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:

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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.

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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 make 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.
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> 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.
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> 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:

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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]

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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.

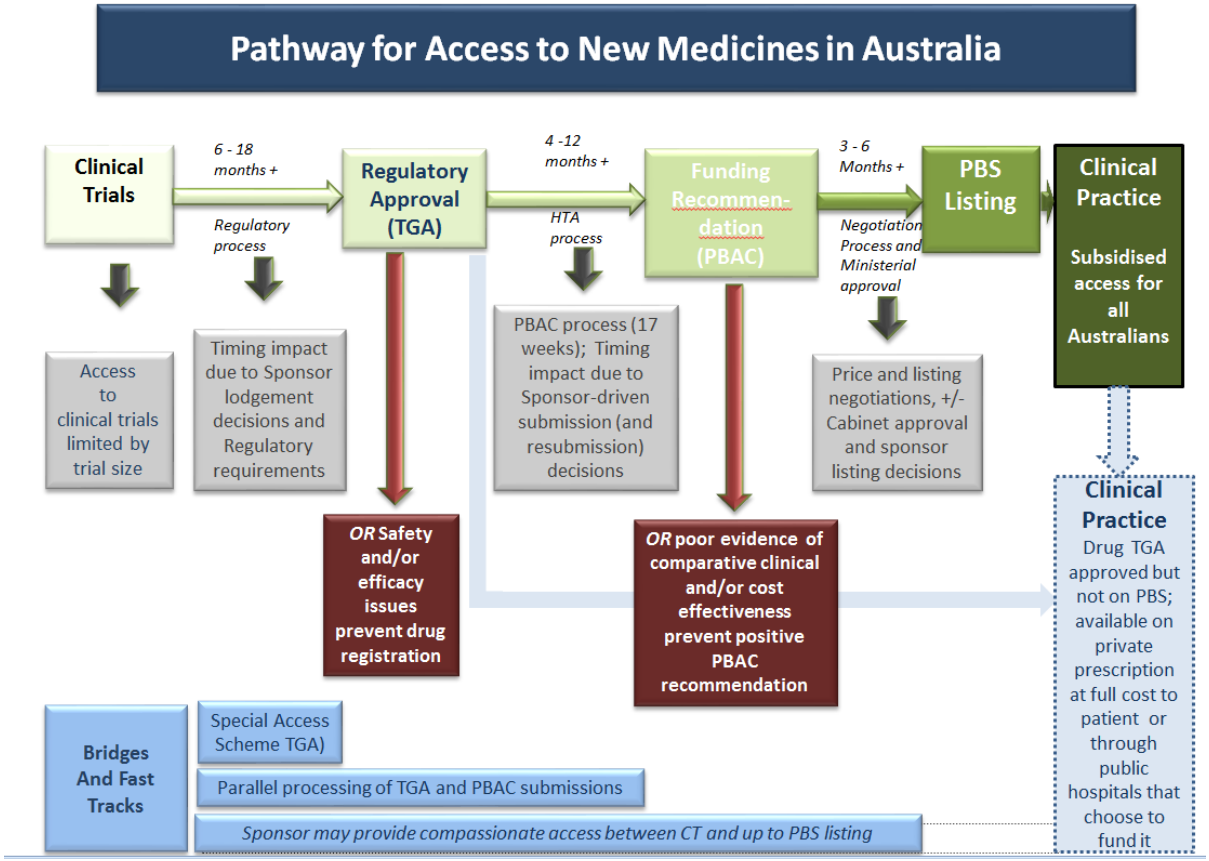
28 MA, *Committee Hansard*, 20 April 2015, p. 2.

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

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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

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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 pembrolizumanb. 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

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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]

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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 availabile 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

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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.
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> 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.
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> …
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> 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]

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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 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

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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

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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.