Availability of new, innovative and specialist cancer drugs in Australia

Submission to the Senate Community Affairs References Committee

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Pharmaceuticals Division, Corporate Affairs, Dee Why

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-four medicines developed by Roche are included in the World Health Organisation Model Lists of Essential Medicines, among them antibiotics, antimalarials and chemotherapy.

In 2014, Roche invested 8.9 billion Swiss francs in research and development worldwide, including over $36 million (AUD) in pharmaceuticals in Australia. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

More information about Roche is available through www.roche-australia.com

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Executive Summary

Innovation in the treatment of cancer has exceeded our system's ability to assess and reimburse medicines. The complexities of cancer medicines provide many "uncertainties" from the perspective of the Pharmaceutical Benefits Advisory Committee (PBAC), which is tasked with recommending medicines for funding. These "uncertainties" may provide many reasons to reject or delay funding applications, in order to minimise risk to the taxpayer of overpaying for medicines. However, a risk averse and inflexible approach misses the full and evolving value of cancer therapies to patients and the community and all too frequently denies patients timely access to important advances in care.

In recent years, delays and access restrictions have become concerning for cancer patients. Not only is Australia now ranked at the bottom of highly-developed countries for access to recent cancer medicines, we frequently do not fund their full range of approved uses. Roche's two recent therapies for metastatic breast cancer have taken more than three times the average for highly-developed countries to be reimbursed following registration, and while expected to be listed soon, they are still not on the Pharmaceutical Benefits Scheme (PBS) nearly two years after registration.

This creates serious inequalities between patients: in time to access treatment, where patients who need innovative therapies now are disadvantaged compared to those who will be diagnosed in the future when these medicines are eventually listed; and where patients requiring the same targeted cancer medicine will have different levels of access because of the organ where their cancer first occurred.

These delays and issues can be attributed to a "one-size-fits-all" approach to assessing the value of medicines, risk-averse management of uncertainty and a narrow conception of what aspects of value matter. Australia is lagging other developed countries that take a more flexible approach, including involving the broader community in considering the important ethical and social issues. The PBS requires urgent review to ensure the system is "fit-for-purpose", aligned with community values and efficiently engages all stakeholders early on in the process, to avoid the delays of multiple submissions.

Roche does not advocate that cancer treatments should inherently be held to different standards than other specialty medicines. Instead, these reforms to the PBS will ensure that all high-burden diseases will have more timely access to new medicines. Nevertheless, as cancer is frequently life-threatening, patients need all stakeholders to collaborate urgently to find solutions.

Australia has engaged in important reforms to the PBS in the last decade that have created significant savings from older medicines, placing the PBS on a sustainable footing. We now have the opportunity to invest in innovative new medicines that will benefit patients in need.

Table of Recommendations

1. **Utilise the significant savings from Pharmaceutical Benefits Scheme (PBS) reform to support continued investment in innovative medicines that lead to improvements in health outcomes, including for cancer.**

2. **Build on the ongoing review of the Therapeutic Goods Administration (TGA) to improve the functioning of parallel regulatory and reimbursement assessments and to support timely PBS listing.**

3. **Introduce a Citizens' Council on health technology assessment (HTA) to collect community input on social and ethical aspects of medicines such as end-of-life care, indirect costs and the value of a quality-adjusted life year (QALY).**

4. **Review the HTA system in Australia to consider the following specific aspects:**

    a. **Fit-for-purpose evaluation of medicines, taking into account budget impact, level of innovation and complexity, rarity of disease, unmet need and clinical benefit;**

    b. **Increased citizen, patient, clinician and academic involvement in decision-making, with improved transparency around decision-making and criteria;**

    c. **Incorporation of societal values and costs/benefits beyond the health system into the decision-making process, as well as a willingness-to-pay in line with other highly-developed countries; and**

    d. **Earlier and increased engagement between all stakeholders.**

1. Introduction

Roche welcomes the opportunity to make a submission to the Senate Community Affairs References Committee inquiry into "Availability of new, innovative and specialist cancer drugs in Australia". This is an important topic for the one-in-two Australians who will develop cancer in their lifetime and the one-in-five who currently die as a result[1], as well as their families and the clinicians, researchers and businesses working to improve patient outcomes.

Roche is a leader in the field of cancer therapeutics, with 10 registered cancer medicines in Australia, and the company continues to invest a significant amount in the search for innovative treatments in areas of high unmet clinical need. Roche has more than 30 cancer drug combinations in development[2] and over 20 novel "immunotherapies" for cancer in the pipeline[2].

Innovation in the treatment of cancer has exceeded our system's ability to assess and reimburse medicines. The complexities of cancer medicines provide many "uncertainties" from the perspective of a health technology assessment (HTA) body such as the Pharmaceutical Benefits Advisory Committee (PBAC). These "uncertainties" may provide many reasons to reject or delay funding applications in order to minimise risk to the taxpayer of "overpaying" for medicines. However, a risk averse and inflexible approach misses the full and evolving value of cancer therapies to patients and the community and all too frequently denies patients timely access to important advances in care.

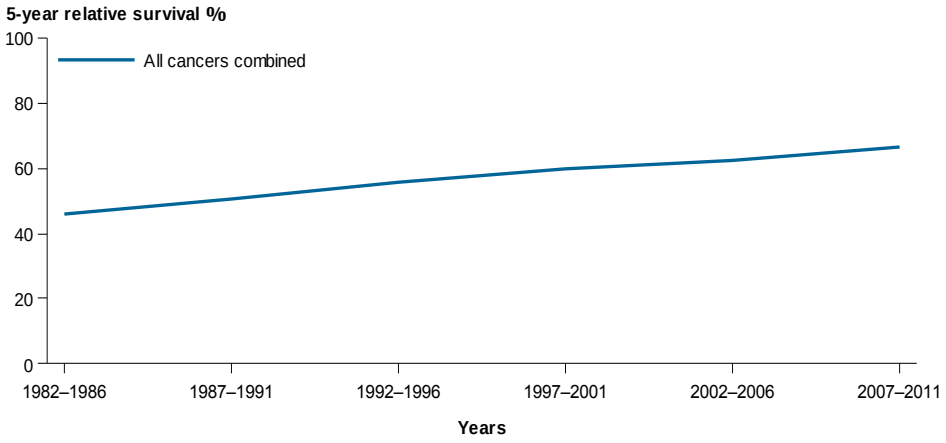
While Roche does not advocate that cancer treatments should inherently be held to different standards than other specialty medicines, cancer faces particular challenges related to the urgency with which patients with terminal illness require treatment, the pace of innovation in this area and the challenges of showing conclusive "overall survival" gains in cancer trials. This submission aims to present solutions that would improve timely access to all specialised medicines, not only cancer, while preserving the sustainability of the Pharmaceutical Benefits Scheme (PBS). As cancer is frequently life-threatening, inaction is not an option.

2. Cancer in context

Cancer is not just one disease: over 200 types of cancer have been identified so far. It accounts for more than a third of the burden of premature death[3], yet in 2008-09, cancer received only 7% of Australian health expenditure on chronic disease[4].

Improvements in diagnosis and care, including innovative medicines, have contributed to significant gains in survival for Australians with cancer[5] (Figure 1 below). Five-year survival rates for bowel cancer improved from 46.9% to 66.9% in the last three decades, with breast cancer improving from 72.2% to 89.6% and prostate cancer from 56.6% to 93.2%[5]. In many cases, improvements have come through multiple incremental gains, rather than medical breakthroughs. Even areas such as lung cancer and advanced melanoma, where outcomes remain poor, have benefited from innovation in recent years, with novel targets and use of the body's own immune system to fight cancer. The challenge has been to make these therapies available to Australian patients in a timely way.

Figure 1 – 5-year relative survival for cancer in Australia



Source: AIHW 2014. "Cancer in Australia: an overview 2014"

In comparison to Europe or North America, Australians commonly experience delays of several years in reimbursement being provided for medicines, or experience limitations on their ability to access funding. Australia was recently ranked 12th out of 13 highly-developed countries for uptake of new cancer medicines, with reimbursement the most likely restriction. Australia was ranked only 9th for access to more established medicines (5-10 years since launch)[6]. An international comparison of 10 cancer medicines in 2012 showed Australia only funded 46% of the approved indications for these medicines, compared to 100% in the USA and Sweden, 92% in Germany, 90% in France, and 88% in Italy[7]. Examples of funding delays from Roche's portfolio are shown in the box below.

Case study: Timelines for reimbursement of treatments for advanced breast cancer

The time to reimbursement in Australia for Roche's two most recent medicines for metastatic breast cancer, pertuzumab (Perjeta®) and trastuzumab emtansine (Kadcyla®), has been notably longer than in other highly-developed countries. These two medicines were recommended by the PBAC late in 2014 and are expected to be listed on the PBS in the near future. However, as of February 2015, it has been 21 months since pertuzumab was approved by the Australian regulator, the Therapeutic Goods Administration (TGA). This is almost three times the average time to access (between registration and reimbursement) seen in 14 other highly-developed countries: the UK, Germany, France, Spain, Italy, Belgium, the Netherlands, Finland, Denmark, Ireland, Greece, Luxembourg, Canada and Switzerland. Likewise it has been 18 months since trastuzumab emtansine was granted regulatory approval in Australia. The average time to access for trastuzumab emtansine in a similar list of 14 countries is less than one third of this time, at only 5 months[8]. Two submissions for pertuzumab and three for trastuzumab emtansine have been made to the PBAC. Roche, clinicians and other stakeholders also engaged with Department of Health staff and members of the PBAC in a stakeholder meeting (May 2014) in order to progress reimbursement of these agents.

Even with these limitations and delays, the expansion of options for managing cancer means that it now constitutes an increasing share of medicines funding in Australia, although still proportionately less than its burden of disease. Recently the Parliamentary Library estimated that while there has been an overall slowing of PBS growth, the "Efficient Funding of Chemotherapy is the fastest growing Section100 program [for specialised hospital drugs] with an average annual growth rate of 62.61%"[9]. This figure should be considered with caution, as it represents only 6% of the $9 billion cost of the PBS[10], excludes company rebates and is only part of PBS expenditure on cancer medicines. Headline expenditure growth figures for small programs must be considered with caution and in the broader context of community need, improved patient health outcomes, innovation and overall value.

Reforms to the PBS since 2007 are expected to deliver nearly $18 billion in savings to 2017-18[11], providing a real opportunity to invest in innovative medicines, such as those for cancer. This inquiry allows for open consideration of the significant value of cancer medicines and the need for reform. Given the significant unmet need that remains in cancer, and the known delays in access that are occurring, the "headroom" provided by PBS savings must be reinvested in the interests of patients.

Recommendation 1: Utilise the significant savings from PBS reform to support continued investment in innovative medicines that lead to improvements in health outcomes, including for cancer.

3. Principles of access and value

3.1 Value of innovation

The value of medicines innovation has many components, including:

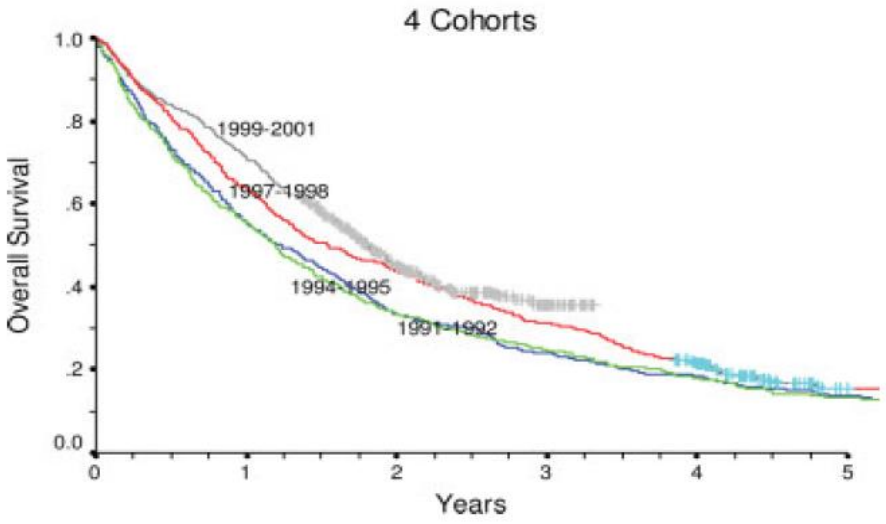
- increased survival and quality of life;
- convenience of delivery and reduced healthcare system costs;
- improved ability to deliver treatment in regional or remote areas;
- replacing inefficient older treatments;
- improved understanding of diseases and medicine targets; and
- improved patient productivity and reduced burden on carers.

Innovation often proceeds incrementally and there is important community value in both specific products and a sustainable medicines industry that continuously improves healthcare. The value of cancer medicines can be found in both the immediate gains for patients and in the longer term improvements in cancer care seen over the last 40 years.

There is "real-life" evidence of the positive impact new agents have had on overall survival (OS) from a Canadian study of patients with metastatic breast cancer (mBC)[12], as shown in the figure below,

which depicts the proportion of patients remaining alive after diagnosis, for cohorts with access to differing standards of care. Between 1991 and 2001, seven new systemic agents were introduced* and there was a significant improvement in median OS by 7.5 months during that period, in a disease where few patients survived beyond two years. Whilst mBC remains incurable, this study suggests that the introduction of new therapy options will translate into further improvements in health outcomes.

Figure 2 – A cohort analysis of incremental survival benefit over time in mBC



Source: Chia S, Speers C et al. 2007.

It is also important to remember the value of a medicine continues beyond patent expiry, often after 10-12 years on the market, when generic and biosimilar competitors lead to subsequent price decreases, and may include many years of improved health benefits at very low cost to payers. Without the initial introduction of a medicine, which depends on a company "sponsor" being able to achieve a return on investment, the full long-term value of the medicine may never be realised.

3.2 Pricing of medicines

The development of a new medicine is highly risky: only a small portion of early-stage research products makes it into clinical trials involving patients, and of those, only one in five results in an approved medicine[13]. Pricing of those medicines that make it to market must take into account the costs of research "failures" and allow investment for future success. The price is also linked to the full value of the medicine, discussed above in Section 3.1.

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* This Canadian study examined 2,150 patients diagnosed with mBC with four cohorts, as follows:

1. Jan. 1991 to Dec. 1992 - which was the baseline comparator
2. Jan. 1994 to Dec. 1995 - the period during which paclitaxel and vinorelbine became available
3. Jan. 1997 to Dec. 1998 - the period after the approval of the aromatase inhibitors and docetaxel for mBC
4. July 1999 to June 2001 - the period of access to trastuzumab and capecitabine.

Cancer medicines are not inherently more expensive to governments or patients than medicines for other conditions. In fact, the average PBS price paid for cancer medicines has declined in the last two years[14], in comparison to an overall health inflation rate of more than 4% per annum and consumer price inflation of nearly 2%[15]. In addition, the development of increasingly targeted cancer medicines means that small subgroups of patients are often treated (such as HER2+ metastatic breast cancer), in which cases the budget impact may be quite small. Only four of the top 50 medicines by cost on the PBS are for cancer[16].

Since Roche sells medicines globally, prices in different markets are interdependent, due to external reference pricing and parallel trade. Many governments and insurers will typically seek to achieve the best price available in similarly developed markets. This restricts the ability of a company like Roche to grant price concessions exclusively to payers that are economically comparable. Roche operates within a global pricing band set by our parent company and has very limited ability to price below this band. In these circumstances, Roche's experience that Australia has a lower "willingness-to-pay" for health gains than other developed countries (see Section 5.1.1) may be acting as a barrier to access.

3.3 Health technology assessment

Roche supports an evaluation and comparison of the value and the costs of different healthcare technologies when allocating health funding, which may include the use of HTA. HTA encompasses a range of different methodologies to determine the relative value of a medicine, in comparison with alternatives. It therefore supports decisions about whether to adopt a medicine, at what price and in which groups of patients. A European collaboration has set out the core "domains" of HTA[17]:

- health problem and current use of technology;
- description and technical characteristics of technology;
- safety;
- clinical effectiveness;
- costs and economic evaluation;
- ethical analysis;
- organisational aspects;
- social aspects; and
- legal aspects.

Not all of these elements are given equal weighting or even considered in the PBAC's use of HTA, and some are easier to assess than others based on the evidence available. As discussed below, a focus on costs and economic evaluation in HTA has the potential to miss important elements of value and lead to underinvestment in new medicines.

4. Timing and affordability of access for patients

4.1 Regulatory processes

In order to be provided to patients in Australia, medicines must first be registered by the TGA. While

the TGA is a competent and well-regarded agency, Roche supports the recommendations for streamlining processes described in the responses to the current review of the TGA. The ability to make regulatory and reimbursement submissions in parallel has been a positive step in recent years, potentially reducing the time from TGA registration to PBS listing for new medicines. However, in practice, the delays in medicines funding remain, regardless of any shortened timeframe from TGA registration to first PBAC consideration. Roche supports the government building on the ongoing "expert review" of the TGA to also consider the connections with the reimbursement process to streamline the entire process for medicines access in Australia.

Recommendation 2: Build on the ongoing review of the TGA to improve the functioning of parallel regulatory and reimbursement assessments and to support timely PBS listing.

4.2 Reimbursement processes

As discussed above in Section 2 and in detail in the Medicines Australia submission to this inquiry, Australia experiences significant delays and limitations in access to new cancer medicines. Not only have success rates for reimbursement submissions diminished in recent years, Roche has medicines that have never been submitted for reimbursement in light of the challenging process (see box below). For several of these products and indications, Roche has received feedback from the PBAC or the Department of Health that a submission based on the global pricing band and the current level of evidence is unlikely to be successful, even if it has been acceptable internationally. In such cases, these medicines/indications are only available through private sales or compassionate access programs, leading to significant equity issues for patients (see Section 6 below).

Examples of Roche cancer medicines not reimbursed in Australia

Initial or subsequent rejection, no further submissions made

- Bevacizumab (Avastin®) for non-small cell lung cancer; and relapsed glioblastoma
- Vemurafenib (Zelboraf®) for BRAF+ metastatic melanoma

Decision made not to submit

- Bevacizumab for metastatic breast cancer; renal cell carcinoma; and relapsed, platinum sensitive ovarian cancer
- Erlotinib (Tarceva®) for pancreatic cancer; and non-small cell lung cancer first-line maintenance
- Vismodegib (Erivedge®) for advanced basal cell carcinoma

Delays and unpredictability are particularly common for targeted cancer therapies that use companion diagnostic tests[18], despite the potential for these targeted treatments to maximise the benefits of treatment and minimise side-effects. Trastuzumab (Herceptin®) for metastatic gastric

cancer was first submitted for reimbursement along with companion testing over four years ago. HTA rejections and negative feedback from evaluators, coupled with the challenge of allocating company resources to a complex submission with low likelihood of success, have led to lengthy delays. For a medicine that would cost the government less than $2 million annually, in an area of significant patient need, the expected six HTA evaluations (three for the medicine and three for the test) do not represent a "fit-for-purpose" or efficient system.

5. Operation of the Pharmaceutical Benefits Advisory Committee and the Pharmaceutical Benefits Scheme

5.1 The PBAC and cost-effectiveness

Roche is concerned that access to medicines is being limited by decision makers' narrow concept of "value", focus on cost containment and expectation that Australia should pay prices significantly lower than in comparable developed nations. Cancer drugs pose particular challenges for the PBAC. Capturing overall survival in trials (see Section 5.1.2), the incremental nature of cancer innovation and the use of companion diagnostics introduce "uncertainty", which is frequently the reason for rejections of reimbursement applications. Yet these should be properly balanced with the significant value of the treatments and the opportunity cost to the community of delaying access for patients.

5.1.1 Assessing value

Under the *National Health Act 1953* s101 (3B), the PBAC is specifically required to only recommend those medicines where additional costs are accompanied by "significant improvement in efficacy or reduction in toxicity over the alternative therapy". Yet in practice, the PBAC goes further and only recommends medicines where the incremental cost-effectiveness ratio (ICER), the ratio of additional costs to additional quality-adjusted life years (QALYs), and the budget impact are "acceptable".

However, there is no universally accepted threshold for what constitutes a "cost effective" ICER. Although not explicit, experience suggests that the PBAC's "willingness-to-pay", or ICER range for the acceptable cost of a QALY, is potentially less than half of that proposed by the World Health Organisation (WHO) as cost effective: 1-3 times gross domestic product (GDP) per capita[19].

As noted in Section 3.3 above, the cost, safety and efficacy components of an ICER are only three possible elements of a comprehensive HTA. Ethical, organisational (impact on health services), social and legal elements are also relevant to these decisions. In practice, many of the value elements of treatments (see Section 3.1) are not given a high priority by the PBAC and it is not transparent whether they have been considered in decisions to fund or not fund treatments. Several examples from Roche's experience where potential benefits may have been insufficiently valued include:

- Benefits for regional and rural patients – 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.
- Improved productivity and benefits for carers – Roche's submission to the PBAC for a

targeted therapy in metastatic melanoma showed a significant improvement in "cost effectiveness" when including the benefits of patients returning to work, reduced travel costs and productivity gains from an oral therapy not requiring medical service attendance.

- Incremental innovation – A first-in-class treatment against a disease target such as EGFR+ lung cancer allows researchers to build on knowledge of how cancer responds to treatment.
- Replacing inefficient older treatments – Recent treatments for metastatic melanoma and lung cancer have replaced therapies that had not moved forward over several decades.
- Rarity of disease and lack of alternative options – Biological treatments target the specific proteins on several different cancers, which may range from common cancers to rarer forms such as gastric cancer, where fewer options are available.

More and more Australia stands alone in continuing to apply a "one-size-fits-all" approach to cost-effectiveness methodology, regardless of medicine or therapeutic area. The PBAC typically seeks to maximise the QALYs gained for a given cost, whereas other countries give greater weight to ethical considerations such as fairness to those in greatest need. Local evidence suggests that this "QALY maximisation" approach is not supported by the Australian community where it harms equity[20]. While Roche understands the PBAC exercises some flexibility in this regard, it is important that the Australian community has a voice in determining what is considered value for money in HTA. Chim et al[21] have asked whether "it is timely and pertinent to question whether the PBAC should allow for a higher cost-per-QALY threshold for cancer drugs" and to align with society's "willingness-to-pay".

The PBAC approach becomes especially challenging when new therapies are added to the existing standard of care. In metastatic breast cancer, Roche performed a calculation to show that a medicine that adds half a year of life and improves quality of life in comparison to the standard of care, was not considered cost-effective even at $4 a vial, or the equivalent of the price of a cup of coffee, under the current PBAC methodology[22]. An ICER-based system with an undifferentiated ICER threshold, by virtue of the mere methodology applied, may never show an acceptable outcome for combination treatments, given the increased cost associated with the extension of treatment duration and follow-up of patients, despite the value to patients.

A "socially-appropriate" willingness-to-pay is related to two factors: ability-to-pay based on economic resources available; and social preferences.

Ability-to-pay can be considered by benchmarking Australia's prices for medicines to other Organisation for Economic Co-operation and Development (OECD) countries with similar levels of economic development, such as Canada, the United Kingdom and those in Western Europe. The WHO principle above of linking ICERs to GDP per capita suggests this is a useful starting point. If the PBAC requires prices significantly lower than other highly-developed countries, and if this comes at the expense of timely access (as seen above), then Australia is likely out-of-step with the rest of the world and patients are being disadvantaged.

Societal values, which are particularly important, can only be derived through a process that allows active participation by citizens and a clear set of decision-making principles. These decision-making

frameworks have been considered in other HTA countries (UK, Canada and the Netherlands). A similar approach has been taken in South Australia for strategic planning issues with the recently-established Citizens' Jury for non-health related matters. The PBAC currently has only one health consumer representative, whereas other countries have found it useful to expand patient input. Roche supports exploration of similar approaches in reassessing the PBAC's decision framework.

Recommendation 3: Introduce a Citizens' Council on HTA to collect community input on social and ethical aspects of medicines such as end-of-life care, indirect costs and the value of a QALY.

5.1.2 Dealing with uncertainty

As noted above, HTA, whether using ICERs or alternative approaches, must grapple with uncertainty around value. While development of additional clinical or "real world" evidence over time may address some uncertainties, this can be expensive, time-consuming and may still leave questions unanswered.

Unfortunately, the PBAC has a low tolerance for uncertainty, likely out of a desire to avoid the risk of the government overpaying for uncertain benefits. Significant uncertainty usually results in a rejection, a re-submission and access delays for patients. There may be real consequences to patients with life-threatening cancers as a result of delaying access on the grounds of avoiding risk. The improved certainty must be balanced against the opportunity cost of those patients who were unable to access the therapy in the interim, and the inequality that this has produced.

One specific example of this narrow approach to managing uncertainty is the PBAC's preference for the use of overall survival (OS) data to derive the cost per QALY. Cancer medicines are typically registered on the basis of progression-free survival (PFS), i.e. the medicine significantly extends the time for the cancer to recur following treatment response. This is a relatively straightforward measure that usually compares between the new medicine and the prior "standard of care". Demonstrating OS in cancer trials is more complex, as it looks at survival of patients beyond progression of their cancer (i.e. until their death), which is influenced by their subsequent treatments. A significant impact comes from the ethical imperative to give access to the new medicine or regimen to patients who progress while on the comparator treatment, known as "cross-over". This masks (i.e. "confounds") the ability to measure the OS from the experimental medicine/regimen versus the comparator and creates uncertainty, because patients on both treatment arms receive the experimental medicine at some time.

The responsibility rests with both the sponsors of new medicines and the PBAC to find constructive solutions to uncertainty. In order to improve timely access and manage uncertainty, Roche supports a more dynamic approach to HTA through the appropriate use of managed entry schemes for innovative medicines. 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 considers 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). Such initiatives are being

considered by the Access to Medicines Working Group (AMWG), which involves the Department of Health and the medicines industry. A proposal by the AMWG has been developed and Roche understands it is scheduled to be reviewed by the PBAC at its March 2015 meeting. It is important that timely action is taken and that deadlines are set for meaningful reform to occur.

There is limited opportunity for frank dialogue with the PBAC to identify uncertainties and other issues ahead of time and avoid the need for multiple submissions. Sponsors are able to meet with Department of Health officials ahead of submissions. However, as Departmental officials are not the ultimate decision-makers, their advice may not reflect the PBAC's views. Evaluation of the submission is also usually undertaken by external academic groups and increasingly does not reflect pre-submission discussions with the Department or even the advice of the PBAC Chair provided following an initial rejection. Earlier and increased engagement between clinicians, academics (including evaluation units), the PBAC, patient groups and sponsors could help address technical and methodological issues in advance of a first PBAC submission and allow for consistency and agreement on treatment algorithm, comparators, model inputs and structure. This could streamline the current process to reduce submission "churn" as was seen in the case of Roche's breast cancer therapies.

5.1.3 Fit-for-purpose evaluation

Roche considers that "fit-for-purpose" evaluation is important, to avoid unnecessary red tape burden for simple submissions and to dedicate appropriate resources to those that are more complex. This would be based around a more comprehensive evaluation for complex applications or innovative medicines that are associated with higher budget impact and therapeutic value, and less comprehensive evaluation for treatments with low budget impact, treatments for rare diseases and simple submissions (e.g. the majority of cost-minimisation analyses).

In order to define the shape of fit-for-purpose evaluation, future discussions involving government and other stakeholders will be needed, to agree on a framework and suitable criteria for defining "complex submissions". A key aspect of comprehensive evaluations would be early stakeholder meetings, which would require more resourcing but could be offset by streamlining less complex submissions, and reducing submission "churn" as previously outlined. The goal of this "fit-for-purpose" approach would be to support timely and equitable access. International best practice suggests that a proactive approach to engaging all stakeholder groups is needed[23], as is allocation of resources (time, personnel and money) to where there is greater need for robust evaluation.

In order to maintain the cost-recovery principle of the PBAC, more complex submissions may require additional fees. All stakeholders should understand why and how a decision is made to utilise the complex or simple evaluation pathways.

5.2 Post-PBAC processes

Roche acknowledges that several government initiatives over the last ten years have focused on reducing listing delays following a positive PBAC recommendation. Post-PBAC steps include negotiations on final pricing, risk-sharing agreements and Cabinet approval of medicines expected to

cost over $20 million per annum. However, Roche notes that the Cabinet threshold remains an arbitrary rule and one that does not add significant value to the process. Risk-sharing agreements are also 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. Roche considers that the industry and government should work together to identify opportunities to further streamline listing processes. It is important to note that these issues apply to cancer and non-cancer medicines alike.

5.3 Need for review

As noted above, there are several areas where the PBAC process needs to be reviewed, facilitating reforms that would improve timeliness, efficiency and patient access. While no country's HTA system is "perfect" for patients, governments, clinicians and industry, there are lessons from other well-established HTA systems.

The Netherlands, Sweden and the province of Quebec (Canada) routinely consider indirect costs and benefits (such as patient and carer work productivity) in the assessment process[24]. While the PBAC Guidelines state that other factors (e.g. societal values) are taken into account, there is no transparency in how final decisions are made by the PBAC, and what weighting is attributed to these other factors. Several countries are now investigating multi-criteria decision making, which incorporates numerous decision criteria and also allows for weighted consideration of the criteria. The UK and Taiwan involve citizens in decision-making, which is critically important to address the issues outlined in Section 5.1.1. There is a growing trend in HTA countries towards adoption of a different or more fit-for-purpose process for medicines for the treatment of rare diseases or with low budget impact.

Recommendation 4: Review the HTA system in Australia to consider the following specific aspects:

- **Fit-for-purpose evaluation of medicines, taking into account budget impact, level of innovation and complexity, rarity of disease, unmet need and clinical benefit;**
- **Increased citizen, patient, clinician and academic involvement in decision-making, with improved transparency around decision-making and criteria;**
- **Incorporation of societal values and costs/benefits beyond the health system into the decision-making process, as well as a willingness-to-pay in line with other highly-developed countries; and**
- **Earlier and increased engagement between all stakeholders.**

6. Impact on the quality of care available to cancer patients

Australians enjoy a high standard of cancer care overall. However, as noted above, Australia lags other nations in access to new, innovative cancer medicines. While in the short term, this is unlikely to impact on population outcomes, the impact is greatest on individuals who are diagnosed early in the lifecycle of a medicine, or those in cancer populations with limited options. As noted in Section 2 above, Australia funds less than half of the indications for which new cancer treatments have been

shown to be safe and effective[7]; meaning entire groups of patients are unable to access innovative medicines.

As discussed in Section 4.2, trastuzumab is reimbursed in Australia for HER2+ breast cancer, but not the less common HER2+ gastric (stomach) cancer, despite being registered for this use. Bevacizumab is reimbursed in colorectal and ovarian cancers, but not in relapsed glioblastoma (a form of brain cancer) or lung cancer. These access gaps can occur in cancers that have significantly poorer prognosis, with five-year survival rates of stomach (27%) and brain cancer (21.6%) falling behind outcomes for colorectal cancer (66.9%) and breast cancer (89.6%)[1].

In such situations, patients rely on standards of care which may involve chemotherapeutic treatments that have not advanced in decades. Delays in access to the newest therapies, where Australia underperforms the developed world[6], most greatly affect those for whom current treatments are unsuitable or ineffective. These might include patients who have attempted all conventional treatments and continued to experience cancer progression, or those who have other illnesses that make more toxic conventional therapies inappropriate.

While in general most cancer medicines are available in Australia, especially older medicines, in practice there are widespread inequalities in access to care if medicines are not on the PBS:

- Patients may need to pay significant out-of-pocket costs.
- Patients may live in states such as Queensland that restrict access to company-funded patient access programs that require a patient contribution.
- Patients may attend or live near hospitals that do not provide some medicines on formulary. In this case they will either need to travel long distances or receive sub-optimal care.
- Patients may need to exhaust more options prior to accessing the newest therapies, even if this sequence of treatment is not supported by evidence or optimal.

In order to address these impacts on cancer patients, some have looked to the UK Cancer Drugs Fund as a suitable model. Roche Australia does not advocate for a cancer drugs fund and considers that it has 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 supports systemic reform that will improve access for all specialised medicines, including cancer. As reform can take time and cancer is often life-threatening, Roche encourages the government to also look at models that would provide interim access to patients awaiting new cancer therapies.

7. Conclusion

Roche supports a comprehensive review of the PBS system as well as urgent implementation of pragmatic solutions to ensure that reimbursement decisions are timely, fair and reflect community values. Many cancer patients face a poor prognosis without access to the most effective treatments. It is essential that they do not face unnecessary delays or restrictions. Only through a collaborative, transparent and fit-for-purpose system can the Australian community have confidence that it is able to access a standard of care for cancer among the best in the world.

References

1. Australian Institute of Health and Welfare (AIHW). 2012. "Cancer survival and prevalence in Australia: period estimates from 1982 to 2010". Cancer Series no. 69. Cat. no. CAN 65. Canberra
2. Roche. 2014. "Annual Report 2014". Basel
3. AIHW. 2015. "Australian Burden of Disease Study: Fatal burden of disease 2010". Australian Burden of Disease Study Series no. 1. Cat. no. BOD 1. Canberra
4. AIHW. 2013. "Health system expenditure on cancer and other neoplasms in Australia: 2008–09". Cancer Series no. 81. Cat. no. 78. Canberra
5. AIHW. 2014. "Cancer in Australia: an overview 2014". Cancer series no. 90. Cat. no. CAN 88. Canberra
6. O'Neill P and Sussex J. 2014. "International Comparison of Medicines Usage: Quantitative Analysis". Report for Association of the British Pharmaceutical Industry, Office of Health Economics, London
7. Cheema PK, Gavura S, Migus M, Godman B, Yeung L and Trudea ME. 2012. "International variability in the reimbursement of cancer drugs by publically funded drug programs", *Curr Oncol*. Jun 2012; 19(3): e165–e176
8. Roche data on file
9. Harvey R and de Boer R. 2015. "Growth in expenditure on high cost drugs in Australia". Research Paper, Parliamentary Library, Canberra
10. Department of Health. 2014. "Expenditure and Prescriptions twelve months to 30 June 2014". Accessed http://www.pbs.gov.au/info/statistics/expenditure-and-prescriptions-30-06-2014, 30/01/15
11. Sweeny K. 2013. "The impact of further PBS reforms: Report to Medicines Australia". Melbourne
12. Chia S, Speers C et al. 2007. "The impact of new chemotherapeutic and hormone agents on survival in a population-based cohort of women with metastatic breast cancer". *Cancer*, 110: 973–979
13. Medicines Australia. 2011. "Innovation for the Health of the Nation". Occasional Paper No. 2, Canberra
14. Calculated from PBS Expenditure Statistics for ATC group "Antineoplastic and immunomodulating agents". Accessed from http://www.pbs.gov.au/info/browse/statistics, 16/09/14
15. Australian Bureau of Statistics. "6401.0 - Consumer Price Index, Australia, December 2014". Accessed from http://www.abs.gov.au/ausstats/abs@.nsf/mf/6401.0, 20/02/2015
16. Department of Health. 2014. "Expenditure and Prescriptions twelve months to 30 June 2014". Table 9. Accessed http://www.pbs.gov.au/statistics/2013-2014-files/table-9a.pdf, 20/02/15
17. EUnetHTA. 2014. "The HTA Core Model®". Version 2.1 Public Draft. Joint Action 2, Work Package 8
18. Medicines Australia. 2013. "Submission to the National Commission of Audit November 2013". Canberra
19. World Health Organisation. 2015. "Cost-effectiveness thresholds". Accessed http://www.who.int/choice/costs/CER_thresholds/en/, 20/02/15
20. Nord E, Richardson J, Street A, Kuhse H, Singer P. 1995. "Maximising health benefits versus egalitarianism: An Australian survey of health issues". Centre for Health Program Evaluation Working Paper 45, Melbourne
21. Chim L, Kelly P, Salkeld G, Stockler M. 2010. "Are Cancer Drugs Less Likely to be Recommended for Listing by the Pharmaceutical Benefits Advisory Committee in Australia?". *Pharmacoeconomics*, 28(6):463-475
22. Roche. 2013. "Access to oncology medicines in Australia: Roche response to Medicines Australia Oncology Industry Taskforce report". Sydney
23. Drummond M, Schwartz J, Jonsson B et al. 2008. "Key principles for the improved conduct of health technology assessments for resource allocation decisions". *Int J Tech Assess in Health Care*, 24 (3): 244-258
24. Kerr A, Todd C, Ulyate K, Hebborn A. 2014. "A Comparison of International Health Technology Assessment Systems – Does the Perfect System Exist?" Presentation to the ISPOR 17th Annual European Congress, Amsterdam