Specialised Therapeutics®

29 September 2020

The Chair
Mr Trent Zimmerman MP
Standing Committee on Health, Aged Care and Sport
PO Box 6021
Parliament House CANBERRA

Dear Mr Zimmerman,

Inquiry into approval processes for new drugs and novel medical technologies in Australia

Thank you for the opportunity to provide a response to the Inquiry – **Approval processes for new drugs and novel medical technologies in Australia.** Specialised Therapeutics Australia (STA) is an independent, wholly-Australian-owned and family-founded pharmaceutical company established in 2008 by internationally experienced pharmaceutical executives Carlo Montagner and Bozena Zembrzuski.

The company began with exclusive rights to market a single oncology product in Australia and New Zealand – a breast cancer medicine known as ABRAXANE. It has rapidly expanded, and now markets a range of specialist medicines and diagnostics spanning oncology, haematology, ophthalmology and neurology. Its efforts ensure patients in Australia, New Zealand and across South-East Asia are afforded critical access to innovative and potentially life-changing therapies and technologies for devastating diseases including breast cancer, pancreatic cancer, multiple myeloma, leukaemia and brain cancer.

The STA mission has always been to provide therapies that fulfill an unmet medical need and sometimes these products are destined for smaller patient populations.

Our submission (attached) to this Inquiry focuses on our company's experience with two products navigating the subsidy processes in Australia via the Medical Services Advisory Committee (MSAC) and the Pharmaceutical Benefits Advisory Committee (PBAC.

These experiences form our view of the system and are the basis of our recommendations for change noting the considerably more efficient and transparent processes of the Therapeutic Goods Administration (TGA).

But this Inquiry is not about our business, it is about Australians who are waiting for access to therapies that are often a standard of care globally, but not in Australia.

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For this reason, we have placed the patient and clinician experience with one of our products at the forefront of our submission, because this is what this Inquiry and our concerns are about – the timeliness of access to safe treatments that could significantly improve health for Australians and how the system could make it a little easier for companies to do that.

Thank you again for launching this Inquiry and providing a platform for meaningful discussion and potential reform.

STA and the people who have contributed to our Submission would greatly welcome the chance to talk directly with the Committee on our experiences and recommendations, and request the opportunity to appear before any hearings held as part of this Inquiry.

Likewise, upon review of our submission if there is any further information the Committee consider would be of use, we would be pleased to make it available wherever possible.

Yours sincerely

[redacted]

Carlo Montagner
Chief Executive Officer
Specialised Therapeutics Australia

Specialised Therapeutics®

House of Representatives Standing Committee on Health, Aged Care and Sport

Inquiry into the approval processes for new drugs and novel medical technologies in Australia

September 2020

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EXECUTIVE SUMMARY

On 18 August 2020, the House of Representatives Standing Committee on Health, Aged Care and Sport established an inquiry into the approval processes for new drugs and novel medical technologies in Australia, with a particular focus on the treatment of rare diseases and conditions where there is high and unmet clinical need

Australians can and should be proud of our health system. It is a system currently split across public and private health, across federal, state and territory and local level delivery, across primary care, acute care and aged care, and specialist outreach services. This diversity provides ample opportunity for both innovation and patient-centric care, but also poses the risk of inconsistency, in terms of access to therapies, or service gaps.

These gaps are further magnified as healthcare innovation gains momentum, particularly in the areas of genomic testing and the advent of translational research, which has heralded a change from an organ-centric concept guiding treatment choice, towards deep molecular analysis, driving a personalised approach to treatments.

However, it now seems that traditional reimbursement processes and pricing strategies are 'out of step' with modern treatment options, particularly in the oncology world and treating cancers.

In 2014, a panel of three experts were tasked with reviewing the regulations and approval processes for medicines, therapies and devices. This review recognised the need to innovate and improve time to market registration, ensuring Australians could access new technologies as quickly as possible, irrespective of whether they were designed to treat a rare or common disease.

Systematic reforms implemented by the Therapeutic Goods Administration (TGA) now ensure faster registration times for all therapies where appropriate. In particular, the Project Orbis initiative, which enables concurrent review of oncology products by international regulators such as the United States (US) Food and Drug Administration (FDA), is a great step forward to fast track approval processes where a high unmet need exists.

Industry and consumers have welcomed these improvements to streamline processes, including the announcement on 22 September 2020 of additional pre-submission engagement meetings to specify data needs and enable expedited registration.

The TGA should be applauded for its work to ensure all treatments and technologies are safely registered in Australia as quickly as possible.

Unfortunately, expedited market registration by the TGA comprises only one critical component for access to emerging novel therapies in Australia. The second critical component is the government funding process, particularly at the federal level. Unlike the improvements implemented by the TGA, this is not an efficient process by any measure, particularly global.

This is reflected in the analytics presented in the 2018 COMPARE report (COMPARE (Comparison of Access and Reimbursement Environments): A report benchmarking Australia's access to new medicines – Edition 4).

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With so many breakthrough medicines and technologies financially outside the reach of most Australians, reimbursement via government is crucial if all Australians are to have equal access to such therapies.

However, the Health Technology Assessment (HTA) processes administered by the Pharmaceutical Benefits Advisory Committee (PBAC) and Medical Services Advisory Committee (MSAC) are increasingly slow and complex. To our knowledge, these processes also incur the highest application and administrative fees in the world.

A patient's medical need is often forsaken in favour of a purely economic rationale which can take years to resolve.

As a result, timely access to cutting-edge medicine and technologies is at best delayed, and often completely unavailable.

This is not an acceptable outcome for Australians living in a first world country. This is more glaring when we see the same therapies reimbursed by other governments with similar HTA processes.

Determining what is value for money for health treatments is an important component of any decision-making process for funding, but it is slowing down the access processes beyond what Australians reasonably expect. It is also too long in comparison to many other first world countries.

As the 2018 Compare report demonstrates, Australia is lagging behind many other countries when it comes to accessing cutting-edge medicines and technologies to improve health outcomes.

- Is being seven years behind the international standard of care in diagnostics for breast cancer acceptable?
- Is waiting three years for subsidised access to a medicine acceptable?
- Is it fair to expect small pharma companies to pay up to $3M to submit a reimbursement application on a product that will not return much more than this per annum?

It is not, if our goal is timely access to new treatments for all Australians that might benefit.

The Government has continued to announce multiple investments in clinical trials in Australia through its Medial Research Future Fund (MRFF). But there appears a misguided belief that this will provide sustained access to treatments for all Australians.

Clinical trials do provide early access to yet-to-be-fully-proven treatments. Patients recruited to these important studies may benefit. But they do not provide universal or ongoing access. Australia's subsidy system means that those patients not enrolled in a trial may wait many years – or forever – to access the same therapy. Unless of course that Australian has the financial resources to afford such treatment.

Clinical trials will drive research, but better timeframes and processes for funding are the only solution for providing all patients with access.

Specialised Therapeutics Australia (STA) is a wholly Australian owned, family-founded and managed company that provides new specialist therapies and technologies to Australian patients where there is a high unmet need. STA usually partners with other smaller US or European Union (EU) based

biotech companies that do not have a presence in this region. This often means that STA products are designed for small patient populations.

Current subsidy systems in Australia are difficult and complex, in terms of lengthy regulatory timeframes due to typically multiple applications required for a positive outcome, and high submission costs in the millions of dollars. These factors, combined with the potential pricing threat resulting from the current Trump Executive Order on favoured-nation pricing, will mean further uncertainty as many companies debate internally the merits of commercialising their medicines in Australia, a market that comprises only 1-2% of the global market.

It is clear that reforms are needed to ensure the Australian healthcare system - and the patients within it - are afforded appropriate access to world-class healthcare.

It is our contention that a lack of process transparency erodes confidence in this system, and the absence of a truly patient-centric view is a cause for concern.

The Australian health budget is a finite resource. This is accepted, but the processes for determining access to life-saving and life-changing technologies need to be faster and more transparent, with fewer administrative and financial barriers.

If the MRFF and TGA can demonstrate significant progress with timeliness, consistency and transparency, why not then can the subsidy processes for universal patient access follow suit?

Australians are waiting too long to cross that final hurdle – universal and equitable access to cutting edge highly personalised treatments and technologies.

RECOMMENDATIONS

As part of its Inquiry, STA asks the Committee to recommend the following:

1. **That Australia recognises that clinical trials potentially attract and retain research and development investment and can provide early access to novel technologies, but the pathways to subsidy need improvement to enable universal access for all eligible patients when these treatments are ultimately approved by the TGA.**
2. **That Australia's subsidy systems need to be aligned with the same timeframes of certainty and transparency as the TGA, and further, that the role of the TGA in determining safety and efficacy should be given higher weighting by the MSAC and PBAC.**
3. **That collaborative meetings between TGA, PBAC and MSAC becomes the standard approach for bringing new or novel technologies to Australia, reducing submission churn and requests for data by subsidy committees.**
4. **That the PBAC and MSAC harness the lessons from the TGA's international collaborative model (eg Project Orbis) to improve data assessment and time to subsidy in Australia.**
5. **That the costs of some of Australia's processes are increasingly prohibitive for smaller companies and therefore technologies supporting rare or small patient populations,**

particularly with multiple rejections of applications by subsidy committees, should provide for:

a. **Exemptions/waiver of fees for subsidy processes on orphan status drugs and technologies should be extended beyond the current 12-month timeframe for application, noting the data and process demands of the subsidy system are significantly longer than the safety and efficacy registration processes in Australia; and that only one application is fee exempt, when typically two or more applications are required for a successful outcome, if achieved.**

b. **Smaller companies with revenue <$50M annually be granted an exemption from paying new fees 'upfront' for at least the first two applications, and when, or if, a drug is listed on the PBS, the company then pays those fees in arrears, in instalments when Pharmaceutical Benefits Scheme (PBS) expense on that drug exceeds $3M per year.**

6. **That the MSAC processes and timeframes be standardised and expedited, including significant improvement in transparency of external data and contributions and time to provision of minutes from the meeting to allow sponsors to re-submit as quickly as possible and improve patient access. (This may require consideration of cost-recovery).**

7. **That an independent review process for MSAC decisions be introduced similar to that of the PBAC and that the PBAC process also be extended to independent review of positive recommendations where that recommendation is not consistent with the original application, and that the fees for independent review be removed so that individual patients and patient groups can seek an independent review.**

8. **That Australia recognise its current 1990s systems lacks the agility, flexibility and responsiveness Australians expect of their health system and consider alternative processes such as:**

   a. **Collaborative working processes such as the Oncology Drug Advisory Committee (ODAC) convened by the United States Food and Drug Administration to improve collaboration between suppliers, clinicians, patients and government to expedite processes; and**

   b. **Explore payer processes such as those employed in Germany and other countries, where pricing is negotiated upon registration, and evaluation of effectiveness is managed with risk share arrangements that both penalise and benefit suppliers based on access and outcomes.**

9. **New objectives for subsidy processes aligned to patient need should be a key deliverable of the delayed Review of Australia's National Medicines Policy.**

WHO WE ARE

Specialised Therapeutics Australia (STA) is an independent, wholly Australian owned and family-founded pharmaceutical company established in 2008 by pharmaceutical executives Carlo Montagner and Bozena Zembrzuski.

The company began with exclusive rights to market a single oncology product in Australia and New Zealand – a breast cancer medicine known as ABRAXANE®. It has rapidly expanded, and now markets a range of specialist medicines and diagnostics spanning oncology, haematology, ophthalmology and neurology. STA efforts ensure patients in Australia, New Zealand and across South-East Asia are afforded critical access to innovative and potentially life-changing therapies and technologies for devastating diseases including breast cancer, pancreatic cancer, multiple myeloma, leukaemia and brain cancer.

The STA mission has always been to provide therapies that fulfill an unmet medical need and sometimes these products are destined for smaller patient populations.

Since it was founded, STA has provided more than 70,000 patients with access to potentially life-changing medicines, which they have been able to access via listings on the PBS and MBS, or via Special Access Programs. We are also strong supporters of research and development, and have provided almost $25 million worth of drugs to patients at no cost on compassionate grounds.

Our submission to this inquiry focuses on our company's experience with two products navigating the subsidy processes in Australia via MSAC and PBAC. These experiences form our view of the system and are the basis of our recommendations for change.

But this Inquiry is not about our business, it is about Australians who are waiting for access to therapies that are often a standard of care globally, but not in Australia.

For this reason, we have placed the patient and clinician experience with one of our products at the forefront of our submission, because this is what this Inquiry and our concerns are about – the timeliness of access to safe treatments that could significantly improve health for Australians and how the system could make it a little easier for companies to do that.

STA CASE STUDIES

Case Study 1: The patient perspective on the need for improved ACCESS to medicines and technology in Australia

Maxine Gladwin's Story

Maxine Gladwin was 47 and a single mum to three teenage daughters when she was diagnosed with breast cancer. When her oncologist advised chemotherapy treatment, she was devastated – fearing it would impact her health, her job and her ability to provide for her family. With support from her family, a sample of Maxine's tumour was tested, using the Oncotype DX Breast Recurrence Score Test.

Maxine explains what happened next.

"I was 47 years old when I was diagnosed with breast cancer in November 2014.

After a mastectomy, my oncologist recommended chemotherapy treatment, along with hormone therapy.

When my family raised concerns about chemotherapy, my oncologist told me about the Oncotype DX test. The cost of this test was well out of my reach, as I am a single parent with three teenage daughters.

My mother was with me at the consultation and she insisted on paying for it, because we were hoping I could avoid chemotherapy if it was safe.

It was such a relief when I got the results. I had a 3% chance of recurrence and I would not be any better off having chemo.

My Dad cried with relief when he heard. Because I am the sole breadwinner, I was terrified of losing my job and I really thought this could happen if I was missing work for treatment.

I had contacted Centrelink prior to receiving my results and was advised that my entitlements would not even cover our rent, so our family could have been homeless.

Two of my girls were doing HSC at the time and moving them away from their school, family and friends would have been hugely disruptive.

Without Mum at my appointment, I would have just gone ahead with chemotherapy.

It's terrible knowing that many women are going through unnecessary treatment.

I consider myself lucky. I am happy to report that five years after my diagnosis, I have had no cancer recurrence. My oldest daughter is married and is a manager for a travel agency, my two younger girls are nearly finished university degrees – one is studying to be a nurse and the other a social worker.

I don't know if any of this would have happened if I had just proceeded through treatment. Having an Oncotype test and getting the results I did, really changed my life."

Case Study 2: The clinician perspective on the need for improved ACCESS to medicines and technology in Australia

Jane O'Brien is a Specialist Oncoplastic Breast Cancer Surgeon who has been practising for over 25 years. She specialises in surgery for breast cancer and also prophylactic/preventative surgery for high-risk individuals.

Jane is a member the Australasian Society of Breast Surgeons, The American Society of Breast Surgeons, The Australasian Society for Breast Disease and the Australia and New Zealand Breast Cancer Trials Group.

"Since the Oncotype DX breast cancer test became available in Australia, I have used it to help guide treatment decisions in more than 50 patients.

This test is not for all breast cancer patients. It is only appropriate for use in cancers which are hormone receptor positive and HER2 negative, and in excess of 65% of breast cancers fall into this category. It is not however required in all women with this breast cancer subtype.

Oncotype DX testing is most appropriately considered in women with relatively low-risk breast cancers, that are hormone receptor positive and HER2 negative, where the additional benefit of chemotherapy over and above anti-hormonal/endocrine therapy may be unclear. Because the cancer is hormone receptor positive – this means it is powered by a woman's own hormones – all of these patients would be given endocrine therapy to cease hormone production. But not all of these women will need chemotherapy.

Standard clinico-pathological criteria can usually reasonably accurately identify who out of this large group of women with hormone receptor positive/HER2 negative breast cancer is high-risk and who is low-risk. With high-risk women, in those who are suitable for, and agreeable to chemotherapy, chemotherapy treatment would usually be recommended.

Conversely, when we can see clearly that a woman is at an obviously low risk of recurrence, we would usually be satisfied with prescribing hormone therapy alone.

There are however many women who are 'stuck in the middle' and for whom a decision could really go either way. It is for these women that an Oncotype test is of most benefit.

Without the detailed specific information provided by Oncotype that would reassure a no-chemo decision, we would most frequently prescribe a three or six-month course of chemotherapy, as clinicians understandably err on the side of caution in the absence of a reassuringly low Oncotype Recurrence Score. But we now know that more than 70% of them may not derive significant benefit from the toxic treatment.

Recommendations regarding post-operative (adjuvant) drug therapies for breast cancer used to be made virtually exclusively on traditional clinico-pathological criteria which relied on "tumour burden" as estimated by tumour size and axillary nodal status. It has become increasingly clear over the last couple of decades, that the biological subtype of the cancer is also of great importance, not only in predicting prognosis, but also in predicting response to different types of drug therapies.

Chemotherapy attacks rapidly dividing cells, and the aim in selecting patients for chemotherapy is to be able to more accurately identify which cancers are likely to be more or less "chemo sensitive" or "chemo responsive". Faster, more aggressive breast cancers tend to obtain more benefit from chemotherapy than slower growing, more indolent tumours. There is no point putting a patient through a gruelling chemotherapy regime if their particular tumour is one which is relatively "chemo resistant".

Many, if not most, breast cancer patients would prefer to avoid chemotherapy unless it is absolutely necessary and undergoing Oncotype DX testing often provides patients with the added degree of reassurance that allows them to more confidently forgo chemotherapy if appropriate.

Alternatively, some patients may have hormone sensitive cancers that are relatively small, and endocrine therapy alone is likely to be safe, but the cancer may have a couple of slightly more adverse pathological features, such as low or absent progesterone receptor positivity or elevation of the proliferative protein Ki67, that leads to consideration of the role of Oncotype DX testing. Occasionally, these cancers come back with an unexpectedly high recurrence score, prompting a recommendation for chemotherapy.

Whilst these patients may have been hopeful to avoid chemotherapy, [running the Oncotype DX test] they are almost always pleased/relieved to have undergone the testing, as otherwise, with endocrine therapy alone, they may have been inadvertently "undertreated". Patients, in my experience, are usually much more accepting of chemotherapy if there is felt to be a strong prediction that it will significantly reduce their risk of recurrence, and they are not just having it to be "safe".

Most medical oncologists make a "default" treatment recommendation prior to Oncotype DX testing about what drug therapy they would recommend in the absence of genomic testing. As the long-term consequences to the patients of cancer "undertreatment" are usually greater than "overtreatment", the natural tendency is if in any doubt to recommend chemotherapy as well as the anti-hormonal therapy. ***In my experience, which is supported by the literature, both nationally and internationally, more women having undergone Oncotype DX testing, manage to avoid chemotherapy than if the test is not done, than the reverse.***

The Oncotype DX test is internationally endorsed and is the only such test recommended for use in clinical practice by the United Kingdom's National Institute of Health and Care Excellence (NICE) and is recommended in five major international oncology treatment guidelines. It is reimbursed in many other countries, including the United States, Canada, England, Ireland, Switzerland, Spain, Israel and Greece. Without a Medicare rebate, the Oncotype DX test costs Australian women around $5,000, which is out of financial reach for many.

Failure to approve this test for reimbursement means that many Australian women may receive chemotherapy when there is little or no benefit. In addition, the women who are currently least able to self-fund Oncotype DX testing are those in whom avoiding chemotherapy may in fact be the most desirable because of their associated medical comorbidities.

Being able to give women every possible opportunity to make informed decisions about which treatments may be best for them is incredibly important. Chemotherapy comes at a huge cost physically, psychologically, socially and financially. Occasionally, the health side effects can be catastrophic. The usual immediate physical effects of chemotherapy are fatigue, nausea, hair loss, nerve changes and low immunity leading to infections and hospital admissions. In the longer term,

chemotherapy can result in infertility and premature menopause. Avoiding chemotherapy and all of the associated toxicities and long-term side effects can therefore make a huge difference to the lives of women with breast cancer and can also mean less time away from family and work.

An examination of the international medical and regulatory landscape tells us that Australian authorities are out of step with the rest of the world when it comes to Oncotype. A greater focus on information sharing between internationally equivalent decision makers may help to ensure Australian women are afforded the same access to sophisticated healthcare technologies as their peers in other developed countries.

Case Study 3: the STA EXPERIENCE in ensuring timely access to medical technology in Australia

Maxine and Jane's patient and clinician testimonies highlight the importance of delivering world-class genomic testing to Australian patients.

Despite multiple consultations with MSAC, STA has now made six unsuccessful attempts over seven years to have the Oncotype DX breast cancer test - an international standard of care genomic test for breast cancer - recommended for government subsidy by the MSAC.

Their contributions to this Submission reflect the potential benefits of this technology to a broader breast cancer population, as well as the devastating impact on this same group when Australia's health subsidy system cannot find a way forward to reimburse this test.

Oncotype DX was registered by the TGA in August 2014.

It is a standard of care and has been reimbursed in the UK, France, Canada and the US for several years. Despite the six submissions – which have cost STA more than a million dollars – Australia is still waiting for subsidised access. It is important to note that STA submitted the very same clinical and population evidence to MSAC that international regulators found so compelling.

No one is benefitting from this impasse.

STA has documented its concerns with the transparency and predictability of both the MSAC system's evaluation of Oncotype DX, as well as the PBAC consideration of a drug for early breast cancer known as NERLYNX®.

These experiences underpin our recommendations for improvements to Australia's health access systems, which determine whether Australians can affordably access potentially lifesaving and life changing treatments.

We must have confidence in the consistency, transparency, and timeliness of these systems if we are to understand and accept the rejections that are integral to what must be stringent, robust and highly scrutinised processes.

STA and the MSAC consideration of Oncotype DX

The Oncotype DX® breast cancer test is a cutting-edge genomic test that examines 21 specific genes within a woman's own tumour.

Very simply, it can accurately identify those early breast cancer patients who can safely avoid chemotherapy and be treated with hormone therapy alone, as well as those women for whom chemotherapy can be lifesaving.

It works by delivering a Recurrence Score™ (RS) result between 1 and 100. This score provides clinicians with sophisticated information about a patient's likelihood of disease recurrence, as well as the benefit of chemotherapy.

This information goes 'over and above' what any other test is able to discern. Critically, it provides information about a woman's own cancer that would otherwise be unavailable.

It is most useful when determining appropriate treatment for women who fall into the 'intermediate' risk category, for whom chemotherapy would be very strongly considered.

The Oncotype DX test is underpinned by strong clinical evidence and is reimbursed and provided as a standard of care in most other developed countries – including in the United States, Canada, the United Kingdom and in many European countries, including Germany and Spain.

It was also the subject of what was the world's largest breast cancer treatment trial ever conducted – an independent study known as TAILORx – that enrolled more than 10,000 women at global sites, including Australia. Researchers followed these patients for 10 years, providing an unprecedented level of evidence.

Results from this US National Cancer Institute-funded and internationally-acclaimed investigation were considered so ground-breaking, they were published in the prestigious New England Journal of Medicine and presented to the global oncology community at the world's biggest cancer congress, the American Society of Clinical Oncology (ASCO) in 2018.

Post-ASCO, international health authorities and peer-reviewed cancer guidelines – including NICE in the UK and the NCCN in the United States - reaffirmed advice to reimburse Oncotype DX to guide treatment decisions. Indeed, the NCCN noted it was now the "preferred" multi-gene test at the core of any breast cancer treatment decision making.

STA, with the support of clinicians via the Medical Oncology Group of Australia (MOGA) and patients via the Breast Cancer Network of Australia (BCNA), has been seeking Medical Benefits Schedule (MBS) subsidy for this test since 2013, with six MSAC submissions. ***It has been rejected for reimbursement six times – even though it is reimbursed and a standard of care in most other developed countries.***

Following the fifth rejection in 2017 and based on MSAC's own feedback cited in the rejection minutes, STA awaited new global evidence released as part of the of TAILORx study, before meeting again with the MSAC Chair and key Department of Health advisors in mid-2018. Following the presentation of the design and results of the TAILORx study, the Chair of MSAC strongly encouraged STA to submit a sixth application based on this long-awaited data.

STA was buoyed by this meeting, and by the positive pre-submission meeting held shortly after with Departmental MSAC advisors. We were further encouraged when MSAC's own Economic Sub-Committee (ESC) delivered its evaluation, acknowledging that Oncotype DX was one of the more rigorously designed gene assays, was cost-effective and confirming there was a clinical need in Australia for this test. The ESC subcommittee further conceded that clinicians should be using a

higher level of evidence based on genomic subtyping of individual cancers to provide tailored treatment for Australian patients.

Specifically, it advised MSAC that the Oncotype DX test was *"one of the more rigorously developed gene assays with good quality control"* that was given a "preferred" rating on the NCCN guidelines and "strongly" recommended by the prestigious American Society of Clinical Oncology following the publication of the TAILORx study in the New England Journal of Medicine in 2018. The ESC report also acknowledged the Oncotype DX test is a standard of care and reimbursed in most other developed countries, including the US, UK and Canada, and conceded that clinicians should be using a higher level of evidence based on genomic subtyping of individual cancers to provide tailored treatment.

The MSAC and PBAC ESC subcommittees are well known for being the more difficult assessment hurdle in the subsidy processes, so any positive feedback from these subcommittees is read with this lens. The positive feedback from ESC on this test in 2019, was a considerable change on the previous five submissions.

However, after the sixth MSAC hearing in August 2019, STA was sent an email two weeks later (as is standard practice) advising the application had been rejected. The email also stated that the minutes of the MSAC hearing, captured in a Public Summary Document (PSD) and outlining the reasons for the rejection, would be provided to STA within six to eight weeks following receipt of this email.

Despite repeated requests from STA, this PSD did not materialise until January 2020, following STA submitting an FOI request. In addition to seeking the PSD, STA requested any documents relating to the internal evaluation or review of its application, to fully understand the rationale behind this particular decision and make commercial decisions moving forward.

These documents, while heavily redacted, subsequently revealed concerning irregularities about how the application had been managed by MSAC.

Critically however, they also revealed what STA perceives as serious flaws in MSAC's expertise, its practises and its review processes. Unless addressed, these concerns will impact how all other technologies are examined for public health benefit moving forward.

The FOI request revealed three key areas of concern about MSAC processes, including:

1. **Transparency: There is no apparent transparency around MSAC decision making**
2. **Reliability: MSAC is not bound to its own stated decision-making time frames, with STA forced to lodge an FOI to have the MSAC minutes disclosed more than six months post the MSAC meeting**
3. **Decision-making Ability: MSAC is not aligned with equivalent global decision-makers, highlighting a potential lack of expertise in assessing novel personalised/genomic medicine and technologies**

Issue 1. MSAC Transparency

As stated above, it was not until STA lodged an FOI request to access the PSD that the PSD was finally received (three days after the FOI request was submitted). Several weeks later, the Department of Health FOI officer released the documents pertaining to STA's FOI request. Most, if not all, the documents released were heavily redacted, with some documents withheld, including critical information requested in the application as to who specifically was evaluating the submission, and their expertise in evaluating such a complex application. STA also queried whether any other internal or external expert advice had been sought.

In addition, despite these significant redactions, the documents further revealed:

- Two days before the MSAC meeting, a third party "consumer comment" was submitted to MSAC by a medical practitioner working for a competitor product who had previously been an MSAC member. The pecuniary interest of this objector was noted in his email to MSAC, however with no reference to his past MSAC membership and possible participation in previous Oncotype DX applications, and STA was given no right of reply to the eleventh-hour objection.
- The FOI trail further indicates that MSAC sought additional evidence/advice AFTER the decision had already been made. This practise is puzzling at best, but more worryingly, suggests a decision was made ***before*** a full collection of evidence to justify any decision or outcome.

While MSAC confidentially advised STA that it had rejected the application two weeks after the decision-making meeting, it failed to disclose meeting minutes or reasons for rejection for more than six months, despite repeated attempts to access this information. STA was consistently told there were "clinical issues" being addressed.

Like all applicants, STA expects MSAC to operate in an open and transparent manner. As described above, this did not happen in this instance. Because the documents were so heavily redacted, it is unclear who MSAC sought additional expert advice from, and who or what information ultimately informed the final decision. This sort of detail should not be redacted.

MSAC must be compelled to reveal the source of any data guiding its decision-making.

In the interests of transparency and MSAC accountability, it is vital that companies making a submission, as well as any public stakeholders including patients, are provided a clear picture of who is guiding ultimate decisions.

In an era of personalised medicine, STA further contends that it is vital MSAC is equipped, or has access to, relevant experts or authorities with the scientific background to accurately assess new personalised medicine and genomic testing technologies. This is particularly relevant not only to Oncotype DX, but to other emerging technologies like CAR-T therapies.

Issue 2: Lack of timeliness and responsiveness to the Australian community waiting for access via MSAC recommendations

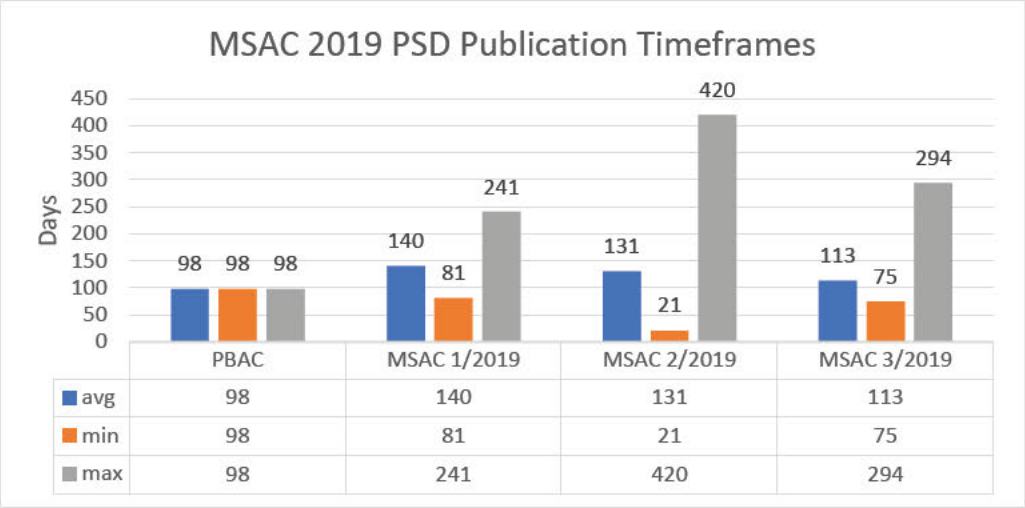
MSAC has shown itself to be unreliable in its ability to deliver decisions in a timely manner.

STA was forced to lodge a FOI request to access the MSAC minutes/ PSD more than six months after it had been confidentially advised the application for subsidy of the Oncotype DX test was unsuccessful.

The PBAC provides applicants with minutes within three to six weeks of the meeting, and a draft PSD within 70 days of the PBAC meeting. The finalised PSD is published within 98 days after the meeting. By comparison, MSAC's provision of the PSD for STA's Oncotype DX submission took more than 190 days.

As the summary data below demonstrates, it appears STA's experience is not unusual for MSAC.

The average number of days for MSAC decisions to be published in a PSD from the August 2019 meeting (meeting at which Oncotype DX was considered) was 140 days, with a range of 81-241 days.[1] For the March 2019 meeting, the average was 131 days, with a range of 21-420 days. For the November 2019 meeting the average was 113 days, with a range of 75 days with one application still not finalised as at 18 September 2020, some 294 days later (see graph below).



The short turnaround PSDs primarily relate to listing variations for already approved technologies, while new technologies are subject to extended delays. Why? If the MSAC is making clear and firm evidence-based decisions at its meetings, why does it take it so long to write up meeting outcomes when there are notetakers present for this very purpose?

It could be inferred that MSAC is making decisions and then conducting research to support those decisions post-meeting. If MSAC is doing this, it is an inappropriate process for an important Australian government health committee which determines whether someone will have access to potentially life-saving, or life-changing medical interventions.

[1] The days are calculated from the first day of the relevant MSAC meeting to the date of publication of the Public Summary Document (PSD) for each application considered at that meeting.

If it is simply a lack of timely processes, this is of equal concern and must be addressed as a matter of urgency, given the time taken to advise a company of an unsuccessful application prolongs the time for a new submission to be lodged.

> ***It is our recommendation that MSAC be required and bound to deliver findings within an appropriate and reasonable time frame, so applications are not drawn out interminably.***

Issue 3: Decision making ability – MSAC is 'out-of-step' with equivalent global decision-makers

MSAC's decision to reject the Oncotype DX breast cancer assay for subsidy and its interpretation of the TAILORx evidence is at odds with how the data are viewed by other key medical, regulatory and reimbursement authorities in the developed world.

This body of evidence is recognised and validated globally by oncology authorities, including the National Comprehensive Cancer Network (NCCN) in the United States and the National Institute for Health and Care Excellence (NICE) in the United Kingdom.

STA contends that greater use of international approval processes, registration and reimbursement processes, as well as post-market assessments, would benefit both MSAC and the PBAC, when it comes to assessing new drugs and novel medical technologies for reimbursement. Taking into account the decisions of internationally equivalent decision makers would alleviate the burden on Australian authorities – in terms of both time and cost – and also ensure a level playing field, enabling Australian patients to access and benefit from new and novel technologies already available and reimbursed internationally.

Ultimately, MSAC's decision to reject Oncotype DX for reimbursement means Australia remains an outlier when it comes to the provision of cutting-edge genomic tests. Australian women are missing out on a technology their peers internationally are provided as a standard of care. The great pity in Australia now, is that only those women who can afford to access this personalised genomic technology have the opportunity to benefit. This is not a level playing field and has led to a situation where a cutting-edge technology is only available to those with the financial resources to pay.

Case Study 4: the STA EXPERIENCE in ensuring timely access to medicines in Australia

STA and the PBAC consideration of NERLYNX®

Since STA was founded in 2008, we have engaged faithfully and diligently with the PBAC seeking reimbursement for some of the specialist therapies and technologies we in-license, so they are affordable and accessible for all Australian patients who might benefit.

But a recent application seeking reimbursement for a new early breast cancer therapy known as NERLYNX® (neratinib) for appropriate and eligible Australian breast cancer patients has highlighted some gaps in the process that we believe need to be addressed to ensure a transparent, accountable and accessible healthcare system.

NERLYNX® (neratinib) is a breast cancer therapy for women with the type of breast cancer that is HER2-positive and hormone-receptor positive, and who have already been treated with adjuvant chemotherapy and trastuzumab-based therapy. Trastuzumab-based therapy is designed to reduce

the risk of recurrence for this group of women and NERLYNX represents a new treatment paradigm – extended adjuvant therapy – to further drive down the ongoing risk of a breast cancer recurrence. International clinical studies have shown that NERLYNX is able to reduce the risk of a breast cancer recurrence by up to 42% in those women who are HER2+/HR+ and who are treated within 12 months of completing adjuvant trastuzumab-based therapy.

NERLYNX is approved and has been reimbursed in countries including the United States, England, Germany and Scotland since 2019.

It was rejected by the PBAC for reimbursement on the Pharmaceutical Benefits Scheme (PBS) at its April 2019 and November 2019 meetings, following Australian Register of Therapeutic Goods (ARTG) registration in early 2019.

In order to understand the rationale for this decision, STA submitted an FOI request, to access the documents that may provide a more complete picture of the decision-making process.

The dossier subsequently supplied has highlighted some critical areas for reform. These are not confined to our company or this particular application, but would improve the system overall for all companies, and ultimately, all patients.

In essence, STA would urge this committee to:

1. ***Review PBAC transparency and recommend improvements***
2. ***Review PBAC engagement processes and recommend new avenues for discussion/engagement/debate such as the FDA ODAC model***
3. ***Recommend alignment/streamlining of subsidy decisions with regulatory decisions, including MSAC, PBAC and TGA***

Issue 1: PBAC Transparency

STA submitted an FOI application to better understand the PBAC's rejection of NERLYNX for subsidy. The minutes as supplied within the PSD, and the brief post rejection meeting with the Chair, did not adequately address a number of key issues used as the basis for rejection.

Given the extremely high cost of submitting a third application, particularly for a small family- owned Australian pharmaceutical company such as STA, it is critical that information is provided enabling a full understanding of the rejection rationale.

Of 29 potential documents, 27 were completely withheld, including relevant information from third parties engaged for expert scientific opinion.

Without access to this kind of information, it is difficult for any company to properly scrutinise the information provided to the PBAC by relevant third parties including its contracted evaluators and committee appointees, nor consider the commercial position of any therapy moving forward.

It is STA's belief that greater transparency and accountability in terms of providing access to decision-making information would improve the integrity of PBAC's decision-making process.

Indeed, the Commonwealth Information Commissioner's own guidelines clearly state that reports of scientific or technical experts, whether employed within an agency or not, should **not** be exempt under an FOI request.

We note that the Department has expressed concerns that third party stakeholders may be compromised as a result of this kind of information being released.

Third party stakeholders engaged to *analyse* complex scientific data are paid contractors appointed via a tender process. It is difficult to envisage how such commercial arrangements would, or could be, compromised. Further the advice of government-employed committee members is also technical advice and should be freely available to those relying on this advice and judgement for access to or rejection of subsidy to health services in Australia – patients, clinicians and the company bringing forward the new technology.

Issue 2: PBAC Engagement Processes

Pharmaceutical companies submitting for reimbursement are currently bound by very strict engagement criteria.

This effectively prevents open, frank dialogue with evaluators once a submission has been lodged. While companies do receive a commentary document from evaluators, they are provided only a week to respond and even then, the response is constrained to four pages.

After this, a sub-committee evaluation is provided and companies may respond again within a week, but with no more than two pages.

In essence, this process means that if evaluators do not understand something within an application, there is limited opportunity provided for ongoing input. This is a pity, as it would enable both applicants and evaluators the opportunity to fully understand a therapy being considered.

In the case of our NERLYNX application, we were required to communicate what was a very complex treatment algorithm.

We are of the belief that additional opportunities for rigorous and robust engagement with evaluators prior to the submission decision (rather than at a post-decision meeting) to address relevant concerns would have provided all parties with a more comprehensive dossier of information.

It is STA's belief that the model currently employed by the Food and Drug Administration (FDA) in the United States is a prudent and appropriate way to enable this kind of high-level interaction. In this jurisdiction, an Oncologic Drug Advisory Committee (ODAC) is convened specifically to make recommendations to the FDA when it is examining the efficacy and safety of oncology products.

This expert committee provides advice based on issues highlighted **during** the review process and its membership must also include a technically-qualified member who is selected by the Commissioner and recommended by a consortium of consumer organisations.

In terms of future PBAC considerations, it is our belief that the establishment of a committee similar to the FDA's ODAC to assist oncologic drug applications would ensure a less autocratic process, paving the way for ongoing discussion and professional dialogue and importantly reduced submission churn thereby improving access for patients.

Issue 3: Inconsistent data Interpretation between regulatory authorities and subsidy committees

The other issue we seek the Committee to address concerns the interpretation of data across regulatory and subsidy processes in Australia at the federal and state levels.

It is clear that PBAC's (and MSAC's) evaluation and interpretation of therapeutic data can significantly differ from the interpretation provided by the TGA.

For example, the TGA may approve a therapy as efficacious and safe, but the same drug and the same data can be interpreted very differently at PBAC review. This was the case with STA's NERLYNX application.

NERLYNX was approved by the TGA as effective and safe, and in the process of its evaluation, consulted with three independent breast cancer experts. In contrast, the PBAC evaluation questioned the efficacy of the compound and determined that risk outweighed benefit when it came to safety.

What this has highlighted is we have two divisions of the Health Department who can provide completely different data interpretations. Further, PBAC's interpretation of the same data set differed markedly from major global regulatory agencies (FDA, EMA) and HTA-based reimbursement agencies (NICE).

> ***STA would urge greater collaboration and information sharing between the TGA, PBAC and MSAC. We welcome the new consultation processes established by the TGA on pre-collation for submission data, and further encourage the engagement of both the MSAC and the PBAC in these processes to streamline processes for government and access for patients.***

Additional PBAC Process Concerns

There are two other areas of fundamental concern that STA would like the Committee to consider closely when recommending reform. Both of these issues impact the ability of STA and all pharmaceutical companies to provide new therapies and technologies to Australian patients.

1. Continuous increases in PBAC fees and creation of new one
2. PBAC orphan drug applications that are not fee exempt following an initial application rejection

Recent fee increases and the introduction of new fees to submit PBAC applications are particularly prohibitive for small, independent pharmaceutical companies.

They will mean the cost of submitting a major submission is now well in excess of $300,000 - even if the application is unsuccessful.

STA has estimated that the combination of fee increases, new fees for various processes and internal costs of submission preparation will mean the real cost per submission is approaching $750,000.

Considering that it typically takes several submissions to achieve a PBS listing, companies need to budget almost $2M for one indication for one drug. If there are further indications in the pipeline these must also be budgeted a further $2M per indication expansion.

For independent, privately-owned companies, this is a major barrier – especially when the outcome of a PBAC submission is highly unpredictable.

STA acknowledge there is never a guarantee of success for any pharmaceutical company when it submits to the PBAC for reimbursement. We further understand there is not an unlimited pool of funding from the government, and also that not every therapy deserves reimbursement.

However, it is now apparent from STA's own experience with four recent major PBAC submissions, that even when a company has attained high-level trial evidence showing a drug has achieved its primary and secondary endpoints and has demonstrated improved survival data and achieved reimbursement from key agencies such as NICE, it can still be rejected multiple times by the PBAC.

History shows it will typically take two, or even three PBAC submissions to achieve a listing, even with the best evidence available.

Given this, the reality is that with the new fees and increases to existing fees, pharmaceutical companies will be spending in excess of $3M for every drug they try to list. It's a vast amount of money when there is no definitive predictor of listing success that a company can rely on to determine the degree of investment risk.

While large multi-national pharma companies may be able to bear this cost and risk, smaller companies such as STA cannot manage this level of 'upfront' payment combined with the high risk of rejection due to the poor predictability of listing success.

STA supports cost recovery, but it must not be an impediment to patient access, and the system must start to acknowledge the variability in make-up of companies and the challenge of treating small patient population.

A potential solution to this situation is to provide special consideration to pharmaceutical companies that are generating annual revenues of less than $50 million.

> ***STA request that smaller companies with revenue <$50M annually be granted an exemption from paying new fees 'upfront' for at least the first two applications, and when, or if, a drug is listed on the PBS, the company then pays those fees in arrears, in instalments when PBS expense on that drug exceeds $3M per year.***

PBAC and Orphan Drugs

The situation is even more difficult with orphan drugs – that is, therapies that treat people with rare diseases and where there is a high unmet clinical need.

These patient populations are frequently denied effective targeted therapies but have the same right to receive precision medicines that may significantly improve their outcomes.

While the PBAC provides an exemption on the initial PBAC submission for drugs that have been orphan-designated, this is not the case for subsequent resubmissions post a rejection.

As stated earlier, it typically takes two to three submissions for a drug to receive a positive PBAC approval.

Given this statistic, STA is now faced with a real barrier for orphan drugs to be PBS listed as the likelihood of success in the only fee exempt round (first submission) is low, and the revenue that

would be generated by the orphan drug insufficient to justify the multi-million dollar outlay required for subsequent submissions.

> ***STA proposes that the first two PBAC submissions for orphan designated drugs are fee exempt, with a further minor submission fee thereafter (if this required following an unsuccessful second major submission).***

CONCLUDING STATEMENT

Australia's life-saving PBS system was once a world-class pillar of what really is an outstanding health system. All of us – including scientists, industry and consumers - must demand that the system continually evolves and adapts to accommodate new science, new therapies and better diagnostics, that can improve health outcomes for patients.

When the PBS was introduced more than 50 years ago, it supplied only a limited number of 'life-saving and disease-preventing' drugs free of charge to the community. Now, it is a far-reaching scheme that provides affordable, subsidised access to all Australians of varied means, to thousands of branded and generic medicines.

These medicines are safe and effective, and as a society we can have the utmost faith in the due diligence process underpinning the availability of these therapies, thanks to the scientific rigour employed by our regulator, the TGA.

The TGA is an organisation that has continually evolved, recognising the need to adapt and update processes to ensure that world-class therapies are recognised and available in Australia.

Making these medicines affordable – once they are TGA-approved – is the next step.

It is our view that both the MSAC and the PBAC should not 'second-guess' the science that has already been examined by the TGA. It must further ensure that the Australian health system is internationally competitive – i.e. that Australian patients are afforded the same standard of care available in other developed countries.

Both the PBAC and the MSAC were established to advise on cost-effectiveness of public funding.

They must be transparent in their decision making, and further recognise that emerging complex therapies and technologies require greater levels of assessment expertise.

It is time for these independent reimbursement organisations to adapt, as the TGA has clearly done. Both MSAC and PBAC must recognise that all patients matter. This includes those patients with common or well-known diseases, as well as those with rarer diseases in smaller patient groups and limited treatment options. Smaller patient populations must also enjoy affordable access to new therapies that have been shown to improve outcomes.

The MSAC and PBAC must also be cognisant of the commercial landscape – not all pharmaceutical companies are multi-national organisations. Industry must be incentivised to continually navigate

the regulatory and reimbursement pathways that will ultimately enable provision of emerging therapies to all Australian patient populations – clinical trials are not enough.

Thank you for considering our submission and we look forward to continuing our quest to make a difference for all Australian patients.