there are challenges associated with clinical trials and for a number of reasons participation in clinical trials is not an option for many cancer patients:

- not all new cancer drugs are tested through clinical trials conducted in Australia;
- patients must be referred to hospitals and clinicians participating in the trial, meaning participation may not be possible due to the patient's location; and
- strict eligibility criteria may mean some patients are ineligible to participate.⁴⁸

4.43 OCA told the committee:

Most ovarian cancer trials are large international studies and getting a spot on one of these trials is itself fraught with difficulty. Australia is often given only a handful of spots at a few hospitals. In addition, the eligibility criteria are often so restrictive as to rule them out as an option for most women, if geography has not done that already.⁴⁹

4.44 Mr Andrew Warden, who has been diagnosed with Waldenstrom's Macroglobulinemia (WM), a type of non-Hodgkins Lymphoma, told the committee that he had been unsuccessful in gaining access to a trial as he did not meet the eligibility criteria:

The consensus of leading world experts identifies WM treatments including IMBRUVICA, Idelalisib, Ofatumumab, Velcade and RIBOMUSTIN. I do not have access to these treatments. There are Australian clinical trials (with limited patient intakes) for all these treatments except Ofatumumab which is only for Chronic Lymphocytic Leukaemia (CLL). My Haematologist late last year unsuccessfully sought my participation in the IMBRUVICA clinical trial. I did not then meet the specified criteria as my relapse had not

46 *Submission 125*, p. 4.

47 *Submission 152*, p. 10.

48 CCA/COSA, *Submission 145*, p. 5; Melanoma Patients Australia, *Submission 116*, p. 3.

49 *Submission 137*, p. 4.

then reached the stipulated level. The trial is now closing before my condition is within the defined criteria, so my chance has passed.⁵⁰

4.45 A number of submitters called for greater access to clinical trials for Australian cancer patients.⁵¹ Mr Anthony Steele told the committee that there is a need to facilitate increased access to clinical trials by simplifying the process for establishing trials, establishing a national ethics approval system and increasing access to international trials.⁵²

4.46 Cancer Voices South Australia told the committee that clinical trials are often undertaken only in limited locations and that access often depends on patients and families searching out the information and asking clinicians to refer them to those locations.⁵³

4.47 The Australian Leukaemia and Lymphoma Group (ALLG) told the committee that one of the reasons more Australian's are not able to access new drugs via the clinical trial framework is because the framework is 'slow, unresponsive to emerging trends, and focused to aid the clinical trial activity generated from the pharmaceutical industry whereby commercial outcomes of the drug in use is at the forefront of the development investment'. ALLG argued for better support for the Australian clinical trial environment, noting that:

Cooperative clinical trial groups, like the ALLG, provide the fertile ground for patients to have access to drugs that are designed for use with the patient and their health outcomes as the focus – not the commerciality of the drug.

4.48 ALLG further stated:

If this continues in this way, Australians will only ever continue to get access to new drugs at the discretion of a company that has valued and determined access by a commercial gain.⁵⁴

4.49 Professor Brendon Coventry, Research Director with the Australian Melanoma Research Foundation, also noted the need for greater support in Australia for clinical trials of innovative approaches to cancer treatment. Professor Coventry, and Mr Martin Ashdown, a Research Fellow in the Faculty of Medicine at the University of Melbourne, told the committee of their research into the operation of the immune system and the importance of accurate timing of cancer treatments. Professor Coventry told the committee:

Martin and I have subsequently identified how the immune system seems to be working, by switching on and switching off repetitively, and that when treatment occurs is vitally important. The delivery of relatively inexpensive

50 Mr Andrew Warden, *Submission 7*, p. 3.

51 See for example: Cancer Voices SA, *Submission 150*, p. 3;

52 *Committee Hansard*, p. 11.

53 *Submission 150*, p. 2.

54 *Submission 159*.

agents at the correct time for the patient can have a dramatic effect on the effectiveness of many therapies for cancers of many different types.

4.50 Mr Ashdown further commented:

Continuing on, this relatively simple approach potentially offers near-immediate and less expensive opportunity to use cheaper off-patent existing drugs and some of the newer drugs more effectively. Timing of therapy seems to govern efficacy and this principle is finding its way into clinical literature year by year. Regarding the use of accurate timing of therapy, according to two highly experienced and prominent New York oncologists who have been reviewing our work, this finding has the potential to dramatically change the treatment landscape of cancer immunotherapy.⁵⁵

4.51 The committee notes that this work has been self-funded and reliant on philanthropic support. Professor Coventry told the committee that the current grants system 'does not really serve original research and innovative research'.⁵⁶

4.52 The committee heard that a lack of information about clinical trials may also contribute to inequities in access to clinical trials. For example, the committee heard that patients may experience difficulty accessing information about clinical trials for medicines that may be suitable for them if the trials are not offered at the hospital or oncology unit where they are receiving treatment. BCNA told the committee:

We know that some women receiving treatment in rural and regional areas, older women and women from lower socio-economic and culturally and linguistically diverse backgrounds are poorly represented in clinical trials.⁵⁷

4.53 The committee notes the establishment of the Australian Clinical Trials website is intended to assist patients to be aware of trials available in Australia and access information about them. The website is also intended to assist trials to recruit participants.⁵⁸

Private funding, fundraising and charitable funds

4.54 For those cancer patients who have not been able to access treatment through trials or compassionate access, the alternatives are limited.⁵⁹ The committee heard evidence of patients travelling overseas to receive treatment at significant expense and personal cost. Submitters noted that the expenses associated with seeking treatment

55 *Committee Hansard*, p. 10.

56 *Committee Hansard*, p. 17.

57 *Submission 90*, p. 7.

58 Joint Media Release, The Hon Sussan Ley MP, Minister for Health and The Hon Ian Macfarlane, Minister for Industry and Science, *Australian-first website to connect more patients with clinical trials*, 20 May 2015. See www.australianclinicaltrials.gov.au (accessed 15 September 2015)

59 *Melanoma Patients Australia, Submission 116*, p. 2.

overseas are 'beyond the capabilities of most Australian families' and noted the associated emotional and social burden.⁶⁰

4.55 While the Australian Government funds a Medical Treatment Overseas Program for proven therapies not available in Australia, the committee heard that treatments on a clinical trial are specifically excluded 'presumably because by definition, if a therapy is still undergoing a clinical trial, its efficacy is not yet proven'.⁶¹

4.56 The committee heard that many cancer patients rely on the generosity and fundraising efforts of family, friends, colleagues and the community to finance the cost of their cancer treatment.⁶² While submitters expressed their gratitude for this support, they noted the personal impact fundraising has on cancer patients and their families.⁶³ Mrs Naomi Brugger told the committee:

We are fundraising at the moment. We have managed to raise close to \$60,000 since January. That has been hard going. I have run the campaign mostly by myself, so that means I have been away from the boys as well. So they are not only missing out on dad; they are also missing out on mum, who is trying to keep dad alive.⁶⁴

4.57 RCA told the committee that it has established a charitable Cancer Medicines Fund to address what it sees as profound inequities in the current system.⁶⁵ In its submission, RCA provided the committee with two examples of patient experience to illustrate how these inequities can arise:

The first of these examples, Anita, has been diagnosed with non-small cell lung cancer and has been diagnosed as having an ALK+ genetic mutation as a contributing factor. Her oncologist prescribed a drug called Crizotinib and Anita has responded well for a number of months. Crizotinib has been recommended for listing by the PBAC for Anita's cancer but as the contractual process unfolds, it may yet take some months for it to be listed. In the meantime our Cancer Medicines Fund continues to fund her treatment at \$7,400 per month.

Our second patient is Lillian who has also been diagnosed with non-small cell lung cancer but in Lillian's case her much rarer mutation is in the ROS1 gene. Her highly respected oncologist has also prescribed Crizotinib as there is substantial evidence of benefit. Lillian is also responding well but

60 *Submission 152*, p. 11.

61 ANZHCHOG, *Submission 152*, p. 13.

62 See for example personal accounts provided in the following submissions: Mr Jason Noble, *Submission 19*, Rare Cancers Australia, *Submission 92*, p. 19 and p. 23; Mr Matthew Story, *Submission 201*, p. 2.

63 See for example: Ms Maureen Austin, *Submission 98*, p. [1].

64 *Committee Hansard*, p. 10.

65 *Submission 92*, p. 1.

because her cancer or indication is so rare there is currently no application to PBS for re-imburement.

Hence we face a situation where both Lillian and Anita need to self fund today at a cost of over \$7,400 per month yet simply because of the random genetic mutations they have, Lillian will never receive funded medicines through the PBS whilst Anita hopefully will.

Same cancer, same treatment but no fairness.⁶⁶

4.58 The fund, which has been established under the campaign banner, is supported by fundraising, corporate support, public donation and events and campaigns under the 'Sick or Treat' banner.⁶⁷ RCA told the committee:

That we needed to establish this site says everything we need to say about the current state of cancer medicines in Australia.⁶⁸

Impact on rural patients

4.59 The committee heard that cancer patients living in rural and remote areas frequently suffer greater challenges in accessing cancer treatment. MA told the committee:

There is commonly a lack of easily accessible diagnostic and treatment services in rural areas where treatment services are often rudimentary compared to large urban centres. They will also likely lack access to current research and clinical trials, which are commonly conducted in larger urban centres. These factors contribute to later diagnosis; diagnoses at more advance stages of disease; and higher mortality rates.⁶⁹

4.60 This is of particular concern for patients with rare or less common cancers, as rural centres are not equipped to treat less common cancers. The Unicorn Foundation, which assists and supports patients with neuroendocrine cancer, submitted that 40 per cent of neuroendocrine cancer patients live in rural areas.⁷⁰

4.61 Medical Oncology Group of Australia (MOGA) and LFA expressed concern that cancer patients receiving treatment outside major treatment centres, such as those from regional and rural areas, may also experience difficulty accessing compassionate and early access programs and clinical trials.⁷¹ LFA told the committee :

In our survey, of the patients who accessed a new drug, 17% had to relocate for treatment at their own cost. However, none of the State or Territory Patient Assisted Travel Schemes (PATS) provides a subsidy to cover rural, regional or remote patients to travel to a metropolitan hospital to take part

66 *Submission 92*, p. 9.

67 Cancer Medicines Fund, www.sickortreat.org.au (accessed 7 September 2015)

68 *Submission 92*, p. 1.

69 *Submission 142*, p. 25.

70 *Submission 130*, p. 2.

71 *Submission 108*, p. 2; *Submission 123*, p. 12.

in a clinical trial. Even if the clinical trial covers the cost of the drug, rural, regional and remote patients must bear ongoing accommodation and travel expenses as well as the cost of other medications. It means accessing new drugs through clinical trials is an inequitable, user-pays system that penalises non-metro patients and their families.⁷²

4.62 LFA underscored this evidence with the following four patient case studies, which demonstrate the additional challenges faced by rural and regional cancer patients seeking to take part in clinical trials:

Patient case study 6:

I made the decision to move from Canberra to Melbourne, where I had no family, to avoid having to commute regularly to receive the drug (which had to be given intravenously as part of the clinical trial program). This was a very hard thing to do, but looking back it doesn't seem there really was any other option for me at the time.

Patient case study 7:

My wife and I had to live in Melbourne for 14 weeks while undergoing the treatment, which wasn't available in our regional centre, 300 km from Melbourne. Our first month cost \$5550 for accommodation. Thereafter we were lucky enough to gain access to Leukaemia Foundation accommodation, which meant a saving in the order of \$10,000.

Patient case study 8:

My treatment regime involved two consecutive days each four weeks. It was too far (and way too exhausting) to travel to and from home two days in a row so I stayed in a motel located near the hospital. It was pretty lonely going back to a motel after an exhausting day of treatment, monitoring any symptoms and then going back in a taxi the next day to do it all again.

Patient case study 9:

I'm taking part in an international clinical trial. This requires driving for treatment every two weeks to Gosford from Tamworth. While in Gosford I live in rented accommodation. Fortunately, our children are old enough to be self-sufficient and my wife's still working, so we're able to pay for the costs from her personal savings. So far, the treatment's been successful.⁷³

4.63 The committee notes that for families of young cancer patients the only option may be to relocate the whole family to be nearer to treatment and support:

To undergo this intense treatment schedule, Zoe's family had to leave their farm – 18,000 acres of mixed cropping and livestock – and relocate to Perth to be closer to the Princess Margaret Hospital for Children. Zoe's older sister...and little brother...(who was born just a few months after Zoe's

72 *Submission 123*, p. 12. The Leukaemia Foundation undertook a survey on new and innovative drugs of 675 blood cancer patients (or their carer) in February 2015, *Submission 123*, p. 2.

73 *Submission 123*, p. 12.

diagnosis), together with her mum...and dad...fought with Zoe all the way.⁷⁴

4.64 Roche Products submitted that the potential benefits for regional and rural patients of new forms of cancer therapy should be accorded greater value in the assessment process. For example, Roche Products stated that 'oral and sub-cutaneous forms of intravenous cancer therapies may be more easily used outside of major metropolitan hospitals and may support patients completing their full course of therapy'.⁷⁵

4.65 Mrs Jill Delahoy's experience taking the drug Ibrutinib as part of her treatment for Chronic Lymphocytic Leukaemia also highlights the impact some new cancer medicines can have on both the quality of care and quality of life for rural patients:

This drug comes in capsule form and is taken by the patient at home. This means no hospital admission required, either for day chemotherapy or by admission. My haematologist is of the view that in a short time this will become the normal treatment for CLL patients. Imagine what this means for rural residents, no going to hospital which may be many hours away at a time when the patient is feeling dreadful. This should reduce costs and pressure on the hospital system.⁷⁶

Impact on patients with rare cancers

4.66 The committee heard that, as research priorities, commercial imperatives and advocacy tend to focus on oncology medicines and treatments for more common cancers, the impacts of a lack of access to subsidised cancer medicines has a disproportionate impact on the quality of care for patients with rare and less common cancers, for whom there are often few treatment options.⁷⁷

4.67 The evidence base for rare cancers, which have small patient populations, is more likely to have some level of uncertainty.⁷⁸ Clinical trials for rare cancers are often conducted through collaborative trial groups with less industry support and the data collected may be less suited to registration and reimbursement requirements.⁷⁹

4.68 Dr Christopher Fraser, Chair of ANZCHOG, told the committee that most drugs for rare cancers, which includes most childhood cancers, are not covered by the PBS and are not likely to be:

The problem is, to get to that PBS approval, the data is almost never going to be available to prove clinical and cost-effectiveness in extremely small patient groups, and the economic incentive to try and collect the data is not

74 The Kids Cancer Project, *Submission 192*, p. 9.

75 *Submission 114*, p. 11.

76 *Submission 79*, p. 1.

77 *MOGA Submission 108*, p. 3.

78 Cancer Action Victoria, *Submission 151*, p. 5.

79 *MOGA Submission 108*, p. 3.

going to be available. The drug company is going to say: 'Let's apply for a listing for breast cancer.' They are not going to be worried about a rare liver tumour in children. At the moment in our system we have to beg our hospital executives to pay for these drugs, and they may or may not approve it. There are inequities amongst different state thresholds. For rare diseases, like just about every childhood cancer, we feel there needs to be an improved mechanism that assesses the eligibility for federal funding or a federal subsidy for these drugs that does not rely upon extremely stringent clinical and cost-effectiveness data and that is not subject to the vagaries of individual jurisdiction or approval.⁸⁰

4.69 In its submission, the Department of Health noted the difficulties associated with funding for treatments for rare cancers:

Making judgements about the level of support for rare cancer patients is especially difficult, noting that it involves spending significant amounts of taxpayer dollars on a very small, but very sick, sub-group. The trend in increasingly expensive, personalised medicines will continue to place pressure on both the family and national budgets.⁸¹

4.70 As Ms Lee McKerracher submitted, an individual's access to medicines should not be dictated by the type of cancer they have or their financial position:

For those diagnosed with a rare cancer, they are in a different position. They are not lucky like I was and have ready access to a range of therapies that are reimbursed. So in addition to the emotional stress they are under, these people need to try and fund treatments to get well. These treatments can be extremely expensive and many can't afford them. Access to medicines should not be dictated by the type of cancer someone has, nor the income they earn. These people do not put their hands up to get cancer, they are a victim of circumstance and should not be discriminated against just because their disease is rare.⁸²

4.71 A number of submitters argued that alternative approval and funding pathways are required to address the particular challenges faced by patients with rare cancers. For example, LFA proposed that consideration be given to automatic conditional acceptance of treatments for rare cancers that have been approved in the United States and Europe. Mr Steele told the committee:

We know there are some life-saving drugs that may be available to rare cancers but are not brought into the country because it is not profitable. We would like to have some other methods to access those drugs for the non-profitable therapies to the rare cancer groups.⁸³

80 Dr Christopher Fraser, Chair, Australian and New Zealand Children's Haematology and Oncology Group, *Committee Hansard*, pp 35 -36.

81 Department of Health, *Submission 197*, p. 20.

82 *Submission 25*, p. 1.

83 *Committee Hansard*, p. 12.

4.72 The account of Mr John Canning summarises the sentiments of many submitters. Mr Canning has inoperable metastatic stage 4 lung cancer. Despite his prognosis, Mr Canning describes himself as mentally and physically fit. Mr Canning has a rare genetic mutation known as anaplastic lymphoma kinase and is being treated with the drug crizotinib:

What does this mean for me? I actually do not feel like a patient. I can take this drug orally, in the form of a tablet twice a day wherever I am, whether I am travelling or out at dinner with family and friends. If I was on the current PBS listed alternative pemetrexed, I would have to book in for an infusion at a public hospital or cancer centre every two to three weeks. The side effects of the targeted therapy that I am on have been proven and shown to be much milder and much more manageable. I have some control over my life as a cancer sufferer. I have quality of life. For me and for patients like me, that is what it is all about: quality of life.

There is no plan B. At this point in time, I do not have other options. I am still working, albeit fewer hours. I continue to carry out the charitable and pro bono work that I have done during my professional career. It means an enormous amount to me emotionally, psychologically and physically, but it makes an enormous difference to my wife and my family, who are my primary carers.

There is a challenge with all this because, although crizotinib was approved at PBAC's November meeting, it is still not listed on the PBS. It is not reimbursed. It is an expensive drug. I am one of very few people in this community who can afford to purchase this drug. For every one of me, there are 30-plus people who cannot. There are currently around 340 people with my cancer in Australia today. There are only around 40 who are likely to be diagnosed each year. What we are after is a fair access scheme for people with rare cancers. It is not an expensive access scheme but it is one which means a truly remarkably different experience than the brutal, debilitating and exhausting process of normal cancer chemotherapy treatments.⁸⁴

4.73 Evidence to the committee indicated a move toward more personalised use of existing medicines in the treatment of rare cancers. For example, CBCF told the committee that it is tackling the paucity of medicines to treat brain cancer through:

- A significant, increasingly global, research collaboration, to accelerate new treatment options for patients.
- A concerted move towards a 'personalised medicine' approach, whereby tumour genetics are established early on and high-throughput screening of existing medicines (many of which are currently PBS listed for other indications) occurs. If any of the screened drugs show activity against an individuals' tumour, then this information is conveyed to the treating

84 *Committee Hansard*, p. 41.

oncologist (and hopefully patient) to be used for (most likely off-label treatment).⁸⁵

4.74 As noted in chapter 2, commercial realities often mean that pharmaceutical companies do not seek registration of cancer medicines for rare indications with small patient populations. Rare Cancer Australia (RCA) told the committee:

The potential outcome is that today we have medicines registered with the TGA for one indication meaning they are deemed safe and for that indication also efficacious. However, their utilisation for other indications is prevented simply by the lack of application for registration.⁸⁶

4.75 RCA expressed the strong view that where a medicine is already registered in Australia for one indication, clinicians/and or patient groups ought to be able to apply to the TGA to extend the registration to additional indications where reasonable evidence of efficacy exists.⁸⁷

Impact on children, adolescents and young adults

4.76 The committee notes that the concerns raised above are amplified in the case of young cancer patients. The committee also received evidence that children, adolescents and young adults (AYAs) diagnosed with cancer face unique challenges in accessing new, innovative and specialist cancer drugs.

4.77 The committee heard that childhood cancers are different from adult cancers. While the most common form of adult cancer is carcinoma, this form of cancer constitutes less than three per cent of paediatric cancers. ANZCHOG told the committee:

Consequently, the molecular targets seen in childhood cancers are often different to those in adult cancers. However, currently the approach taken to applying targeted therapy to paediatric oncology is to see which drugs being developed for adult cancers might have some activity in children. The paediatric oncology community would argue that children deserve their own drugs developed specifically for their diseases. The explosion of new agents, a relative lack of pre-clinical research and the small numbers of paediatric patients makes prioritisation of agents for clinical trials extremely challenging.⁸⁸

4.78 CanTeen submitted that AYAs face exceptionally difficult cancer journeys, noting that the number of young people aged between 15-24 years is higher than in the younger age groups. AYAs present with a greater range of cancer types and, due to delays in diagnosis, the prognosis for AYAs is not as good:

85 *Submission 187*, p. 1.

86 *Additional Information*, received 16 September 2015.

87 *Additional Information*, received 16 September 2015.

88 The Australian New Zealand Children's Haematology/Oncology Group in partnership with The Kids Cancer Project, The Kids Cancer Alliance and the Children's Cancer Institute (ANZCHOG) *Submission 152*, p. 1

The number of young people aged 15-24 years diagnosed with cancer is 1.5 times the number of children aged 0-14 years that are diagnosed. Young people have significantly poorer survival rates than children and older adults in some of the cancers common in this age group. Many of the cancers that affect young people are rare. Young people also present with a larger array of cancer types compared to older adults: 90% of the cancer burden is accounted for by 20 different cancer types. Furthermore, young people also tend to present with cancer at a more advanced stage due to longer delays before diagnosis and suffer higher rates of inferior psychological outcomes compared to other age groups. This in turn, is associated with poorer prognosis and a heightened risk to survival. Consequently, for some cancers, young people show a much poorer response with the same treatments given to older adults or younger children.⁸⁹

4.79 Similarly, AYAs encounter disproportionate difficulty in accessing new and innovative cancer medicines. There is a lack of clinical trials for the cancer subtypes commonly seen in AYAs because pharmaceutical companies do not usually devote the same research effort to rare diseases. CanTeen noted that, unlike the United States and Europe, where legislation has been passed encouraging pharmaceutical companies to develop drugs with paediatric indications, Australia has not provided a legislative incentive for pharmaceutical companies to seek the PBS listing of indications relating to cancers in children and adolescents.⁹⁰

4.80 One young submitter told the committee:

There are no drugs for kids like Eva to try and save their life. The big drug companies need help from the government to find better ways to help kids get new drugs. The government needs to help out scientists find drugs for little kids so they don't just have to use drugs for old people. Kids are different and the government needs to treat them differently to grown up people.⁹¹

4.81 The Kids Cancer Project submitted:

Australia now needs to develop a policy for incentives and/or require industry to participate in the supply of drugs for childhood cancer and eliminate inequities. The fear is that Australia will not keep pace internationally with improvements in survival rates and children and families will continue to seek international options.⁹²

4.82 The rarity of the cancers that affect children and AYAs means it is extremely challenging to conduct trials necessary to satisfy the requirements to achieve

89 *Submission 146*, p. 2.

90 See for example: Best Pharmaceuticals for Children Act, 2002, Paediatric Research Equity Act, 2003, and European Paediatric Medicine Regulation, 2007.

91 Name withheld, *Submission 115*, p. 2. The submitter is 12 years old. Her six year old sister Eva died from rhabdomyosarcoma in 2014.

92 *Submission 192*, p. 6.

subsidised funding through the PBS.⁹³ It is not economically attractive for pharmaceutical companies to invest in drug development for childhood cancers:

The success of frontline therapy and the fact that new therapies target smaller sub-groups of already rare diseases means that there are fewer patients eligible to test these therapies and makes the conduct of trials to prove clinical effectiveness extremely challenging.⁹⁴

4.83 While noting the dramatic improvement in survival rates for children with cancer 'from less than 30% in the 1960s to 80% currently', ANZCHOG states that the most important factor in this improvement, has not been access to new cancer medicines, but global collaboration in incorporating clinical research as an essential part of the care of children.⁹⁵ The committee heard that all of Australia's major paediatric hospitals have access to international trials and it is estimated that more than 50 per cent of Australian children with cancer will participate in a US or European originated children's cancer clinical trial.⁹⁶

4.84 However, meeting the costs associated with treatment of childhood cancers poses significant challenges for hospital operation budgets. ANZCHOG told the committee 'most Australian paediatric oncologists would be very reluctant to ask a family to pay for a high cost therapy themselves because of the ethical challenges that this presents'.⁹⁷

4.85 Reliance on childhood cancer clinical trials based and funded in the United States and Europe is also not without its complications. Unlike adult trials, which are often initiated by the pharmaceutical industry, childhood cancer clinical trials are initiated by organisations such as the United States based Children's Oncology Group and the European based Consortium for Innovative Therapies for Children with Cancer funded by the United States and European governments. The committee heard that Australia's access to some childhood cancer clinical trials funded by the Children's Oncology Group is being limited due to budgetary constraints.⁹⁸

4.86 The committee also heard that there can be difficulties associated with children under the age of 18 gaining access to trials. CBCF noted that children are often not allowed to enter trials because the medicines must be tested on adults first.⁹⁹ CanTeen argued that there is no valid biological justification for age-eligibility criteria and told the committee that the practice has been criticised internationally by AYA

93 *Submission 152*, p. 1.

94 ANZCHOG, *Submission 152*, p. 1.

95 *Submission 152*, p. 1

96 Kids Cancer Project, *Submission*, 192, p. 15.

97 *Submission 152*, p. 10.

98 Kids Cancer Project, *Submission 192*, p. 5; CanTeen, *Submission 146*, p. 3.

99 Ms Michelle Stewart, Head of Research Strategy, Cure Brain Cancer Foundation, *Committee Hansard*, p. 14.

cancer advocacy groups.¹⁰⁰ The Kids Cancer Project told the committee that decisions to register and subsidise drugs for use in adults but not children can also lead to inequities. For example, the drug clofarabine, used in the treatment of acute lymphoblastic leukaemia, is subsidised for use in adults but not in children. The annual cost of treatment for a child can be as much as \$100 000 compared to \$37 for an adult.¹⁰¹

4.87 Finally, as noted earlier, many childhood cancers are rare and patient populations are small. This lack of a commercial incentive can hamper the development of trials to test the effectiveness of drugs used in the treatment of adult cancers in treating the types of cancers seen in AYAs. For example, CanTeen said Ruxolitinib, a drug developed for older adults with myeloproliferative disease has been reported to be effective in some AYAs with Philadelphia-like acute lymphoblastic leukaemia. Despite the apparent effectiveness of this drug in treating this disease, CanTeen stated it is unlikely that the PBAC will approve the indication without clinical trials and there is currently no incentive for pharmaceutical companies to undertake trials in such a comparatively small market.¹⁰²

Committee view

4.88 The committee notes that for cancer patients and their families, maintaining a normal life and enhancing the quality of that life is of utmost importance. The uncertainty and significant financial cost associated with off-label use of cancer drugs results in significant physical, emotional and financial stress associated with the uncertainty of securing that access. As Ms Robyn Lindley noted:

You can't work, your husband needs to work less to help so his income is lower. Then you also have the expenses of pharmacy products to counteract side effects. So where do we get this money from? You're so worried about surviving and beating this dreaded disease and wondering if you are going to be here for your children to then add another huge stress of MONEY.¹⁰³

4.89 The committee understands that often the patients with the highest medical need are also the patients with the least capacity to fund their own treatment.¹⁰⁴ Many patients are already experiencing financial difficulty and do not have the capacity to meet significant out of pocket costs. Access to new treatments through clinical trials and compassionate programs is by no means certain, and in the case of the latter, can involve a significant contribution on the part of the cancer patient. The burden is even greater for those cancer patients with rare or less common cancers, particularly children and young adults, or who live in rural and regional Australia, who have fewer treatment options to begin with.

100 *Submission 146*, p. 3.

101 *Submission 192*, p. 6.

102 *Submission 146*, p. 2.

103 Quoted in Bowel Cancer Australia, *Submission 149*, p. 4.

104 Mr Paul Hobson, *Submission 6*, p. 2.

4.90 Special access schemes, compassionate access programs and clinical trials are an important source of assistance, but help only a small minority of cancer patients and are neither sustainable nor equitable alternatives to subsidised access through the PBS. Over reliance on such schemes also risk creating a two tiered health system in which some cancer patients can afford treatment and others cannot.¹⁰⁵

4.91 The committee is particularly concerned about the impact of delays in access to innovative cancer medicines to treat patients diagnosed with rare and less common cancers, including children and young people and those with brain cancers. Proportionally, research in these areas of cancer research is less well supported than other areas of cancer research, while at the same time expenditure on treatment for these forms of cancers is much greater. For example, the committee notes that treatment of brain cancer costs more per person than any other form of cancer, yet receives only a small fraction of Australian Government cancer research funding.¹⁰⁶

4.92 In this context, the committee recognises the importance of supporting innovative research that may lead to more effective use of existing cancer treatments with consequential savings in the longer term. The committee notes that work described by Professor Coventry and Mr Ashdown in relation to a locally produced vaccine to treat advanced metastatic melanoma highlights the potential for the delivery of relatively inexpensive agents at the correct time for an individual patient to have a dramatic impact on the effectiveness of many therapies for many different types of cancers.¹⁰⁷

4.93 The committee considers the long-term implications of research of this type merit further investigation. Similarly, the committee considers that there is merit in considering the extent to which legislative and other incentives implemented overseas might have application in an Australian context to encourage greater focus on the development of cancer treatments for rare and less common cancers.

105 Takeda Pharmaceuticals Australia Pty Ltd, *Submission 122*, p. 4.

106 Cure Brain Cancer Foundation, *Submission 187*.

107 *Committee Hansard*, p. 10.

Chapter 5

Alternative access models for new and innovative cancer drugs

5.1 As noted in earlier chapters, while submitters consider that the current system for providing subsidised access to medicines has served Australia well, they also consider it is in urgent need of review and modernisation. Submitters noted that the particular plight of cancer patients highlights the need for a substantive overhaul of the current system to improve flexibility and timeliness of decisions, while retaining the rigour of the existing process.¹

5.2 Throughout the inquiry, the committee heard a range of evidence regarding approaches used by other countries that might be considered as models for alternate approaches to providing access to cancer drugs. Submitters noted that some countries have introduced specialist mechanisms to facilitate wider and more-timely access to cancer drugs. For example, the United Kingdom established the Cancer Drugs Fund (CDF) in 2010 as a temporary fund to meet the costs of some cancer drugs either rejected by the National Institute for Health and Care Excellence (NICE) or not yet evaluated by them.²

5.3 As noted in Chapter 1, Canada established the pan-Canadian Oncology Drug Review as a cancer specific national drug review process separate from the Common Drug Review (CDR) in response to concerns that the CDR process for consideration of oral oncology products was not meeting the needs of patients and clinicians.³

Establishment of a specialist cancer drug fund

5.4 Many submitters emphasised the need for Australia to implement a specialist early access program for cancer drugs. However, a number of submitters recommended the establishment of such a fund as a temporary measure pending 'modernisation' of the Pharmaceutical Benefits Scheme (PBS) and Pharmaceutical Benefits Advisory Committee (PBAC) processes.⁴

5.5 The Private Cancer Physicians of Australia (PCPA) expressed support for the formation of a separate, novel funding mechanisms for high cost drugs outside the PBS prior to drugs being considered by the PBAC. PCPA proposed that once a drug

1 See for example: Rare Cancers Australia (RCA), *Submission 92*; p. 10; Pharmaceutical Society of Australia (PSA), *Submission 176*, p. 6.

2 Department of Health (DOH), *Submission 197*, p. 17.

3 Angela Rocchi, Isabelle Chabot and Judith Glennie, Evolution of health technology assessment: best practices of the pan-Canadian Oncology Drug Review, *Clinicoecon Outcomes Res.* 2015, 7:287-289, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4461134/> (accessed 7 September 2015)

4 See for example, Mr Peter Carr, *Submission 13*, p. 1; See also Cancer Drugs Alliance, *Improving Access to Cancer Medicines*, White Paper, March 2015, p. 25.

receives PBAC approval, such funding would no longer be required and suggested that cost recovery mechanisms could be applied in the event that a drug failed to gain approval.⁵

5.6 The Tasmanian Government submitted that a cancer drug fund which supports access to cancer medications that are not available via the PBS, like that established by the National Health Service (NHS) in England, could provide an expedient way of enabling access to cancer medications and could be preferable to the creation of separate administrative arrangements for specific cancer medicines:

[T]he creation of new administrative arrangements for some newly listed medicines, as has been seen with the introduction of Herceptin and more recently Eculizumab, should be avoided as it created an additional level of administrative burden and access ambiguity for clinical staff and patients to overcome.⁶

5.7 Medicines Australia (MA) told the committee that the UK and Canada, having recognised that the value-for-money measure of cost-effectiveness does not deliver access to cancer medicines in line with community or political expectations, had established interim access measures while continuing the search for a better system. Mr Timothy James told the committee:

I think it is fair to say, without reflecting too much on the public policy decisions of other governments, that in both the UK and Canada they saw that a one-size-fits-all approach did not work and that, indeed, that approach was failing cancer sufferers. Hence, they determined that there should be a dedicated, specifically focused, resourced part of their system and a particular capacity to enhance access to cancer medicines. We believe that sort of focus, the resourcing, the consideration of processes and decisions, the engagement of stakeholders in a range of respects obviously to have that greater enhanced focus upon cancer medicines and the particular challenges and indeed opportunities around cancer medicines, that is obviously something we would welcome in the local context.⁷

5.8 A number of submitters advocated the establishment of an interim access scheme within or closely aligned with the existing PBAC/PBS mechanisms.⁸ The Tasmanian Government was not supportive of the establishment of a separate funding stream specifically for cancer medicines outside the PBAC process, stating that it is preferable for the PBAC process to be streamlined and tailored where possible.⁹

5 *Submission 117*, p. 4.

6 *Submission 188*, p. 4.

7 Mr Timothy James, *Committee Hansard*, p. 6.

8 See for example: Rare Cancers Australia, *Submission 92*, pp 10 – 12; Unicorn Foundation, *Submission 130*, p. 4; Cancer Drugs Alliance (CDA), *Submission 53*, p. 1; Tasmanian Government, *Submission 188*, pp 4-5.

9 *Submission 188*, p. 5.

5.9 The Cancer Drugs Alliance (CDA) proposed the establishment of an interim access scheme while 'the Government commences the process of PBS modernisation'.¹⁰ Like the Tasmanian Government, the CDA considers that an interim access scheme should be established within the existing PBAC/PBS mechanisms and should:

- be designed to provide access to medicines between Therapeutic Goods Administration (TGA) registration and PBS reimbursement;
- time-limited and operate until revised PBS/PBAC measures have been implemented;
- operate within and in parallel to the existing PBS system, which would continue to execute its obligations to approve and fund cancer drugs based on the existing framework;
- include clinically driven guidelines for listing and de-listing drugs;
- include clear guidelines around acceptable pricing taking account of issues faced by all stakeholders; and
- be supported by the establishment of a database of outcomes following the use of chemotherapy and targeted medicines.¹¹

5.10 Some submitters saw benefits in establishing an interim fund to provide expedited access to treatments for rare and less common cancers, including treatments already listed on the PBS for other indications.¹² Rare Cancers Australia (RCA) proposed that an interim access scheme should be administered by the Department of Health (DOH) for the interim approval of medicines not listed on the PBS. RCA proposed the following process:

- applications to be made by a suitably qualified clinician; and
- for indications considered to be rare or less common and for which the company will not be making a submission to the PBAC for that indication; and
- reviewed by a panel of clinicians and patient advocates who would provide feedback to the DOH on each drug's safety, efficacy and potential value; and
- that the supply of approved medicines could be subject to a range of other considerations, including a limited time period; a price agreed to between

10 CDA, *Improving Access to Cancer Medicines*, White Paper, March 2015, p. 25.

11 CDA, *Improving Access to Cancer Medicines*, White Paper, March 2015, p. 25. In March 2014, the CDA hosted a forum of stakeholders from across the cancer community to discuss and build strategies to support both short and long-term access to cancer medicines. The CDA Forum identified five priority areas for improving access to cancer medicines for Australian patients and established work-streams to address these. The outcomes of these work-streams are set out in the White Paper; www.cancerdrugsalliance.org.au (accessed 7 September 2015)

12 See for example, Mr Andrew Warden, *Submission 7*, p. 2.

DOH and the manufacturer, and an agreement with regard to any outstanding amounts paid to the company in the event the drug is listed by the PBAC.

5.11 RCA also stated that it may be necessary to implement some form of time-limit penalty to ensure that applications are considered in a timely manner.¹³

5.12 However, some submitters cautioned against the establishment of a dedicated cancer fund, noting that overseas experience suggests that such funds have not necessarily alleviated issues around cost and access to high cost medicines.¹⁴ For example, Cancer Council of Australia and Clinical Oncology Society of Australia (CCA/COSA) noted that while the CDF had improved access to new listings, the fund was over budget and has been criticised for not addressing the issue of price negotiation with manufacturers.¹⁵

5.13 The Society of Hospital Pharmacists of Australia (SHPA) was also not supportive of the establishment of alternate funding programs for specific patient groups such as oncology:

SHPA believes that the current standard assessment and approval systems are essential to ensuring the safety and cost effectiveness of medicines funded by public monies or through the PBS. We do not believe that these evidence-based decision-making principles should be compromised for any patient group.

5.14 SHPA further stated

...if the Australian government was to expand the range of medicines funded outside the PBS, the limitations and capacity of systems such as the Australian Life Saving Drugs Program and the Cancer Drugs Fund in the United Kingdom must be examined in detail.¹⁶

5.15 In its submission, SHPA noted a range of concerns about the CDF, including:

- the fund's use of less stringent approval processes compared to the standard NICE process;
- a tendency for the price paid by the fund to result in the UK paying a higher price for cancer medicines than most European countries;
- the diversion of funds away from potential treatment alternatives;
- overspending has resulted in only 59 of 84 currently listed medicines being funded in 2015-16; and

13 *Submission 92*, pp 10-11.

14 See for example, Pharmaceutical Society of Australia, *Submission 176*, p. 6; Dr Agnes Vitry, *Submission 128*, p. 8.

15 *Submission 145*, p. 10.

16 *Submission 112*, p. 2.

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- the CDF has undermined the NICE and the principle of evidence-based decision making.¹⁷

5.16 Roche Products also considered that the CDF has its limitations, 'principally the lack of an acceptable method of prioritising medicines to list, and the perception of discrimination against other high-burden health conditions'. Roche Products submitted that it supports systemic reform that will improve access for all specialised medicines, including cancer. However, Roche Products noted that, as reform would take time, the government should consider models for providing interim access to new cancer therapies.¹⁸

5.17 Ms Simone Leydon from the Unicorn Foundation told the committee that, notwithstanding the difficulties encountered with the CDF, there was merit in considering such a scheme as an interim measure:

There have been different mistakes probably made with that, but the essence of it is that it provides an interim model—and we would stress that these are interim models—while we look at reviving or changing some parts of the PBS. They would not be there for the long term, which, unfortunately, I think has happened overseas. And they would be more strictly controlled. So, again, there would have to be some sort of restrictions put on what drugs could go in there and how much and that sort of thing.¹⁹

The Cancer Drugs Fund

5.18 A significant number of submitters suggested that an interim specialist fund could be modelled on the United Kingdom's CDF.

5.19 As noted above, the CDF was established in response to criticism over the timeliness of access to new cancer medicines, to fund access to cancer drug treatments which:

- were not approved by NICE due to insufficient cost effectiveness;
- had not yet received final NICE guidance;
- were for rare cancer licensed drug indications not selected for NICE appraisal; or
- were planned to be used off label (and therefore could not be assessed by NICE).

5.20 The current operating model for the scheme is due to end on 31 March 2016. Initial funding for the CDF was originally capped at £200 million per year. In 2013-14, the fund was overspent by £30.5 million. The UK government announced that it would increase the CDF budget to £280 million in 2014-15 (and to £340 million

17 *Submission 112*, pp 7-8.

18 *Submission 114*, p. 16.

19 *Committee Hansard*, p. 45.

in 2015-16), and that the list of drugs on the CDF would be reviewed, with a focus on 'value for money'.²⁰

5.21 NHS England told the committee that while the CDF had substantially increased access to cancer drugs, particularly for the treatment of rare cancers or rare cancer indications which had not been assessed by NICE, the CDF has had unintended consequences:

An unintended consequence of the CDF has been to initially reduce the incentive for drug manufacturers to reduce the prices of their drugs to make their drugs cost effective via a NICE appraisal. However, the recent incorporation of drug cost when added to an assessment of clinical impact into the overall CDF decision-making process has restored this need. The consequence of the setting up of the CDF has also been to have an ever increasing number of CDF drugs without final decisions as to whether they should be in baseline commissioning or not and only definitively making such decisions when the CDF funding envelop is threatened. An additional observation has been the recent trend for drugs to be licensed on relatively preliminary data which creates much uncertainty in NICE's assessment of cost effectiveness. This phenomenon is an additional factor in explaining the recent higher rate of NICE negative recommendations.²¹

5.22 In December 2014, a CDF Working Party was established, comprised of NHS England, NICE, the Department of Health and representatives of the pharmaceutical industry and cancer charities, to co-produce a proposal for a framework for the long-term sustainable evaluation and commissioning of cancer drugs. The framework is expected to be ready for public consultation during 'the summer of 2015' and for implementation from April 2016.²²

5.23 One of the potential solutions being considered by the Working Party is a 'managed access' approach to the CDF 'with clear entry and exit criteria and procedures which would be run jointly between NHS England and NICE.

5.24 NHS England told the committee:

The proposal recognises NICE's strength in the determination of overall clinical and cost effectiveness and the ability of NHS England to produce robust clinical commissioning policies for rare or off label cancer drugs. Both of these routes of assessment in the new process will incorporate an initial consideration of clinical promise and thus prioritisation of drugs which deliver the most important, favourable and meaningful outcomes.²³

5.25 NHS England said the managed access approach is considered to allow the potential for immediate access to funding on licensing and the collection of further clinical outcome data if the NICE technology appraisal concludes that longer term

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

21 NHS England, *Answer to written question on notice*, received 15 June 2015, p. [2]

22 NHS England, *Answer to written question on notice*, received 15 June 2015, p. [2]

23 NHS England, *Answer to written question on notice*, received 15 June 2015, p. [2]

data are required. NHS England describes this as a 'Commissioning through Evaluation' model.²⁴

Managed access models

5.26 A number of submitters proposed the adoption of a model for managed access to medicines as a means of addressing concerns regarding evidence gaps and timeliness in the PBAC assessment process.²⁵ For example, Roche Products expressed support for the more dynamic approach to Health Technology Assessment (HTA) that a managed access scheme may provide:

Currently, under managed entry, an initial subsidy is provided at a price justified by the existing data, pending the submission of more conclusive evidence. Roche consider that the initial price must reflect the value of the product and be in step with launch prices in other developed markets. The totality of available evidence needs to be considered, and subsequent evidence collection must be fit-for-purpose (i.e. address the identified uncertainties).²⁶

5.27 The committee notes that Australia has had a framework for a Managed Entry Scheme (MES) since 2011. Under this framework, the PBAC has had the ability to recommend PBS coverage for a drug at a price justified by the existing evidence, pending submission of more conclusive evidence of cost-effectiveness.²⁷ The expectation this measure is that the price of the drug could subsequently be adjusted, either up or down.²⁸

5.28 The PBAC provided the following explanation of how managed entry works:

In managed entry, a provisional price for the drug is set on the basis of the sponsor's estimate of effectiveness and toxicity, while data on outcomes are systematically collected from patients and prescribing doctors. In this way the clinical risk of lack of benefit and potential for harm are countered, because those outcomes are detected early because national data are collected. The financial risks associated with PBS-listing a drug whose effectiveness is uncertain, but which the PBAC believes is not likely to be cost-effective at the sponsors' preferred price, are shared between sponsor and government because the sponsor agrees to repay money if the drug is less effective in actual use than was predicted.²⁹

24 NHS England, *Answer to written question on notice*, received 15 June 2015, p. [2]

25 See for example: Janssen-Cilag Pty Ltd, *Submission 140*, p. 10.

26 *Submission 114*, p. 13.

27 DOH, *The Pharmaceutical Benefits Scheme, Framework for the introduction of a Managed Entry Scheme for submissions to the Pharmaceutical Benefits Advisory Committee*, www.pbs.gov.au (accessed 10 June 2015).

28 See for example: Dr Katherine Nielsen, Director, Research and Advocacy, Ovarian Cancer Australia, *Committee Hansard*, p. 10.

29 *Submission 196*, p. 14.

5.29 However, evidence to the committee was that the MES had not been enthusiastically embraced by industry. The Leukaemia Foundation of Australia (LFA) noted the limited use made of the MES to date and that the scheme is currently under review:

The PBAC requires greater flexibility to list new drugs, such as TGA listed orphan drugs, which have limited clinical data due to small patient cohorts. The Managed Access Scheme was introduced as a solution to this in 2011. However, the program has not been a success and is under review. A less restrictive scheme is essential, allowing conditional listing with further data to be supplied to demonstrate clinical benefit.³⁰

5.30 DOH told the committee that changes, such as the MES and 'pay for performance', are slowly being taken up by industry 'as their value is recognised'.³¹ DOH submitted that:

...the increasingly expensive price of [cancer medicines] represents marginal value and that it is difficult to justify continuing acceptance of high costs for treatments that offer very small benefit. It is vital that PBS pricing policies continue to put pressure on medicine pricing and further consideration of 'pay for performance' (ensuring that the price reflects available evidence of the health benefit) is also warranted.³²

5.31 DOH further stated:

The PBS has adopted innovative pricing models to provide access to new drugs whilst also supporting the development of a stronger evidence base. For example, the existing 'managed access' approach is being reinvigorated to provide options for medicines that are used to treat rare cancers by allowing a phased evaluation and listing, linked to progressive payments. Earlier access than would otherwise be obtained could be granted, where safe to do so, for use in those patients who have no other treatment options. The health outcomes would be tracked and reviewed, with approval for broader use only once sufficient evidence of effectiveness becomes available.³³

5.32 MA told the committee that the industry is open to working with 'public policy makers' on the development of the MES scheme, but noted:

There is a balance to be struck between getting access to patients who need those medicines most as early as possible and being prepared to submit to requirements for both clinical and cost effectiveness.³⁴

5.33 Notwithstanding the limited use made of the MES to date, submitters noted the potential for such an approach to address concerns regarding the collection of

30 *Submission 123*, p. 7.

31 *Submission 197*, p. 1.

32 *Submission 197*, p. 21.

33 *Submission 197*, p. 20.

34 Mr Timothy James, Chief Executive Officer, Medicines Australia, *Committee Hansard*, p. 8.

clinical data and the consideration of broader social and economic factors, by capturing 'real world' experience of new cancer treatments. Mr Richard Vines, Executive Chair, RCA told the committee that the solution requires a bit of flexibility:

I go back to where you were talking about 'once a submission is lodged'. Once it is registered and we know there is going to be a submission, and the TGA says it is safe and the pharmaceutical company is definitely making a submission, from that point on, if we can run a managed entry scheme after PBAC consideration, we ought to be able to put something in place beforehand, not that corrupts the PBS process—it has served us well for a very long time—but allows it to go through the one to two years, if that is necessary, and patients still have access. The issue is not the delay; the issue is the patients who do not get it while the delay takes place.³⁵

5.34 Mr John Cannings, who appeared in a private capacity, told the committee:

The issues are that currently, under the present guidelines and PBAC rules, PBAC are not able to take into account some of both social factors and economic factors in their determination around cost-effectiveness. Those rules need to be modernised to allow earlier access. Part of that could be through a managed entry scheme arrangement, where this real-world evidence is then obtained, accumulated and put back into the system for all cancer sufferers.³⁶

5.35 The PBAC noted that there are a number of issues that need to be considered in formulation recommendations based on a managed entry approach:

- the PBAC must have confidence that the clinical data provided at the initial application shows evidence of likely benefit of treatment to patients;
- the sponsor should have additional studies in progress that will potentially confirm this benefit and allow accurate assessment of the size of the benefit over existing treatments;
- alternatively, the sponsor needs to be prepared to collect data from Australian patients to establish the benefits, harms and costs of treatment. Clinicians and patients therefore need to agree to have such data collected; the committee notes that this raises issues of privacy that are beyond its remit, but that optimal implementation of managed entry may require legislative change;
- the sponsor needs to propose a price that is potentially cost-effective, on the basis of the data available at the time of PBAC consideration; and
- the sponsor and DOH need to execute a contract to ensure all of these issues are agreed, as well as a strategy for delisting the product and/or recovering excess payments if the hoped-for benefits are not confirmed. This process,

35 *Committee Hansard*, p. 40.

36 *Committee Hansard*, p. 44.

including the fact the drug may be delisted, need to be very clearly communicated to patients.³⁷

5.36 The committee notes that some of the PBAC's more recent recommendations have been on the basis of a MES. For example, in announcing the listing of the drug Crizotinib, used to treat anaplastic lymphoma kinase – positive non-small cell lung cancer, on 1 July 2015, the Minister for Health, the Hon Sussan Ley MP, stated that listing through a MES would speed up access for patients with the highest need for treatment.³⁸ In chapter 4, the committee noted evidence from RCA and Mr Cannings regarding delays in the listing of Crizotinib.³⁹ The PBAC recommended listing of Crizotinib following its November 2014 meeting, having first considered an application for its listing at its November 2013 meeting. The drug was registered by the TGA on 27 September 2013.⁴⁰

5.37 In evidence to the committee, Dr Suzanne Hill, former Chair of the PBAC, indicated that the PBAC is continuing to make recommendations for listing in certain circumstances on the basis of managed entry, while the future application of managed entry is being considered:

In terms of actual managed entry schemes, the committee has recommended already a couple of products with listings that are effectively managed entry. One was ipilimumab for melanoma, nearly 18 months ago, where the agreement was that the price would be set on the basis of the data that was available to the committee at the time for the cost-effectiveness evaluation; that survival data would be collected; and then, when the two years survival data was available, that the cost-effectiveness would be re-evaluated on the basis of the survival and toxicity data seen in the real world. Subsequently, the committee has made another couple of recommendations from November in a similar vein.

So there are two parts to it. There are the recommendations that are already coming out of the committee that are effectively managed access or managed entry schemes, and then there is some more general discussion of managed entry or managed access.⁴¹

5.38 The committee notes that the discussion around the development of managed access mechanisms appears to be centred in the work of the Access to Medicines

37 *Submission 196*, p. 14.

38 The Hon Sussan Ley MP, Minister for Health, Media Release, New breast and lung cancer drugs available from today, 1 July 2015.

39 See paragraphs 4.56 and 4.70 respectively.

40 PBS, Crizotinib; 200 mg capsule, 60 and 250 mg capsule, 60; Xalkori®, *Public Summary Document – November 2014 PBAC Meeting*, p. 2, www.pbs.gov.au (accessed 7 September 2015).

41 *Committee Hansard*, pp 75-76.

Working Group (AMWG).⁴² Since June 2014, the Managed Access Programme Sub-Group of AMWG has been developing a framework for a Managed Access Programme. At its December 2014 meeting the AMWG noted substantive progress on the project and anticipated broader review of the framework early in 2015. The PBAC reviewed the draft framework at its March 2015 meeting.⁴³ It is not clear if broader consultation with clinicians and consumers is contemplated in finalising the draft framework.

Alternate models

5.39 The committee notes evidence emphasising that managed access is only one possible avenue for addressing demand for early access to new medicines. Submitters noted a managed access scheme would work well alongside other mechanisms currently provided for within the PBS such as risk sharing between the Australian Government and the sponsor of a medicine.⁴⁴

5.40 Submitters also noted that the long-term challenge of funding subsidised access to cancer medicines requires the consideration of a range of new approaches. The committee received evidence suggesting that regulatory models used in other policy domains may serve as useful models for addressing challenges created by rapid scientific advances in cancer treatment. The committee received evidence regarding two such models: the licensing of oncology medicines and social impact bonds.

Risk sharing agreements

5.41 The committee notes risk sharing agreements are intended to help maintain the appropriateness and cost-effectiveness of listed medicines.⁴⁵

5.42 CCA/COSA expressed support for use of risk-sharing arrangements as a means of incorporating the use of surrogate endpoints into the evaluation of cancer drugs:

As recommended against ToR a), a scheme based on surrogate endpoints (also known as performance-based, risk sharing arrangements) could be implemented in Australia. The scheme could involve new cancer drugs being submitted for funding based on surrogate endpoints (such as progression-free survival) with an upfront agreement (not subject to appeal)

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- 42 The Access to Medicines Working Group was formed by DOH and MA as part of the PBS reforms announced in 2006 to assist them to work together more effectively and to consider issues regarding timely and appropriate access to new medicines for the PBS. The membership of the working group comprises DOH and MA, but has agreed to consult with other stakeholders when issues may impact on them. See: DOH, Access to Medicines Working Group, www.health.gov.au. (accessed 15 September 2015).
- 43 DOH, The Pharmaceutical Benefits Scheme, March 2015 PBAC Minutes for the Managed Access Program Framework, www.pbs.gov.au (accessed 15 September 2015).
- 44 See for example: Ovarian Cancer Australia, *Answer to question on notice*, 20 April 2015 (Received 22 May 2015).
- 45 DOH, The Pharmaceutical Benefits Scheme, *Step 7, Entering agreements to share risk*, www.pbs.gov.au (accessed 15 September 2015).

that funding would be reduced if the drug, in post-market evaluations, did not realise a major endpoint such as overall survival or improved quality of life.

Post-marketing surveillance under this type of scheme would need to be strictly conducted, as the earlier a drug is marketed, the greater the risk of uncovering unusual or adverse effects.⁴⁶

5.43 However, Roche Products submitted that while risk-sharing agreements are aimed at reducing listing delays following a positive PBAC recommendation, they are frequently one-sided and may impose requirements that are not based on clinical best-practice but simply reducing financial costs to government beyond what is required for cost-effectiveness. However, Roche Products recommended that industry and government should work together to identify opportunities to further streamline listing processes.⁴⁷

5.44 Merck Sharp and Dohme (MSD) also stated that the reason for the poor take up of the original MES was the perception that 'all risk in participating in the scheme would be borne by the companies, with little hope of price increases even if conclusive evidence was forthcoming'. MSD expressed hope that the development of a new framework through the AMWG would formalise a more effective way of giving patients access to new products.⁴⁸

Licensing innovative oncology medicines

5.45 RCA questioned whether the current approach of treating medicines as products and seeking approval on an individual product basis remains an appropriate model. RCA suggested that treating innovative medicines as intellectual property and applying a 'service' model, similar to that used for software, music and film:

The proposition is that, in order to address the failings and delays of the current system and to avoid the future capacity issues that seem likely, we look at the model of "Medicines as a service". In other words instead of pricing and costing each tablet or ampule as a separate exercise we examine the possibility of licensed usage for a medicine.⁴⁹

5.46 RCA states that this type of funding model has the capacity to deliver benefits in terms of certainty, flexibility and simplicity.⁵⁰

Social impact bonds

5.47 The CDA White Paper proposed further consideration of social impact bonds (SIBs) as means of providing incentives from investments in cost-saving preventive services. CDA stated that SIBs can ensure that public funding goes only to

46 *Submission 145*, p. 10.

47 *Submission 114*, p. 15.

48 *Submission 120*, pp 4-5.

49 *Submission 92*, p [14]

50 *Submission 92*, p. [14].

interventions that demonstrate their impact through rigorous outcome-based performance measures.

Under the most common social impact bond model, the government contracts with a private sector intermediary to obtain social services. The government pays the intermediary entirely or almost entirely based upon achievement of performance targets.⁵¹

5.48 The CDA considered that SIBs offer innovative solutions for funding health initiatives and could have long-term benefits beyond the funding of access to cancer medicines. Australia's first SIB is the Newpin Social Benefit Bond, funded by the NSW Government.⁵² The CDA states that in proposing consideration of alternate access models such as SIBs, it is not attempting to design alternative funding models external to the PBS. Its intention is to identify models that might 'relieve pressure on already constrained resources, while ensuring we improve access for Australian patients'.⁵³

Improved monitoring and data collection

5.49 Evidence to the committee underscored the importance of improved data collection and greater integration of existing data bases to improving the speed with which cancer drugs are assessed for registration and reimbursement and the level of information available to assist clinicians. Evidence to the committee noted that the success of managed access programs for new medicines is dependent on accurate data capture systems.⁵⁴

Post marketing surveillance

5.50 Submitters stressed that it is important to continue to monitor clinical and cost effectiveness of all medicines after they are listed on the PBS and recommended the application of greater use of post-market review processes.⁵⁵ The committee heard that currently little is known about patterns of use, patient outcomes or safety following the grant of marketing approval.⁵⁶

51 CDA White Paper 2015, p. 27.

52 Newpin Social Benefit Bond is a long-term, centre-based, intensive support program that works with families to improve parenting so children can live safely at home. The CDA White Paper states that in August 2014 it was reported that Newpin's maiden return to investors had a yield of 7.5 per cent on the \$7 million bond.

53 CDA White Paper 2015, footnote d, p. 26.

54 See for example: Delivering Affordable Cancer Care: A Value Challenge to Health Systems, Report of the World Innovation Summit for Health (WISH) Delivering Affordable Cancer Care Forum 2015, cited in DOH, *Submission 197*, p. 16.

55 See for example, Cancer Voices Australia, *Submission 49*, p. 1; MSD, *Submission 120b*, pp 5-6; CCA/COSA, *Submission 145*, p. 10; Cancer Voices SA, *Submission 150*, p. 2

56 See for example: CDA White Paper, p. 19.

5.51 CCA/COSA told the committee that while they consider there is an excess level of rigidity in the pre-market assessment of medicines, the same rigour is not applied to assessing the efficacy and cost-effectiveness of medicines once listed:

The absence of rigorous, ongoing post-listing review can lead to unnecessary expenditure and suboptimal use of listed medicines. Greater rigour in post-market review is a potential cost offset that could allow for the listing of new medicines which, while vitally important to a comparatively small number of patients, do not currently meet cost-effectiveness criteria. Greater rigour in post-market evaluation would also be a necessary tool for accepting surrogate endpoints other than disease-free survival as indicators of efficacy when assessing new PBAC applications – as recommended in response to the problems of timing and delay.

Agreed future milestones could be monitored through regular post-market assessment using agreed, pre-determined reporting mechanisms. It would require a commitment from the sponsor to provide results of ongoing studies and greater monitoring of safety and efficacy post-market by the TGA.⁵⁷

5.52 SHPA also expressed concern that under the current system of post-marketing surveillance products are reviewed in an ad hoc manner in response to stakeholder concerns about a particular product. SHPA recommended that all medicines funded through the PBS should be systematically and routinely assessed against the criteria that was initially used to approve the product for listing, as well as any newer, relevant evidence which has been published since the time of listing.⁵⁸

5.53 COSA member Ms Suzanne Kirsa told the committee that improved post-market surveillance to ensure that listed medicines are continuing to provide value for money, could help to offset some of the costs associated with the listing of new medicines via more flexible evaluation processes.⁵⁹

5.54 A system of post-market reviews was introduced following the 2011-12 budget to assist with improving the sustainability of the PBS. Post-market reviews provide a means of monitoring medicines in use to inform decision making at all levels throughout the medicine cycle, from registration to its use by consumers. The committee notes the post-market review program is intended to contribute to:

- improved patient safety through better understanding of adverse events and medicine-related harms;
- ensuring the ongoing viability of the PBS through targeted medicines usage and avoiding preventable wastage or inappropriate prescribing;
- a better understanding of medicines utilisation, to review intended clinical benefit and inform medicines evaluation processes;

57 *Submission 145*, p. 7.

58 SHPA, *Answer to question on notice*, 22 April 2015 (received 22 May 2015).

59 *Committee Hansard*, p. 52.

- ongoing cost-effectiveness, including through better management of clinical and economic uncertainty; and
- overall improvements to the quality of use of medicines and education for patients and prescribers.⁶⁰

5.55 The committee notes that new guidance for post-market reviews of medicines listed on the PBS were announced in March 2015. The new guidance was produced by the AMWG and has been agreed by the pharmaceutical industry, MA and DOH.⁶¹

Cancer registries

5.56 Submitters noted that governments in other countries are increasingly recognising the value of a coordinated national approach to data collection to justify expenditure on cancer treatments, to provide a framework for earlier access to new treatments and drive improvements in the delivery of better outcomes for cancer patients.⁶² Ms Carlene Todd of Roche Products said:

What we can learn from other countries though is around collection of clinical data in the real world. Italy and the Netherlands do this well. They have cancer registries in place and they can collect evidence in clinical practice over time for medicines.⁶³

5.57 In its White Paper, CDA advocated the establishment of an Australian national chemotherapy registry (NCR) to enable identification of trends in clinical practice and patient outcomes. CDA noted that this information could be used to inform and improve the quality of care across the country:

The NCR's focus will be to improve patient outcomes by monitoring and improving quality of care. The main purpose of the data collection would be to:

- Monitor current relevant patient information and linking to medicine use and patient outcomes, including safety and efficacy;
- Report risk-adjusted benchmarked data with the purpose of improving quality of care and delivering optimal patient outcomes;
- Facilitate decision-making for access to new cancer medicines on the pharmaceutical benefits scheme (PBS);
- Provide a framework that would support earlier access to cancer therapies such as through managed entry schemes/managed access programs;
- Provide a framework for the collection of real world data to measure cost effectiveness in Australian clinical practice; and

60 DOH, The Pharmaceutical Benefits Scheme, *Post-Market Reviews of Pharmaceutical Benefits Scheme Subsidised Medicines*; www.pbs.gov.au (accessed 15 September 2015)

61 The Hon Sussan Ley MP, Minister for Health, Media Release, *Positive progress and achievement from AMWG*, 18 March 2015.

62 CDA White Paper, p. 6.

63 *Committee Hansard*, p. 28.

- Monitor and report on delivery of equitable cancer care across Australia.⁶⁴

5.58 MSD also supported the establishment of a NCR to continually assess the efficacy of medicines and to help demonstrate the value that medicines bring to society:

At present, despite significant expenditure on cancer medicines, no comprehensive picture exists of what happens to patients once they are placed on therapy, as no national database exists which captures this information. As well as empowering clinicians with information to improve cancer care, such data provides a framework to monitor real world cost effectiveness and to support Managed Access Schemes. This would enable the health community to continually monitor whether it is getting value for money out of its investment.⁶⁵

5.59 However, the committee also heard that, before investing in a national clinical cancer registry, there is a need to address mechanisms for the collection of data on a national basis.

We do not have a national database. There are a lot of disparate registries. What the Medicines Australia submission talks about and some of the others as well is the need to link some of those registries together to make sure that they are talking to each other so we can access the data within those registry silos. That is a big issue at the moment, and something we should probably look at first before we invest in a national registry.⁶⁶

Greater integration of existing datasets

5.60 Submitters noted that greater integration of existing datasets would provide a means of harnessing the potential of real time monitoring of outcomes, both from clinical trials and post-PBAC approval, to support managed entry and improved patient care. For example, COSA suggested the 'integration of post market surveillance and reporting to track cancer medicines introduced into the market early, as well as the ongoing effectiveness of approved medicines and technologies'.⁶⁷

5.61 Dr Hill told the committee that more effective collection of clinical outcome data such as fact of death or adverse effects would be 'an enormous advance' in supporting the use of managed entry schemes:

Equally, being able to collect clinical outcomes such as fact of death or adverse effects more effectively than we can at the moment would be an enormous advance in trying to arrange what we have called managed entry schemes, where we need to try and monitor drugs that are made available to

64 CDA White Paper, pp 22- 23.

65 *Submission 120*, p.5.

66 Ms Carlene Todd, Director, Market Access and Pricing, Roche Products, *Committee Hansard*, p. 28.

67 COSA, *Answer to question on notice*, 20 April 2015 (received 22 May 2015),

the community early to make sure that the benefits and harms are the same as what we see in the clinical trials.⁶⁸

5.62 In its submission to the inquiry, the PBAC emphasised the importance of linking data sets to support early access.⁶⁹ Professor Zalcborg of CDA also emphasised the merit in linking existing databases to enable a more comprehensive understanding of cancer drugs:

Clinical trial data is often incomplete at the time. For example, long-term survival issues are not available; the true toxicity or safety profile is not understood; we have heard about progression-free survival and overall survival; there may be interim end-points. So there is a need to get further data. The way to collect that data is to link existing databases—like Medicare, like PBAC, like the Australian Cancer Database—in a way that protects people's privacy but allows information that has already been collected and information that can be collected into a comprehensive picture about what these drugs are doing and what they are not doing.⁷⁰

5.63 The Australian Cancer Database (ACD) is a data collection of all primary, malignant cancers diagnosed in Australia since 1982. The ACD is compiled by the Australian Institute of Health and Welfare (AIHW) from cancer data provided by state and territory cancer registries through the Australasian Association of Cancer Registries, which in turn receive information on cancer diagnoses from a variety of sources including: hospitals, pathology laboratories, radiotherapy centres and registries of births, deaths and marriages. Data from the ACD is used to report on national cancer statistics such as incidence, trends, projections, survival and prevalence. While the AIHW acts as custodian of state and territory registry data for the purposes of producing national cancer statistics, the cancer registries retain ownership of their jurisdiction's data at all times. The AIHW is able to make available a broad range of cancer statistics subject to a scientific and ethical review process.⁷¹

5.64 DOH noted that the increasing use of e-health records may also assist in data collection.⁷²

5.65 LFA expressed concern that without access to good information some patients may be being offered treatments that are no longer considered to be 'best practice'. LFA submitted that Australia needs a centralised process for all drug access inquiries:

Without a national clinical cancer database, factually-based information about which therapies are best practice in the Australian community remains unknown. Therefore, therapy decisions are essentially educated

68 *Committee Hansard*, p. 75.

69 *Submission 196*, p. 15.

70 *Committee Hansard*, p. 64.

71 Australian Institute of Health and Welfare, *Australian Cancer Database (ACD)*, www.aihw.gov.au (accessed 15 September 2015).

72 *Submission 197*, p. 16.

guesswork and doctor preference, and may be subjected to conflicts of interest.⁷³

5.66 Professor Brendon Coventry of the Australian Melanoma Research Foundation also described the difficulty in accessing data:

It is really hard. In the melanoma foundation we have been trying to get the information about complete response rates, outcomes, stuff that you should be using to make your decision, your informed choices. We find it really hard to get. It is buried in papers, it is in tables, it is in supplementary information and so on. This is extremely difficult for an experienced clinician and a group of clinicians to do. The patient has almost no hope of doing it on their own, unless they have the experience. We are trying to distil that information, compare the studies, compare the trials, put the information on the table so they walk up to one source and get that information that they need to have at their fingertips in order to make an informed choice in the clinic when the clinician starts speaking to them.⁷⁴

5.67 Mr Martin Ashdown, Research Fellow in the Faculty of Medicine at the University of Melbourne suggested that the AIHW might play a role in facilitating access to clinical data:

It would be very valuable if the Australian Institute of Health and Welfare could also collect survival and complete response data for different drug treatments and their associated costs to enable closer evaluation of clinical effectiveness for patients and clinicians, and especially to permit better informed choices.⁷⁵

5.68 Leukaemia Foundation of Australia (LFA) noted the emergence of private pay-for-service models, such as Biogrid, which collects data from patients with a range of cancers and other health conditions that are being treated in a number of hospitals in Victoria, Tasmania, South Australia, ACT and Queensland. LFA stated that an example of the value of such clinical databases was 'the analysis of outcomes for patients with metastatic colorectal cancer' which had 'enabled differences in practice between centres to be identified, and practice reviewed and standardised to improve patient outcomes'.⁷⁶

5.69 However, LFA argued that such databases need to be established on a national scale so that they can form part of everyday cancer care delivery and not be 'available just to the small number of patients who find out about it, either through their health provider, or online'.⁷⁷ LFA noted that a national clinical database could also facilitate

73 LFA, *Answer to question on notice*, 22 April 2015, (received 22 May 2015), p. 3.

74 *Committee Hansard*, p. 17.

75 *Committee Hansard*, p. 10.

76 LFA, *Answer to question on notice*, 22 April 2015, (received 22 May 2015), p. 3. LFA referred the committee to the Biogrid Annual Report 2013-14: http://biogrid.blob.core.windows.net/assets/uploads/files/BioGrid_Annual_Report_2013_2014_v2.pdf (accessed 15 September 2015).

77 LFA, *Answer to question on notice*, 22 April 2015, (received 22 May 2015, pp 2- 3.

the review of changes in indication, extending approval to other cancers with the same genetic mutations and survival benefits, by providing the TGA and the PBAC with access to extensive data, over and above that provided by the drug sponsor.⁷⁸

Capturing data from off label use of medicines

5.70 Submitters also noted the importance of capturing information about outcomes from off label use of cancer drugs. For example, Cancer Voices Australia recommended the use of post-marketing surveillance of real-life use of medicines, not just in clinical trials, to assess cancer drugs' effectiveness and impact on quality of life.⁷⁹

5.71 Cancer Voices SA submitted:

We need routinely collected comprehensive, high quality data to monitor outcomes of all cancer patients. This data should be analysed and reviewed to ascertain the effectiveness of treatments, particularly high cost treatments. We need to be able to assess cancer drugs' effectiveness and impact on quality of life, not just in clinical trials, but through comprehensive post marketing surveillance. We are missing the information about the outcomes from all those who access these high cost drugs outside of clinical trial situations (eg via family and community fundraising) or special access schemes. We need to ascertain if the expected benefits are achieved when these drugs are used outside the clinical trial population.⁸⁰

5.72 Ms Michelle Stewart of Cure Brain Cancer Foundation told the committee:

People are taking lots of different things and none of that data is being collected. For the larger group of patients, there is little benefit. We believe we could capture this off-label use, which is happening anyway, through a registry. Patients would then disclose what they are taking and we could track their responses on those treatments.

Clinical trials are set up for a good reason and that is to gain evidence for using a certain treatment. If you start using off label you must make sure that you are collecting the data as well.⁸¹

Committee view

5.73 The committee notes strong support for the introduction of an interim specialist cancer drug fund, pending review of the current system for listing medicines on the PBS and the examination of other models for providing expedited access to medicines. Evidence to the inquiry is that the introduction of specialist schemes overseas has resulted in both faster approval times and the availability of a greater range of medicines to cancer patients. However, the committee notes concerns, both in

78 *Submission 123*, p. 10

79 *Submission 49*, p. 2.

80 *Submission 150*, p. 2.

81 *Committee Hansard*, p. 18.

Australia and overseas, that existing specialist schemes have not necessarily alleviated issues around cost and access to cancer medicines and that such funds have the potential to undermine the rigour of existing evaluation processes.

5.74 Evidence to the committee has emphasised the potential for a managed access program to address concerns regarding the availability of clinical data to demonstrate the case for listing medicines on the PBS without undermining the PBAC process. However, the committee notes the importance of effective monitoring of both clinical and cost effectiveness after PBS listing, both as a means of improving patient outcomes and as a basis for delisting medicines where appropriate.

5.75 Finally, the committee notes the importance of effective collection of clinical data and the merit in linking existing databases to enable more comprehensive analysis of the benefits of cancer medicines by the PBAC and clinicians and to support best practice in patient care.

Chapter 6

Conclusions and recommendations

6.1 As noted in this report, Australia has the highest incidence of cancer in the world. While Australia also has some of the best cancer survival outcomes in the world, the provision of timely and affordable access to new and innovative cancer medicines provides a significant challenge for the Australian Government, clinicians and patients. These challenges stem in part from the fact that cancer medicines are among the most expensive medicines, and from Australia's relatively small patient populations.

6.2 These challenges are also a consequence of an increasingly sophisticated understanding of cancer as not one, but many hundreds of diseases requiring an equally sophisticated and individualised method of treatment. The committee heard that advances in the treatment of cancers are frequently incremental and increasingly targeted at small patient populations. More targeted medicines and therapies have the ability to increase the range of treatment options for cancer patients, resulting in improved quality of life and survival for many patients. At the same time, cancer is an area of high clinical need meaning that, even with access to subsidised medicines, many cancer patients face significant financial hardship. These challenges are exacerbated for those patients with rare or less common cancers, particularly children and young people, and those who live in rural and remote communities.

6.3 These factors pose a significant challenge for all governments as they seek to facilitate affordable cancer care while maintaining the sustainability of the overall health budget. The current trends in cancer research can be expected to continue.

6.4 Throughout this inquiry, the committee has been acutely aware that cancer patients are not the only patients who experience difficulty in accessing new and innovative medicines in a timely way. The committee considers that the concerns identified in this inquiry could easily apply to those diagnosed with a range of chronic or less common diseases. What sets cancer patients apart from many other patients is time. The vast majority of cancer patients do not have time on their side.

6.5 The committee considers that if the process for the assessment and listing of medicines can be enhanced to address the particular concerns that arise in relation to cancer medicines, it will inevitably serve the needs of all Australians more effectively.

6.6 Evidence to the inquiry has underscored the fact that access to medicines ultimately depends on the ability of patients to pay for them. The listing of medicines on the Pharmaceutical Benefits Scheme (PBS) plays a significant role in ensuring this access is equitable for all Australian patients.

6.7 As mentioned earlier, evidence to the inquiry has demonstrated that for many cancer patients access to new and innovative treatments comes at significant personal and financial cost. Those who require access to cancer medicines not currently listed on the PBS must resort to access through compassionate programs or clinical trials.

Evidence to the committee has demonstrated these avenues of access are neither equitable nor certain and frequently incur significant cost.

6.8 The committee heard that the inability to access cancer medicines, either because the preferred course of treatment is not registered in Australia or is not subsidised via the PBS, has significant flow on consequences for cancer patients and the people who care for them. The committee received numerous accounts describing the personal experience of cancer patients. These accounts underscored the grim reality that for cancer patients delays in access to new and innovative cancer medicines can be measured in loss of quality life years and lives lost.

6.9 The committee notes that a key factor in the timely availability of new cancer medicines is the timing of applications for registration and reimbursement by pharmaceutical companies. This is a commercial decision made in the context of a global industry. The committee understands the commercial imperatives that may lead a pharmaceutical company to seek regulatory approval in the United States or Europe in the first instance, in preference to a country with a small population, like Australia.

6.10 However, while the timing of the lodgement of applications is outside the control of Australian regulatory authorities, the committee notes that there is scope for the Australian Government to ensure that the regulatory processes in place for the consideration of applications are efficient and do not act as a disincentive to companies to seek listing and reimbursement.

Enhancing the operation of the TGA and the PBAC

6.11 Evidence to the inquiry has stressed the value that stakeholders place on the PBS and the Pharmaceutical Benefits Advisory Committee (PBAC) system. Submitters noted the importance of decisions regarding the registration and reimbursement being based on a rigorous, evidence based assessment of safety, efficacy and value.

6.12 However, while submitters consistently emphasised that the current PBS and PBAC process has served Australia well, they also emphasised the need for the system to be reviewed to ensure that it is capable of dealing with the challenges posed by the rapid development of cancer treatments in particular.

6.13 While some submitters expressed concern that a one-size-fits-all assessment process is no longer fit for purpose, the committee considers that the concerns raised in relation to the current process should be able to be addressed without creating a parallel process. The committee also notes that there is considerable commitment and goodwill within the pharmaceutical industry and the stakeholder community to work with government to explore avenues for addressing these concerns.

More streamlined and flexible processes

6.14 While the committee has noted that the current assessment processes are appropriately rigorous and based on clearly cyclical timelines, the committee notes that there is scope to improve the timelines for consideration of applications. The committee also notes that greater flexibility regarding evidentiary requirements and provision for entities other than the sponsor of a medicine to seek registration of new indications for medicines in appropriate circumstances may address concerns

regarding the responsiveness of the current registration system to changes in the clinical setting.

6.15 The committee notes evidence to the inquiry regarding fast track processes employed by overseas regulators and has noted that key features of such programs are early and frequent engagement between the regulator and the sponsor to address any issues associated with assembling data in support of an application and some form of 'rolling review'.

6.16 The committee also notes concerns regarding the evidential requirements of the current system. The committee considers that greater formal emphasis should be placed on quality of life considerations. In this context, the committee welcomes the current review of Parts II and III of the PBAC Guidelines and notes that the review provides a timely opportunity clarify the information requirements for applications for PBAC assessment. The review also offers an opportunity to identify new developments with regard to current methodology, along with any issues of scientific debate and consideration of Australian and international best practice.

6.17 The committee also supports greater collaboration between the TGA and the PBAC, along with continued examination of current parallel processing arrangements, to identify options for streamlining processes and minimising duplication in order to achieve compressed timeframes where possible.

Improved managed access programs

6.18 The committee notes the potential for managed access programs to address some of the concerns raised in relation to evidential requirements while at the same time providing more timely access to subsidised medicines. While Australia's initial managed entry scheme has not been enthusiastically embraced, the committee welcomes the work of the Access to Medicines Working Group (AMWG) in developing a new framework for a managed access program. The committee encourages the AMWG to consult closely with clinicians and consumers in finalising the framework.

6.19 The committee also notes evidence emphasising the need for consideration of a number of possible avenues to address demand for early access to new medicines. The committee notes that the provision of sustainable subsidised access to medicines, particularly expensive cancer medicines, will continue to pose a significant challenge for the Australian Government. The committee therefore supports the examination of a range of possible access models.

An increased role for consumers and clinicians

6.20 The committee considers that consumers and clinicians should play a more substantial role in the evaluation of new medicines. The committee commends the PBAC for its efforts to facilitate consumer engagement through the introduction of consumer and patient hearings.

6.21 The committee considers that consideration should be given to avenues for facilitating more formal discussion with the Australian community. The committee notes evidence received regarding the operation of formal mechanisms overseas to capture community expectations around broader moral and ethical considerations and

considers there is merit in considering how similar mechanisms might operate in the Australian context.

Greater transparency

6.22 The committee considers that greater transparency throughout the regulatory system will enhance the engagement of all stakeholders and will support a clearer understanding of the reasons for delays in listing of particular cancer medicines. Greater transparency also has the potential to support greater procedural efficiency and a commitment continuous improvement.

6.23 The committee notes the PBAC's commitment to increasing the transparency of its processes and the level and clarity of information available to consumer and patient groups. The committee notes the implications of commercial in confidence considerations for these initiatives, but encourages the PBAC and industry to work together to address these.

Improved monitoring and data collection

6.24 The committee notes the importance of establishing effective mechanisms for collecting and analysing clinical data in relation to the use of cancer medicines.

6.25 Evidence to the committee has underscored the importance of effective review of medicines after their listing on the PBS as a means of supporting the listing of medicines through managed entry programs. The committee welcomes the new guidance for post market reviews produced by the AMWG. The committee encourages the AMWG to continue to consult widely on the operation of the post market review program as greater use is made of managed access programs and more flexible assessment criteria to explore ways in which the program could support such initiatives.

6.26 The committee notes calls for the establishment of a national cancer registry, and, while it sees merit in this proposal, considers that a review of existing data collection mechanisms is a necessary precursor to the establishment of such a registry. The committee considers that a review of data collection must consider options for linking existing databases, facilitating wider access to the data collected and avenues for collecting data regarding the off-label use of cancer drugs.

The case for an interim specialist cancer drug fund

6.27 Evidence to the committee stressed that, while a comprehensive review of the current PBAC processes was necessary, such a review would take time to complete and cancer patients do not have time on their side. Submitters advocated the introduction of an interim cancer drug fund pending completion of a review, particularly for patients diagnosed with rare cancers.

6.28 The committee is cautious around suggestions that advocate for the establishment of separate regulatory mechanisms specifically to deal with cancer drugs. The committee is mindful of concerns raised about the operation of such funds overseas. In particular the committee is concerned at the potential for such funds to exacerbate some of the issues identified with the current PBAC system around cost

and access to cancer medicines, and the impact of separate assessment processes on the rigour and integrity of the PBAC system.

6.29 The committee notes NHS England's current review of its Cancer Drug Fund and the unintended consequences arising from the operation of the fund. The committee notes that NHS England is considering a managed access pathway as an alternative to a cancer fund.

6.30 The committee considers that if such a fund were to be established, it is preferable that it is established within the current regulatory framework and operates consistently with existing processes. The committee considers that the current Life Saving Drugs Programme (LSDP) may offer a basis for the delivery of an expanded government funded compassionate access program for patients with rare or less common cancers.

6.31 The operation of the LSDP is currently the subject of a post-market review. While a technical assessment of the LSDP has raised questions regarding the sustainability of the program in its current form, it has also highlighted options for enhancing its operation. The committee considers that there is merit in drawing on this current review to examine the scope for modifying the administration of the LSDP to provide an interim means of subsidised access to medicines for the treatment of rare cancers.

The need for a coordinated review of access pathways for cancer medicines

6.32 The findings of this inquiry are not new. Similar findings have been identified in previous reviews initiated by the Parliament and the Australian Government. However, the evidence to this inquiry has underscored the importance of acting to address the concerns raised in order to ensure that Australia has a system that is capable of meeting both the challenges posed by rapid developments in medical research and the demand for subsidised access to new and innovative medicine in a way that is timely, equitable and sustainable.

6.33 The committee has acknowledged that the current work of the independent Review of Medicines and Medical Devices Regulation also overlaps with the terms of reference of this inquiry and has produced findings that are consistent with the evidence the committee has received. The committee notes that the review panel has made recommendations to:

- expand the pathways by which sponsors can seek marketing approval for a medicine or medical device, including making provision for utilisation of assessments conducted by comparable regulators, and for expedited assessments in defined circumstances;
- identify comparable overseas national regulator authorities using transparent criteria;
- enhance post-market monitoring of medicines and medical devices and streamline post-market requirements in respect of products in the Australian Register of Therapeutic Goods; and

- improve transparency and predictability of processes and decisions to build trust and confidence in the NRA's ability to ensure Australians have timely access to high quality, safe and efficacious products.¹

6.34 The committee urges the Australian Government to give careful consideration to the implementation of these recommendations.

6.35 The committee also acknowledges work undertaken by the pharmaceutical industry and other key stakeholders. In particular, the committee notes the outcomes of the work streams initiated by the Cancer Drugs Alliance as a result of its forum in March 2014. The work of the AMWG in relation to the managed access program, transparency of PBS processes and post-market reviews, also has the potential have a positive impact on access to new cancer medicines. The committee considers that this work within the stakeholder community speaks to the considerable value placed on the PBAC system and the commitment and good will expressed by all stakeholders to working closely with government to improve its operation.

6.36 The committee has also noted initiatives that have the potential to impact on the assessment of medicines for listing on the PBS. While some of these, such as the review of the PBAC Guidelines and initiatives to enhance consumer engagement throughout the PBAC process, are positive interim steps towards enhancing the operation of the current system, the impact of others, such as the Pharmaceutical Benefits Scheme Access and Sustainability Package, are not yet known.

6.37 The committee recognises the importance of timely, interim changes but is concerned that an incremental approach to reform in this area risks being piecemeal and may squander the opportunity to identify synergies and efficiencies that a more coordinated and comprehensive review could identify. The committee considers that it is incumbent on the Australian Government to respond to the challenges facing the operation of the PBAC and the ongoing sustainability of the PBS in a comprehensive and considered manner.

6.38 The committee also wishes to emphasise the importance of consulting widely in the development and implementation of changes to the current system. In particular, while the committee welcomes the work of the AMWG, the committee encourages broader consultation with all relevant stakeholders prior to the implementation of changes as a result of the AMWG's work program.

6.39 Finally, as noted above, while this inquiry has focussed on access to cancer medicines, the committee considers that its findings have broader application. A review that seeks to address the concerns raised with regard to access to new and innovative cancer drugs, will inevitably address the concerns of all of those patients who rely on the PBS for timely and affordable access to best practice medical treatment.

Recommendation 1

1 Review of Medicines and Medical Devices Regulation, Report on the regulatory framework for medicines and medical devices, March 2015, www.health.gov.au (accessed 14 September 2015).

6.40 The committee recommends that the Australian Government initiate a comprehensive review of the system for the registration and subsidisation of medicines. The review should examine:

- all available pathways for the registration and listing of new medicines, or new indications for medicines already registered on the ARTG and listed on the Pharmaceutical Benefits Scheme, including making provision for utilisation of assessments conducted by comparable overseas regulators; provision for clinicians and/or patient groups to apply for an extension of existing registrations to additional indications, managed access programs and risk-sharing, and the adoption of more flexible evidential requirements;
- options for improving the operation of assessment processes including:
 - enhancing engagement with sponsors and other stakeholders to better tailor their applications to the requirements of the PBAC, including consideration of pre-application planning meetings;
 - applying tiered assessment processes as a means of matching resources to the complexity of applications;
 - encouraging greater cooperation between the PBAC, the TGA and the Medical Services Advisory Committee, including examination of options for enhancing the operation of parallel processing arrangements; and
 - ensuring greater transparency throughout the assessment process;
- options for expanding the post-market review of medicines;
- enhancing and formalising mechanisms for consumers and clinicians to play a more central and substantial role in the evaluation of new medicines and new indications for already listed medicines, including:
 - consideration of options for expanding consumer and clinician representation on the PBAC;
 - enhancing existing avenues for stakeholder input, including the use of consumer and patient hearings; and
 - avenues for incorporating public perspectives on overarching moral, ethical and opportunity cost considerations into PBAC decision making processes, including consideration of models employed by comparable overseas regulators; and
- options for ensuring that the necessary administrative and technical resources are available to support the implementation of an enhanced PBAC system.

Recommendation 2

6.41 The committee recommends that the Australian Government commission a review of current data collection mechanisms for cancer medicines, including identification of:

- **obstacles to the integration of existing databases and potential avenues for addressing these;**
- **opportunities to incorporate data from post-market evaluations; and**
- **avenues for capturing data relating to the off-label use of cancer medicines.**

Recommendation 3

6.42 The committee recommends that the Australian Government establish a Steering Committee to examine the feasibility of establishing a national register of cancer medicines.

Senator Rachel Siewert

Chair

APPENDIX 1

Submissions and additional information received by the Committee

Submissions

- 1** Bayer HealthCare Pharmaceuticals
- 2** CanSpeak
- 3** Ms Kerry Drinkwater
- 4** Mr John Dowling
- 5** Mr David Prestridge
- 6** Mr Paul Hobson
- 7** Mr Andrew Warden
- 8** Mr Doug Meiklejohn
- 9** Ms Jan Darby
- 10** Mr George Curr
- 11** Mrs Karen Cowley
- 12** Mr Janis Kinne
- 13** Mr Peter Carr
- 14** Name Withheld
- 15** Mr Peter Renwick
- 16** Haematology Society of Australia and New Zealand
- 17** Mr Michael Cochrane
- 18** Mr Leroy Lai
- 19** Mr Jason Noble
- 20** Capt. Michael Cottell
- 21** Mr John Perz
- 22** Mr Mark Usher

- 23 Mr Ken Young
- 24 Mr John Betts
- 25 Ms Lee McKerracher
- 26 Professor John Zalcborg OAM
- 27 Mr Michael Armessen
- 28 Urey Lau
- 29 Name Withheld
- 30 Ms Lorraine Hoskin
- 31 Ms Fanny Lai
- 32 Mr Luke Boyd
- 33 Mrs Ligia Matic
- 34 Mr Geoffrey Olsson
- 35 Mr Michael East
- 36 Ms Leah Graeve
- 37 Ms Lara Chapman
- 38 Ms Michelle East
- 39 Miss Natasha Jauncey
- 40 Name Withheld
- 41 Mr Peter Brown
- 42 Ms Jennifer Shepherd
- 43 Mr Neville Black
- 44 Ms Tracy Magiatis
- 45 Ms Kym Short
- 46 Specialised Therapeutics Australia
- 47 Mr Trevor Olsson
- 48 Ms Pauline Grant
- 49 Cancer Voices Australia (plus a supplementary submission)

- 50 Mr Glenn Stoddart
- 51 Mr Allen Sibley
- 52 Ms Ashley Jeffery
- 53 Cancer Drugs Alliance
- 54 Mr Russell Broadbent
- 55 John Logan Cancer Treatment Foundation
- 56 Mr Tony Maxwell (plus three attachments)
- 57 Mr Allan Davies
- 58 Mr Alan Barlee
- 59 Mr Patrick Coughlan
- 60 Name Withheld
- 61 Mr Trevor Brown
- 62 Mr and Mrs Paul and Maureen Thompson
- 63 Mr Alan Kearon
- 64 Brain Tumour Alliance Australia Inc
- 65 Ms Lillian Leigh
- 66 Dr Janet Wale
- 67 Name Withheld
- 68 Mr Bob Schmidt
- 69 Ms Janet Humphery
- 70 Mr and Mrs Peter and Eileen Brown
- 71 Rev Dr Noel Preston AM
- 72 Ms Chantal Tierney
- 73 Name Withheld
- 74 Mr and Mrs David and Pauline Armstrong
- 75 Ms Anita Rollinson
- 76 Mr John Shaw

- 77 Mrs Maureen Meiklejohn
- 78 Confidential
- 79 Mrs Jill Delahoy
- 80 Ms Linda Wilson
- 81 Mr Darren Smith
- 82 Ms Gail McGuinness
- 83 Palliative Care Australia
- 84 Ms Helen Scalzo
- 85 Ms Jennifer Litsas
- 86 Ms Louise Manoe
- 87 Novartis Oncology
- 88 CanSpeak Queensland
- 89 Confidential
- 90 Breast Cancer Network Australia
- 91 Mr Duncan Mitchell
- 92 Rare Cancers Australia (plus an attachment)
- 93 Ms Josie Muller
- 94 Mrs Claire Murnane
- 95 Ms Sharon Ryan
- 96 Ms Elizabeth Olsson
- 97 Ms Marion Davis
- 98 Ms Maureen Austin
- 99 Ms Tereena Cocks
- 100 Mr Damian Lech
- 101 Ms Catherine Arena
- 102 Name Withheld
- 103 Geelong Prostate Support Group

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- 104** Mr Scott Beyer
- 105** Advanced Prostate Cancer Support Group
- 106** Mr Jim Marshall
- 107** Name Withheld
- 108** Medical Oncology Group of Australia
- 109** AbbVie
- 110** Mrs Joanne Wills
- 111** Mr Michael Cook
- 112** Society of Hospital Pharmacists of Australia
- 113** Ms Lesley Royle
- 114** Roche
- 115** Name Withheld
- 116** Melanoma Patients Australia
- 117** Private Cancer Physicians of Australia Limited
- 118** Merck Serono Australia
- 119** Amgen Australia Pty Ltd
- 120** Merck Sharp and Dohme Australia (plus two attachments and a supplementary submission)
- 121** Pfizer Australia
- 122** Takeda Pharmaceuticals Australia
- 123** Leukaemia Foundation of Australia
- 124** Mr and Mrs Gerald and Suzanne Whitty
- 125** Link Healthcare
- 126** GI Cancer Institute Consumer Advisory Panel
- 127** Mr Eric South
- 128** Dr Agnes Vitry
- 129** Mrs Laura Carrington

- 130 The Unicorn Foundation
- 131 Gilead Sciences (plus a supplementary submission)
- 132 IVD Australia
- 133 Mr Terry Crook
- 134 Mr Ray Chilton
- 135 Dr Ian Musgrave
- 136 Ms Cindy Davenport
- 137 Ovarian Cancer Australia
- 138 Bristol-Myers Squibb
- 139 Ms Jolanda Visser
- 140 Janssen-Cilag Pty Ltd (plus a supplementary submission)
- 141 Ms Cathy Watt
- 142 Medicines Australia (plus two attachments and a supplementary submission)
- 143 Mrs Karen van Gorp
- 144 Australian Melanoma Consumer Alliance
- 145 Cancer Council Australia and Clinical Oncology Society of Australia
- 146 CanTeen
- 147 Novo Nordisk
- 148 Mr Wallace Donald
- 149 Bowel Cancer Australia
- 150 Cancer Voices South Australia
- 151 Cancer Action Victoria Inc
- 152 Australian and New Zealand Children's Haematology Oncology Group (plus a supplementary submission)
- 153 Dr James McIntosh
- 154 Name Withheld
- 155 Ms Roselyn King

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- 156** Mrs Lesley Hondrakis
- 157** Ms Caeleigh Hancock
- 158** Hepatitis Australia
- 159** Australasian Leukaemia and Lymphoma Group
- 160** Ms Tess Hemeter
- 161** Mr Rob Royle
- 162** Ms Monique Prior
- 163** Ms Kelly Hill
- 164** Mr Malcolm Trim
- 165** Ms Fiona Jewell
- 166** Genomics For Life
- 167** Lymphoma Australia
- 168** Mr Graham Evans
- 169** Mr Richard Harrison
- 170** Mr David Simcox
- 171** Ms Kim Watts
- 172** Mr Mark Haspels
- 173** Ms Teresa Cilona
- 174** Mr Jim Gruchy
- 175** Ms Nathalie Cook
- 176** Pharmaceutical Society of Australia
- 177** Dr Scott Chapman
- 178** Ms Allison McMaster
- 179** Ms Kate McIntosh
- 180** Ms Jane Casey
- 181** Mrs Anna Hickey
- 182** Mr Trevor Stenner

- 183** Australian Institute of Health and Welfare
- 184** Meni Stefanovski
- 185** Ms Deb Twomey
- 186** Ms Irene Ormsby
- 187** Cure Brain Cancer Foundation
- 188** Tasmanian Government Department of Health and Human Services
- 189** Mr Laurance Cook
- 190** Consumers Health Forum of Australia
- 191** Eli Lilly Australia
- 192** The Kids' Cancer Project
- 193** Generic Medicines Industry Association
- 194** Ms Elizabeth Smith
- 195** Mr Temple Kehoe
- 196** Pharmaceutical Benefits Advisory Committee
- 197** Australian Government Department of Health
- 198** Mr Peter Jones
- 199** Australian Melanoma Research Foundation
- 200** Name Withheld
- 201** Mr Matthew Storey
- 202** Name Withheld
- 203** Cancer Council Victoria's Clinical Network
- 204** Mr Brian Pound
- 205** Ms Angela Willett

Additional Information

- 1 Pharmacy tax invoice, from Chris Brugger, received 20 April 2015
- 2 Stakeholder perceptions study, by GA Research, from Rare Cancers Australia, received 22 April 2015
- 3 Information in relation to access to medicines for rare cancer patients in Australia, from Rare Cancers Australia, received 16 September 2015

Answers to Questions on Notice

- 1 Answers to Questions taken on Notice during 20 April public hearing, received from Advanced Prostate Cancer Support Groups, 24 April 2015
- 2 Answers to Questions taken on Notice during 20 April public hearing, received from Roche, 6 May 2015
- 3 Answers to Questions taken on Notice during 20 April public hearing, received from Australian Melanoma Research Foundation, 15 May 2015
- 4 Answers to Questions taken on Notice during 20 April public hearing, received from Cancer Drugs Alliance, 19 May 2015
- 5 Answers to Questions taken on Notice during 20 April public hearing, received from Novartis Oncology, 21 May 2015
- 6 Answers to Questions taken on Notice during 20 April public hearing, received from Ovarian Cancer Australia, 22 May 2015
- 7 Answers to Questions taken on Notice during 20 April public hearing, received from Clinical Oncology Society of Australia, 22 May 2015
- 8 Answers to Questions taken on Notice during 20 April public hearing, received from Leukaemia Foundation of Australia, 22 May 2015
- 9 Answers to Questions taken on Notice during 20 April public hearing, received from Society of Hospital Pharmacists of Australia, 22 May 2015
- 10 Answers to Questions taken on Notice during 20 April public hearing, received from Australian and New Zealand Children's Haematology and Oncology Group, 22 May 2015

- 11 Answers to Questions taken on Notice during 20 April public hearing, received from CanTeen, 22 May 2015
- 12 Answers to Questions taken on Notice during 20 April public hearing, received from Private Cancer Physicians of Australia, 22 May 2015
- 13 Answers to Questions taken on Notice during 20 April public hearing, received from Merck Sharp and Dohme, 24 May 2015
- 14 Answers to Questions taken on Notice during 20 April public hearing, received from Medicines Australia, 25 May 2015
- 15 Answers to Questions taken on Notice during 20 April public hearing, received from Unicorn Foundation, 25 May 2015
- 16 Answers to Questions taken on Notice during 20 April public hearing, received from Pharmaceutical Benefits Advisory Committee, 28 May 2015
- 17 Answers to Questions taken on Notice during 20 April public hearing, received from Merck Sharp and Dohme, 28 May 2015
- 18 Answers to Written Questions on Notice, received from NHS England, 16 June 2015
- 19 Answers to Questions taken on Notice during 20 April public hearing, received from Department of Health, 5 August 2015

Tabled Documents

- 1 Picture, tabled by Naomi Brugger, at Canberra public hearing 20 April 2015

APPENDIX 2

Public hearings

Day, date, month, year

Venue, City

Witnesses

Medicines Australia

JAMES, Mr Timothy, Chief Executive Officer

GALLAGHER, Mr David, Board Member; and Chairman and Managing Director,
Pfizer Australia

TENNYSON, Dr Mark, Board Member; and Executive Medical Director, Amgen
Australia Pty Ltd

Ovarian Cancer Australia

NIELSEN, Dr Katherine, Director, Research and Advocacy

Australian Melanoma Research Foundation

COVENTRY, Professor Brendon, Research Director

ASHDOWN, Mr Martin, Research Fellow, Faculty of Medicine, University of
Melbourne

Leukaemia Foundation of Australia

STEELE, Mr Anthony, Head of Blood Cancer Support

BRUGGER, Mr Christopher, Private capacity

BRUGGER, Mrs Naomi, Private capacity

Cure Brain Cancer Foundation

LITTLEFIELD, Mr Barrie, Head of Engagement

STEWART, Ms Michelle, Head of Research Strategy

Novartis Oncology Australia and New Zealand

LOREZ, Mr Christoph, General Manager

THOMAS, Ms Jodie, Head of Access to Medicines and Pricing

Merck Sharp and Dohme Australia

SELLARS, Mr Christian, Director, Market Access and Public Affairs

RICHARDS, Ms Nicola, Head of Public Affairs

Roche Products

PULLAR, Mr David, Manager, Government Affairs and Public Policy

TODD, Ms Carlene, Director, Market Access and Pricing

CanTeen Australia

ORCHARD, Mr Peter, Chief Executive Officer

OSBORN, Dr Michael, Lead Clinician, Youth Cancer Service South Australia and Northern Territory

Australian and New Zealand Children's Haematology and Oncology Group

FRASER, Dr Christopher, Chair

DALLA-POZZA, Dr Luciano, Board Member

The Kids' Cancer Project

NEILSON, Mr Peter, Director, Strategy and Partnerships

ANDERSON, Ms Susan, Representative

Rare Cancers Australia

VINES, Mr Richard, Executive Chair

CANNINGS, Mr John, Private capacity**The Unicorn Foundation**

LEYDEN, Ms Simone, Chief Executive Officer

Society of Hospital Pharmacists of Australia

DIPROSE, Ms Emily, Federal Councillor

ALEXANDER, Ms Susan, Member

Cancer Council Australia

GROGAN, Mr Paul, Director, Public Policy and Advocacy

Clinical Oncology Society of Australia

KIRSA, Mrs Suzanne, Adviser and Member

Palliative Care Australia

BRESNAN, Ms Amanda, National Policy and Programs Manager

Australian and New Zealand Society of Palliative Medicine

CHAPMAN, Dr Michael, Secretary

Medical Oncology Group of Australia

STEER, Dr Christopher, Member

Private Cancer Physicians of Australia

STEER, Dr Christopher, President

Cancer Drugs Alliance

ZALCBERG, Professor John, Co-Chair

Melanoma Patients Australia

ANDERSEN, Ms Hayley, Chief Executive Officer

Advanced Prostate Cancer Support Groups

MARSHALL, Mr James, Convenor

Australian Melanoma Consumer Alliance

MARSHALL, Ms Louise, Founding Member

Breast Cancer Network Australia

WELLS, Ms Kathryn, Head, Policy, Research and Advocacy

COWLEY, Mrs Karen, Consumer Representative and Cancer Survivor

Pharmaceutical Benefits Advisory Committee

HILL, Dr Suzanne, Former Chair

WARD, Prof. Robyn, Member

WATSON, Ms Jo, Member

Department of Health

STUART, Mr Andrew, Deputy Secretary

McNEILL, Ms Felicity, First Assistant Secretary, Pharmaceutical Benefits Division

PLATONA, Ms Adriana, Assistant Secretary, Pharmaceutical Evaluation Branch,
Pharmaceutical Benefits Division