Senate inquiry into equitable access to diagnosis and treatment for individuals with rare and less common cancers, including neuroendocrine cancer

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Glossary of Terms

ALCL	Anaplastic Large Cell Lymphoma
ALK	Anaplastic Lymphoma Kinase
ALL	Acute Lymphoblastic Leukaemia
ANSTO	Australian Nuclear Science And Technology Organisation
ANZCHOG	Australian And New Zealand Children's Haematology And Oncology Group
COG	Children's Oncology Group
CT	Computerised Tomography
FDA	Food And Drug Administration
FTE	Full Time Equivalent
HSTs	Highly Specialised Therapies
IMT	Inflammatory Myofibroblastic Tumour
INRC	International Neuroblastoma Response Criteria
KOALA	Kids Oncology And Leukaemia Trials
MBS	Medicare Benefits Schedule
MIBG	Metaiodobenzylguanidine
MRD	Measurable Residual Disease

MRI..... Magnetic Resonance Imaging

MSAC..... Medical Services Advisory Committee

NHRA..... National Health Reform Agreement

NTRK..... Neurotrophic Tyrosine Receptor Kinase

PBAC..... Pharmaceutical Benefits Advisory Committee

PBS..... Pharmaceutical Benefits Scheme

ROS..... Reactive Oxygen Species

SCHN.....Sydney Children's Hospitals Network

SIOP..... International Society For Paediatric Oncology

TGA..... Therapeutic Goods Administration

Executive Summary

Each type of childhood cancer is a rare or uncommon cancer. The incidence rate of individual childhood cancers ranges between 0.16-4.25 cases per hundred thousand population per year. Melanoma is the rarest childhood cancer with an incidence rate 0.16 cases per hundred thousand per year, and acute lymphoblastic leukaemia is the most common childhood cancer with an incidence rate 4.25 cases per hundred thousand per year[1]. A detailed table of childhood cancer incidence rates is included at the end of the submission (Annexure 1). Over the period 1983-2015 there was a mean of 770 new cancer cases per year in children under 15 years of age in Australia[1].

As paediatric haematologists & oncologists we would like to address 4 issues which specifically impact on children and young people with cancer and provide recommendations relevant to the Committee's Terms of Reference to enable our health system to provide world class care for our patients. These issues are:

1. Equitable funding of complex diagnostic tests and complex therapeutics for cancer patients which disproportionately impacts on children and young people with cancer
2. Staffing within paediatric haematology and oncology centres
3. Availability and access to radionuclides for diagnosis, staging, monitoring response to treatment and therapy for neuroendocrine tumours, specifically – I^{123}-MIBG (diagnosis, staging and monitoring) & I^{131}-MIBG (therapy)
4. Extending the registered indications and funding for drugs for rare cancer in Australia

It is the collective viewpoint of the oncologists within the paediatric cancer centres across the Sydney Children's Hospitals Network (SCHN) and the Australian and New Zealand Children's Haematology and Oncology Group (ANZCHOG) that the below recommendations be considered by the Standing Committee on Community Affairs.

Recommendations

The report provides context and makes several recommendations relating to the inquiry's Terms of Reference. The recommendations are summarised below.

Recommendations to address barriers to screening and diagnosis and barriers to accessing appropriate treatment:

a) Equitable funding of complex diagnostic tests and therapeutics is essential for patients with rare cancer
b) Consideration of adapting the joint Federal-State government highly specialised therapies (HSTs) funding model, to allow public funding of complex diagnostic tests and therapeutics which have been approved by Medical Services Advisory Committee (MSAC) for admitted inpatients within a public hospital

Recommendations to address barriers to accessing appropriate treatment:

a) Australia develops and retains the sovereign capacity to produce radionuclide and theranostics such as I^{123}-MIBG and I^{131}-MIBG
b) Australia's current and future capacity to deliver I^{131}-MIBG therapy is reviewed and funding for additional capacity secured if required
c) Consideration be given to allowing flexibility in the mechanisms to modify indications on Therapeutic Goods Administration (TGA) registration and Pharmaceutical Benefits Advisory Committee (PBAC) funding for effective drugs for rare cancers

Recommendations to address all Terms of Reference:

a) Consideration be given to undertaking population-based workforce and staff benchmarking for children's cancer services to accurately identify optimal staffing levels to provide multidisciplinary research enabled care that should be recurrently funded by the Australian healthcare system
b) Consideration be given to securing recurrent funding for staffing within paediatric oncology centres and children's cancer clinical trials units

1. Equitable funding of complex diagnostic tests and complex therapeutics for cancer patients disproportionately impacts on children and young people with cancer

Addressing Terms of Reference items:

a) barriers to screening and diagnosis
b) barriers to accessing appropriate treatment

The structure of Australian health care funding, defined by the federal-state funding model, creates inequalities in accessing some publicly funded treatments and tests for patients admitted to public hospitals which disproportionately impacts on health care funding for children and young people with cancer. Different components of health funding are split between the Federal and State Governments. State Governments have the responsibility to fund all aspects of inpatient care in public hospitals whilst the Federal Government has the responsibility for funding outpatient health care costs, including Medicare Benefits Schedule (MBS) funding, which covers pathology including complex diagnostics, and the Pharmaceutical Benefits Scheme (PBS) funding outpatient medications.

For MBS approved tests, funding is only available for tests where the patient is an outpatient at the time of sample collection. The MBS cannot be used to fund tests for patients who are admitted

inpatients in public hospitals at the time that samples are collected. Therefore, the cost for any test requested for admitted inpatients in public hospitals is not covered by MBS funding but is expected to be paid by either (i) the public hospital; or (ii) the oncology department; and/or (iii) the patient or family.

Almost every child diagnosed with cancer has their diagnostic work-up, including tumour biopsies, and treatment performed whilst an admitted inpatient in public hospitals, which makes them ineligible for MBS funding. This is a particular problem for complex diagnostic tests, particularly genetic and genomic tumour analyses, and monitoring tests which are increasingly required for appropriate diagnosis, staging and management of cancer. These complex diagnostic and monitoring tests are regarded as not being covered by the block funding provided to each State to treat publicly admitted patients in public hospitals.

Whilst the intent of Australian health care funding is to provide equitable access to appropriate tests for all eligible patients, in practice admitted inpatients in public hospitals are disadvantaged as they cannot access MBS funding for specialised tests nor do public hospitals cover the costs of these tests. This leads to intrinsic inequality and disparity in funding diagnostic tests which particularly affects cancer patients treated in children's cancer centres.

As a specific example, for acute lymphoblastic leukaemia (ALL), the most common cancer in children, the MSAC has recommended approving funding a specialised monitoring test for ALL called measurable residual disease (MRD) in Australia. MRD is an internationally recognised standard of care test. Currently MRD testing for children with ALL is being paid by individual oncology departments in children's cancer centres. However, despite the MSAC recommendation for MRD funding through the MBS, patients treated for ALL in Children's Cancer Centres will continue to be unable to access MBS funded MRD as patients treated in Children's Cancer Centres have bone marrow samples collected for MRD whilst admitted as inpatients in a public hospital. In contrast, in the adult haematology setting, patients generally have their bone marrow for MRD collected as outpatients and thus will be able to access publicly funded MRD testing through the MBS.

Despite a positive recommendation for MRD funding, half the patients in Australia eligible for MRD testing will be unable to access publicly funded MRD testing.

The same issue arises for children and young people with solid and brain tumours where tumour samples are collected whilst patients are admitted as inpatients in public hospitals and are thus unable to access MBS funded diagnostic tests which are required for appropriate diagnosis and staging. Biopsy tests are painful/stressful and standard of care principles/approaches are to provide the sedation/analgesia which necessitates inpatient admission for lymph node biopsy, thyroid gland biopsy, bone marrow examination, lumbar punctures in children where these would be done as outpatient investigations in adults. For the same diagnostic tests in identical clinical circumstances, adults are subsidised, while children are not, effectively penalised by virtue of age and appropriate approach. The following item numbers cannot currently be accessed by children despite potential need in those with rare cancers because of inpatient nature of tissue collection: 73338 melanoma, 73301 Ovarian cancer, 73376 Sarcoma, 73373 Glioma IDH1/2 variant testing, 73373 Glioma methylation testing and 73433 neurotrophic tyrosine receptor kinase (NTRK) Fusion<18

Similarly, there are a number of PBS approved, complex therapeutics which are funded by the PBS where the administration requires at least a portion of the therapy to be administered whilst patients are admitted to hospital (*eg* blinatumomab and inotuzumab ozogamicin) yet the PBS approval specifically states: "This drug is not PBS-subsidised if it is administered to an in-patient in a public hospital setting". Although PBS approved and funded, there is no specific Federal or State

government funding program outside the PBS to ensure that admitted inpatients in public hospitals could access these therapies when indicated.

Whilst the intent of the government funding is to provide equitable access to therapy and testing, the current structure of Federal-State health funding means that **not all patients who would be eligible to access these services and therapies can access them equally**. This has a disproportionate impact on children and young people with cancer due to the high number of occasions **where they are managed as admitted inpatients within public hospitals** where the current funding model does not allow access PBS or MBS funding for complex medications and diagnostic tests and there are currently no alternative funding mechanisms in place.

An exception to the principle of not using PBS funding for admitted inpatients in public hospitals has been established. Eculizumab, a drug used to treat atypical haematolytic uraemic syndrome is funded on the PBS to treat admitted patients in public hospitals due to the high clinical need of these patients. There is an additional example of a joint Federal-State government funding model, outside of the MBS and PBS, specifically the Highly Specialised Therapies program which funds therapies recommended for delivery in a public hospital setting recommended by the MSAC. The Highly Specialised Therapies program funds Kymriah and Yscarta (for ALL and lymphoma), Qarziba (for high risk neuroblastoma) and Luxturna (for Leber congenital amaurosis). Additionally, the complexity of funding health care in Australia has been recognised by the creation of 2020–25 National Health Reform Agreement (NHRA). All Australian governments agreed to progress long-term system-wide health reforms under the NHRA, with one of the agreed areas of reform being:

- paying for value and outcomes – enabling new and flexible ways for governments to pay for health services (https://www.health.gov.au/our-work/2020-25-national-health-reform-agreement-nhra)

Therefore, we recommend that (i) equitable funding of complex diagnostic tests and therapeutics is essential for patients with rare cancer and (ii) consideration of adapting the joint Federal-State government highly specialised therapies (HSTs) funding model, to allow public funding of complex diagnostic tests and therapeutics which have been approved by Medical Services Advisory Committee (MSAC) for admitted inpatients within a public hospital.

2. Staffing within paediatric haematology and oncology centres

Addressing Terms of Reference items:

a) barriers to screening and diagnosis
v. availability of treating practitioners
b) barriers to accessing appropriate treatment
c) the adequacy of support services after diagnosis
d) the adequacy of Commonwealth funding for research into rare, less common and neuroendocrine cancer

Paediatric haematology and oncology centres provide specialist, complex care for children and families with cancer and blood disorders. Treatments range from simpler outpatient anti-cancer therapy, more complex inpatient anti-cancer care and highly complex therapies including cellular therapies and stem cell transplantation. Children's cancer centres require a large, diverse team of specialist health-care practitioners to be able to provide the level of care required by their patients and families. Children's cancer care in Australia and the developed world is centralised into highly specialised centres which work closely with networks of referring centres across the country. Many children and families affected by cancer, particularly those living in regional and rural Australia experience prolonged periods of dislocation during acute phases of treatment.

The care of children with cancer therefore requires a complex workforce covering different clinical, clinical research, and settings of care covering:

a) the spectrum of newly diagnosed patients, active treatment, early post treatment surveillance and long-term survivorship health care;
b) initial treatment of newly diagnosed patients, treatment of relapsed / refractory cancer, palliative care for patients with terminal cancer;
c) providing anti-cancer treatment as well as supportive care including practical supports (allied health e.g. social work), nutritional support, psychologic support, educational and vocational assistance, bereavement support;
d) inpatient care, outpatient care, outreach clinics, outreach nursing to support families in the community and services including support and education for health care practitioners in metropolitan, regional and rural settings;
e) participation in clinical trials ranging from large, international phase 3 clinical trials to refine the standards of care to early phase trials for patients with relapsed & refractory disease;
f) each unit has complex staffing across multiple disciplines including: specialist oncologists, haematologists and transplant physicians, junior medical officers, clinical nurse consultants, nurse educators, nursing unit managers, ward nursing staff, care navigators, clinical support officers, bereavement counsellors, clinical psychologists, dietitians, occupational therapists, physiotherapists, pharmacists, pharmacy technicians, social workers, research managers, research nurses, clinical research associates, clinical trials assistants, clinical trials coordinators, business managers, administration managers, administration officers and quality managers.

A significant issue facing all children's cancer services is that only a proportion of staff members are funded by permanent, recurrent funding, leaving a significant proportion of staff with their positions funded by "soft funds", *ie* philanthropic donation and/or other short term funding mechanisms such as grants. There are just over 350 FTE staff employed across the paediatric haematology & oncology services at the SCHN. A substantial proportion of core staffing is not adequately resourced by recurrent salary funding. Every Children's Cancer Centre in Australia is in a similar position and relies on philanthropy and other funding sources to bridge the funding required to cover core staff salary each year. As a result, there is a significant requirement to attract recurrent philanthropic funding every year. Consequently, many positions which are important in providing services to children with cancer and their families, remain reliant on uncertain year-to-year funding. This has a negative impact on staff retention, staff satisfaction, service planning and staff turnover. This reduces the availability of treating practitioners required across the health care disciplines (*eg* oncology pharmacists, pharmacy technicians, specialist nurses *etc*) required for paediatric oncology and particularly has a negative impact on being able to provide supportive care (*eg* social work, psychology, allied health, care navigators *etc*) to children with cancer and their families.

An over reliance on philanthropic funding for staffing has a significant negative impact on building a sustainable workforce for the future, both for clinical and clinical trials staff. Highly qualified nurses, researchers and allied health staff want to be employed in permanent positions, rather than be employed on contracts which need to be renewed on a year-by-year basis. Consequently, it often means that it is not possible to attract the right skilled workforce member to each position. Uncertainty of funding means that there is also a higher staff turnover as well as a longer time to successfully recruit to open positions, which in turn means many positions are often empty for long periods of time.

Effective funding of clinical research and clinical trials staff is particularly important as improved survival and outcomes for children and young people with cancer has been driven by access to, and

participation in clinical trials. Results of clinical trials continue to set the standards of care for cancer treatment and have been a mechanism to provide access to effective therapies for Australian cancer patients. Investigational therapies from recent clinical trials which were open at Australian children's cancer centres, including Kymriah, Qarziba and Vitrakvi, have been registered by the TGA, approved by the MSAC and publicly funded within Australia. The registration and funding of these therapies has been driven by the participation of Australian children's cancer centres in the preceding clinical trials. Clinical trials participation can be particularly important for children with rare cancers and those with relapsed or refractory disease. All children's cancer centres have active clinical trials programs, which have provided an ongoing capacity for Australian children with cancer to participate in clinical trials. Effective Australian participation in clinical trials requires:

- Local Australian clinical trials organisations to sponsor and monitor clinical trials (*eg* the Australian and New Zealand Children's Haematology and Oncology Group, ANZCHOG, https://anzchog.org/);
- Academic research organisations which assist in the development and management of investigator initiated early phase clinical trials (*eg* Kids Oncology and Leukaemia Trials (KOALA, https://koalatrials.org/koala/);
- Clinical trials units based within each hospital including clinical trials staff

However, funding mechanisms for children's cancer clinical trials units is highly variable across Australia with many cancer clinical trials units relying on philanthropic funding to fund staff positions. Unlike adult oncology services, the majority of clinical trials that are conducted for children with cancer are investigator-initiated trials sponsored by large international academic trials consortia such as the Children's Oncology Group (COG) and the International Society for Paediatric Oncology (SIOP). As such it is not feasible that children's cancer clinical trials would be effectively funded on a cost recovery model by participation in pharmaceutical company sponsored trials. Furthermore, many children's cancer clinical trials units recognise the importance of opening clinical trials for patients with rare cancers.

Therefore, children's cancer services face particular challenges raised by partial funding of their staff which impacts all areas of their operation and impacts on the availability of treating practitioners; accessing treatments (through clinical trials); the adequacy of support services after diagnosis; & highlight inadequate & inconsistent funding for clinical research including clinical trials research for children with cancer.

Equitable access to children's cancer services across Australia also requires that each children's cancer service is funded to an equivalent level to support the numbers of patients that they treat. In the Canadian context, the human resources committee of the Council of Canadian Pediatric Hematology/Oncology Directors (C17 Council) established a population based ratio for paediatric oncologists, haematologists and transplant physicians[2]. Defining population based workforce recommendations **was to ensure that patients would have equal access to specialist care and cancer clinicians would have a similar workload across the Canada**[2]. The Canadian workforce recommendations were developed from longitudinal surveys across all 17 Canadian cancer centres considering clinician demographics, full time equivalent (FTE) positions, and work patterns (time spent in clinical, research, education, and administrative activities) with the survey results being reviewed at the C17 national meetings to obtain national consensus on workload ratios for oncology clinicians. In the Australian context it is important to ensure that each children's cancer service has adequate staffing across all disciplines (medical, nursing, allied health, education support, clinical research).

We recommend that Australia undertake a national process of population-based workforce and staff benchmarking for children's cancer services to accurately identify optimal staffing levels to

provide multidisciplinary clinical services that should be recurrently funded. This work will serve to inform a research embedded model of care fit for purpose in the Australian context.

Therefore we recommend consideration be given to (i) undertaking population-based workforce and staff benchmarking to define optimal staffing levels across medical, nursing, allied health, education support, clinical research disciplines for children's cancer services; (ii) securing recurrent funding for staffing within paediatric oncology centres including children's cancer clinical trials units.

3. Availability and access to radionuclides for diagnosis, staging, monitoring response to treatment and therapy for neuroendocrine tumours – I^{123}-MIBG (diagnosis, staging and monitoring) & I^{131}-MIBG (therapy)

Addressing Terms of Reference item:

(a) barriers to screening and diagnosis

The most common neuroendocrine cancer in paediatrics is neuroblastoma. The diagnosis is made using a combination of tests including anatomical imaging (computerised tomography (CT) or magnetic resonance imaging (MRI) scan) and functional imaging with metaiodobenzylguanidine (MIBG) scanning.

Radionuclides are an important component of the diagnosis, monitoring and management of children with neuroendocrine tumours, particularly neuroblastoma. Hence the regular supply of radionuclides for diagnosis, monitoring and therapy is critical to care of children with rare cancers.

MIBG functional imaging is the gold standard investigation for the diagnosis, staging and follow-up of paediatric neuroendocrine tumours including neuroblastoma, ganglioneuroblastomas, ganglioneuromas, phaeochromocytomas and paragangliomas[3,4]. There are ≈50 children diagnosed with neuroblastoma each year in Australia[5]. Half of these have high-risk neuroblastoma which requires prolonged and intensive therapy with a current survival rate of around 50-60%. Most children with neuroblastoma are young with 90% of neuroblastoma cases diagnosed in children under 5 years of age[5]. I^{123}-MIBG scans are used for diagnosis, staging and treatment monitoring in neuroblastoma[3,4]. I^{123}-MIBG scanning is the most important test to identify metastatic neuroblastoma at diagnosis and is a central component of the internationally standardised neuroblastoma response assessment, called the International Neuroblastoma Response Criteria (INRC). INRC response is used by paediatric oncologists to direct the ongoing treatment of children with neuroblastoma[4].

I^{131}-MIBG is used to treat children with high-risk neuroblastoma. I^{131}-MIBG therapy is used to treat relapsed and/or refractory high-risk neuroblastoma for symptom palliation, providing disease control and extending survival. For children with newly diagnosed high-risk neuroblastoma there is current clinical trial examining whether adding I^{131}-MIBG to chemotherapy improves survival (ANBL1531, NCT03126916)[6]. ANBL1531 is being run in the United States by the Children's Oncology Group Trial. Results from the ANBL1531 clinical trial are not known currently but are expected within the near future. If the combination of I^{131}-MIBG and chemotherapy is more effective than chemotherapy alone, then the ANBL1531 trial will change practice for children with high-risk neuroblastoma and set a new standard of care for children with high-risk neuroblastoma, including Australian children.

There are two broad issues relating to access and availability of radionuclides for children with cancer. First, there is a sovereign risk in the manufacture and supply of both I^{123}-MIBG and I^{131}-MIBG as neither are manufactured within Australia and Australia remains reliant on overseas supply, from

Japan for I^{123}-MIBG, and from Poland for I^{131}-MIBG. Previously, Australian Nuclear Science and Technology Organisation (ANSTO) had manufactured I^{123}-MIBG locally (Australian Register of Therapeutic Goods registered product MIBGEN iobenguane[^{123}I] sulfate 100MBq/mL injection vial, https://www.tga.gov.au/resources/artg/101670) but it is not currently available. The Japanese I^{123}-MIBG product is only clinically available on a 2nd weekly basis meaning that patients, families and clinicians managing children with neuroblastoma often have to wait for MIBG scans as there isn't a local Australian manufacturing process for I^{123}-MIBG. Similarly, there are inherent risks in reliance on overseas supply of I^{131}-MIBG for therapy. The second issue relates to capacity and staffing to deliver I^{131}-MIBG therapy in Australia. Administration of I^{131}-MIBG is complex as most patients requiring I^{131}-MIBG are young children. Administration requires a specialised facility including an appropriate shielded room, a prolonged general anaesthetic for young children after I^{131}-MIBG administration and the appropriate multidisciplinary care team including paediatric oncologists, nuclear medicine physicians, medical physicists, intensive care staff, anaesthetists, nursing staff *etc* for the safe administration of I^{131}-MIBG. Currently there are three centres in Australia which can administer MIBG therapy but are restrained in their capacity to deliver therapy. If the ANBL1531 clinical trial shows I^{131}-MIBG and chemotherapy is more effective than chemotherapy, then there would be the reasonable community expectation that I^{131}-MIBG therapy would be made available to all patients with high-risk neuroblastoma in Australia. So, the important resourcing issues going forward are to (i) manage sovereign risk in the supply of radionuclides / theranostics including I^{123}-MIBG and I^{131}-MIBG and (ii) ensure that there is sufficient capacity (facilities and staff) to deliver I^{131}-MIBG therapy in the future.

We recommend that (i) Australia develops and retains the sovereign capacity to produce radionuclide and theranostics such as I^{123}-MIBG and I^{131}-MIBG; and (ii) current and future capacity to deliver I^{131}-MIBG therapy is reviewed and fund additional capacity if required.

4. Extending the registered indications and funding for drugs for rare cancer in Australia

Addressing Terms of Reference item:

(b) barriers to accessing appropriate treatment

The Australian registration and funding of drugs requires that each drug has a TGA registration for each treatment indication and an application to the PBAC for PBS funding for each clinical indication. Currently, the drug sponsor, usually the pharmaceutical company, is the only entity which can apply to the TGA to modify the registered indication for a drug. Although there are pathways for clinicians to make a submission to the PBAC for PBS funding it is not possible to apply to the PBAC for PBS funding for a drug unless it is TGA registered for that indication. This system is a disincentive to the public funding of effective therapies for rare cancers.

A specific example is the anaplastic lymphoma kinase (ALK) inhibitor, crizotinib, which is TGA registered and PBS funded to treat high stage ALK- and/or reactive oxygen species (ROS)-rearranged lung cancer. Crizotinib is an effective drug for other ALK- and ROS- rearranged cancers including the rare sarcoma ALK-rearranged inflammatory myofibroblastic tumour (IMT) and ALK-rearranged anaplastic large cell lymphoma (ALCL). In the US, crizotinib has been Food and Drug Administration (FDA) approved for both unresectable IMT (in 2022) and relapsed / refractory ALCL (in 2021). However, in Australia, there is no mechanism for crizotinib to be funded for cancers other than lung cancer, unless the sponsoring pharmaceutical company is willing to reapply to the TGA to extend the registered treatment indications of crizotinib to include other rare cancers.

Both unresectable IMT and relapsed / refractory ALCL are rare diseases meaning that there is no commercial incentive for the pharmaceutical company to extend crizotinib's TGA registration for

other rare cancers. So, there is no current mechanism to apply to the PBAC to consider PBS funding crizotinib for other rare cancer such as IMT or ALCL.

This puts patients who have rare ALK- or ROS- rearranged malignancies that could be treated with crizotinib at a disadvantage in accessing crizotinib compared to patients with ALK- or ROS-rearranged lung cancer. Whilst this is a specific example, there are other targeted agents where the initial TGA registration will not reflect the groups of patients who may benefit from that therapy. Another example is the use of BRAF and MEK inhibitors which are currently approved for melanoma but are not approved for high-grade glioma and low-grade gliomas despite clinical evidence of their effectiveness in brain tumours[7-9]. Therefore, it is important to consider allowing flexibility in the mechanisms of modify indications on TGA registration and applications for PBAC approval of funding for effective drugs for rare cancers.

This submission has been reviewed and endorsed by and on behalf of:

Adjunct Associate Professor Cathryn Cox PSM, Chief Executive, Sydney Children's Hospitals Network
Robyn Strong, Chief Executive, Australian & New Zealand Children's Haematology/Oncology Group

References

1. Youlden DR, et al. Med J Aust 2020;212(3):113-120.
2. Halton JM, et al. Pediatr Blood Cancer 2013;60(4):564-9.
3. Matthay KK, et al. Br J Cancer 2010;102(9):1319-26.
4. Park JR, et al. J Clin Oncol 2017;35(22):2580-2587.
5. Youlden DR, et al. J Paediatr Child Health 2020;56(7):1046-1052.
6. Children's Oncology Group. NCT03126916 Testing the Addition of 131I-MIBG or Lorlatinib to Intensive Therapy in People With High-Risk Neuroblastoma (NBL). 2023-05-23 (https://clinicaltrials.gov/search?term=ANBL1531).
7. Hargrave DR, et al. Clin Cancer Res 2019;25(24):7303-7311.
8. Wen PY, et al. Lancet Oncol 2022;23(1):53-64.
9. Bouffet E, et al. J Clin Oncol 2023;41(3):664-674.

Annexure 1

Table 1. Mean annual numbers and incidence rates of childhood cancers by diagnostic group/subgroup, Australia, 2011–2015		
	Mean annual number of cases	Incidence rate (per million population per year)* (95% CI)
Diagnostic group/subgroup†		
Lymphoid leukaemias	188 (24.4%)	42.5 (39.8–45.3)
Acute myeloid leukaemias	31.6 (4.1%)	7.2 (6.1–8.4)
Hodgkin lymphomas	26.2 (3.4%)	6.3 (5.3–7.5)
Non-Hodgkin lymphomas (other than Burkitt lymphomas)	24.4 (3.2%)	5.8 (4.8–6.9)
Burkitt lymphomas	15.0 (1.9%)	3.5 (2.8–4.4)
Ependymomas and choroid plexus tumours	19.4 (2.5%)	4.4 (3.6–5.4)
Astrocytomas	73.2 (9.5%)	17.0 (15.3–18.8)
Intracranial and intraspinal embryonal tumours	33.4 (4.3%)	7.6 (6.5–8.9)
Other gliomas	22.0 (2.9%)	5.1 (4.2–6.1)
Neuroblastoma and other peripheral nervous cell tumours	45.8 (5.9%)	9.9 (8.6–11.2)
Retinoblastoma	20.0 (2.6%)	4.3 (3.5–5.2)
Renal tumours	36.2 (4.7%)	7.8 (6.7–9.1)
Nephroblastoma and other non-epithelial renal tumours	35.0 (4.5%)	7.7 (6.6–8.9)
Hepatoblastoma	10.0 (1.3%)	2.2 (1.6–2.9)
Osteosarcomas	14.2 (1.8%)	3.4 (2.7–4.3)
Ewing tumours and related bone sarcomas	14.8 (1.9%)	3.5 (2.7–4.4)
Rhabdomyosarcomas	23.2 (3.0%)	5.3 (4.4–6.3)
Germ cell tumours,‡ trophoblastic tumours, and neoplasms of gonads	27.0 (3.5%)	6.2 (5.2–7.3)
Melanomas	6.6 (0.9%)	1.6 (1.1–2.2)

CI = confidence interval. * Age-standardised to the 2001 Australian standard population. † Defined according to the International Classification of Childhood Cancers (ICCC-3). ‡ Includes intracranial and intraspinal tumours of benign or uncertain behaviour.

Source: Adapted from Table 1: Danny R Youlden *et al* "The incidence of childhood cancer in Australia, 1983–2015, and projections to 2035" MJA 212 (3) ▪ 17 February 2020 113-120 doi: 10.5694/mja2.50456