Australian Government

Department of Health

Application Form

(New and Amended

Requests for Public Funding)

(Version 2.4)

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires in order to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Phone: +61 2 6289 7550
Fax: +61 2 6289 5540
Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):
Corporation name: **The Royal College of Pathologists of Australasia (RCPA)**
ABN: **Redacted**
Business trading name: **Redacted**

Primary contact name: Redacted

Primary contact numbers
Business: **Redacted**
Mobile: **Redacted**
Email: **Redacted**

Alternative contact name: Redacted

Alternative contact numbers
Business: **Redacted**
Mobile: **Redacted**
Email: **Redacted**

2. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☒ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Somatic gene testing for the diagnosis of Gliomas, Gliobastomas, and Soft Tissue and Bone Tumours

4. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Central nervous system tumours of glioma and gliobastoma subtype, and soft tissue and bone tumours.

5. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

The latest World Health Organisation (WHO) classification of brain tumorus has highlighted the critical importance of molecular diagnostic in the accurate diagnosis and proper classification of brain tumours. For some entities, molecular information is required to provide an "integrated" diagnosis and only a descriptive histological diagnosis is acceptable if no molecular diagnostic testing is available. Identification of co-deletion of chromosome 1p/19q regions is important for accurate diagnosis of oligodendroglial tumours, IDH1/2 mutations and MGMT promoter methylation add important prognostic and predictive information to the histopathological diagnosis of gliomas.
Identification of gene rearrangements, copy number aberrations and mutations is also increasingly important in the diagnosis of bone and soft tissue tumours . Important genes in this setting to be tested include beta catenin, EWSR1, SS18, FOX01, PAX3, PAX7, MDM2, FUS, DDIT3, FLI1, ERG, ETV6, NTRK3, COL1A1, PDGFB genes.

6. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☒ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

N/A

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

N/A

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☒ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)

iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

(g) If yes, please advise:

N/A

7. What is the type of service:

☐ Therapeutic medical service
☒ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☐ Co-dependent technology
☐ Hybrid health technology

8. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☒ Assists in establishing a diagnosis in symptomatic patients
iii. ☒ Provides information about prognosis
iv. ☒ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☒ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

☐ Pharmaceutical / Biological
☐ Prosthesis or device
☒ No

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

N/A

☐ Yes
☐ No

(b) If yes, please list the relevant PBS item code(s):

N/A

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

N/A

☐ Yes (please provide PBAC submission item number below)
☐ No

Insert PBAC submission item number here

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

N/A

Trade name: Insert trade name here
Generic name: Insert generic name here

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

N/A

☐ Yes
☐ No

(b) If yes, please provide the following information (where relevant):

N/A

Billing code(s): Insert billing code(s) here
Trade name of prostheses: Insert trade name here
Clinical name of prostheses: Insert clinical name here
Other device components delivered as part of the service: Insert description of device components here

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

N/A

☐ Yes
☐ No

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

N/A

☐ Yes
☐ No

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

N/A

Insert sponsor and/or manufacturer name(s) here

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables:

Brain tumours:
A number of different assays that all require the use of consumables can be used to detect the genetic changes described above including fluorescent in situ hybridisation (FISH), polymerase chain reaction (PCR), Sanger sequencing, and next generation sequencing (NGS).
Further information can be provided if required.

Soft Tissue and Bone Tumours
A wide number of assays and techniques can be used to detect the genetic changes described above including polymerase chain reaction (PCR), Sanger sequencing, next generation sequencing (NGS) and fluorescent in situ hybridisation (FISH). FISH is the most commonly employed assay.
An exhaustive listing is beyond the scope of this application given the multiple assays/ techniques that can be used. These will continue to evolve as new diagnostic changes are reported across tumour types.
Further information can be provided if required.

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good: In-vitro diagnostic test
Manufacturer's name: Various
Sponsor's name: Not applicable

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☒ Class III
☐ AIMD
☐ N/A

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☒ No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

☒ Yes (if yes, please provide details below)
☐ No

ARTG listing, registration or inclusion number

ARTG licence numbers for Acquired genetic alteration IVDs including but not limited to:

AA-Med Pty Ltd 214482
Abacus ALS Pty Ltd 255352 256572 262298
Abbott Australasia Pty Ltd Molecular Division 196286
Biomerieux Australia Pty Ltd 217781
Bio-Strategy Pty Ltd 226487
Carl Zeiss Pty Ltd 266568
Cepheid Holdings Pty Ltd 226631
Dako Australia Pty Ltd 199420 264573
In Vitro Technologies Pty Ltd 225995
Key Diagnostics Pty Ltd 270292
Leica Microsystems Pty Ltd 191254
Qiagen Pty Ltd 214994 226453 238792
Roche Diagnostics Australia Pty Limited 180933 192394 192395 194319 196363 Thermo Fisher Scientific Australia Pty Ltd 227503 256113
Vela Diagnostics Australia Pty Ltd 228024 235394

TGA approved indication(s), if applicable:
TGA approved purpose(s), if applicable:

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

N/A

☐ Yes (please provide details below)
☐ No

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

N/A

☐ Yes (please provide details below)
☐ No

PART 4 – SUMMARY OF EVIDENCE

17. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

Gliomas

	Type of study design*	**Title of journal article or research project (including any trial identifier or study lead if relevant)**	**Short description of research (max 50 words)****	**Website link to journal article or research (if available)**	**Date of publication*****
1.	Clinical practice guidelines	Louis DN, Perry A, Burger P, et al: International Society Of Neuropathology--Haarlem consensus guidelines for nervous system tumour classification and grading. Brain Pathol 24:429-35, 2014.	International clinical practice guidelines on the classification of nervous system tumours by expert consensus.	International Society of Neuropathology-Haarlem Consensus Guidelines for Nervous System Tumor Classification and Grading	10 Sep 2014
2.	Clinical practice guidelines	Louis DN, Ohgaki H, Wiestler OD, et al: WHO Classification of Tumours of the Central Nervous System (ed 4th). Lyon, IARC Press, 2016	International practice guidelines endorsing the use of Haarlem recommendations for the classification of CNS tumours.	Book –no URL	May 2016
3.	Study of diagnostic accuracy	Cahill DP, Louis DN, Cairncross JG: Molecular background of oligodendroglioma: 1p/19q, IDH, TERT, CIC and FUBP1. CNS Oncol 4:287-94, 2015	A study into molecular identification of oligodendroglioma as a subcategory of gliomas. The findings provided a foundation for the consistent diagnosis of the tumor type, for which there is a strong evidence base for effective treatment with radiation and chemotherapy.	Molecular background of oligodendroglioma : 1p/19q, IDH, TERT, CIC and FUBP1	7 Nov 2015
4.	Clinical trial	van den Bent MJ, Brandes AA, Taphoorn MJ, et al. Adjuvant procarbazine, lomustine, and vincristine	Long-term follow-up findings of a randomized phase III study on the addition of six cycles of procarbazine, lomustine, and	Adjuvant Procarbazine, Lomustine, and Vincristine Chemotherapy in Newly Diagnosed Anaplastic	2013

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
		chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC brain tumor group study 26951. J Clin Oncol. 2013;31(3):344-50.	vincristine (PCV) chemotherapy to radiotherapy (RT) (368 patients, median follow-up 140 months) In the 80 patients with a 1p/19q codeletion, OS was increased, demonstrating benefit of adjuvant PCV with RT. IDH mutational status was also of prognostic significance.	Oligodendroglioma: Long-Term Follow-Up of EORTC Brain Tumor Group Study 26951	
5.	Meta analysis	Hu N, Richards R, Jensen R. Role of chromosomal 1p/19q co-deletion on the prognosis of oligodendrogliomas : A systematic review and meta-analysis. Interdisciplinary Neurosurgery. 2016;5:58-63.	A systematic review and meta-analysis on the prognostic effect of 1p/19q co-deletion affects prognoses of WHO grade II/III oligodendrogliomas. The study demonstrated the beneficial prognosis of chromosomal 1p/19q co-deletion in these tumours.	Role of chromosomal 1p/19q co-deletion on the prognosis of oligodendrogliomas: A systematic review and meta-analysis	2016
6.	Observational study	Staedtke V, Dzaye ODA, Holdhoff M. Actionable Molecular Biomarkers in Primary Brain Tumors. Trends Cancer. 2016;2(7):338-49.	Study of actionable biomarkers available in the diagnosis of brain tumours. (i) MGMT promoter methylation as a prognostic and predictive marker in glioblastoma; (ii) codeletion of 1p and 19q differentiating oligodendrogliomas from astrocytomas; (iii) IDH1/2 mutations; and (iv) select pathway-associated mutations.	Actionable Molecular Biomarkers in Primary Brain Tumors	2016
7.	Observational study	Rare Cancers Australia: Just a Little More Time Rare Cancers Update Report. 2016	A review of available cancer data investigating the disparities existing for incidence, mortality and survival across the cancer spectrum. The study provided a definition for rare	Just a Little More Time Rare Cancers Update Report	2016

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
			cancers, and the burden of disease that rare and less common cancers pose across all ages in Australia		
8.	Health economics study	Sabatini LM, Mathews C, Ptak D, et al: Genomic Sequencing Procedure Microcosting Analysis and Health Economic Cost-Impact Analysis: A Report of the Association for Molecular Pathology. J of Mol Diagn 2016;18:319-328.	US Study by Association for Molecular Pathology on cost and value analysis of specific genomic sequencing procedures (GSPs) gathered from representative laboratories' data. Cost-impact models for three clinical scenarios were generated - advanced non–small-cell lung cancer sensorineural hearing loss, and paediatric neurodevelopmental disorders of unknown genetic aetiology.	Genomic Sequencing Procedure Microcosting Analysis and Health Economic Cost-Impact Analysis: A Report of the Association for Molecular Pathology	2016

Gliobastomas

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
1.	Clinical practice guidelines	Louis DN, Perry A, Burger P, et al: International Society Of Neuropathology--Haarlem consensus guidelines for nervous system tumour classification and grading. Brain Pathol 24:429-35, 2014.	International clinical practice guidelines on the classification of nervous system tumours by expert consensus.	International Society of Neuropathology-Haarlem Consensus Guidelines for Nervous System Tumor Classification and Grading	10 Sep 2014
2.	Clinical practice guidelines	Louis DN, Ohgaki H, Wiestler OD, et al: WHO Classification	International practice guidelines endorsing the use of Haarlem	Book –no URL	May 2016

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
		of Tumours of the Central Nervous System (ed 4th). Lyon, IARC Press, 2016	recommendations for the classification of CNS tumours.		
3.	Observational study	Sturm D, Witt H, Hovestadt V, et al. Hotspot mutations in H3F3A and IDH1 define distinct epigenetic and biological subgroups of glioblastoma. Cancer Cell. 2012;22(4):425-37.	A study of 136 cases of glioblastoma (GBM) that identified H3F3A and IDH1 molecular subgroups.	Hotspot Mutations in H3F3A and IDH1 Define Distinct Epigenetic and Biological Subgroups of Glioblastoma	2012
4.	Study of diagnostic accuracy	Cahill DP, Louis DN, Cairncross JG: Molecular background of oligodendroglioma: 1p/19q, IDH, TERT, CIC and FUBP1. CNS Oncol 4:287-94, 2015	A study into molecular identification of oligodendroglioma as a subcategory of gliomas. The findings provided a foundation for the consistent diagnosis of the tumour type, for which there is a strong evidence base for effective treatment with radiation and chemotherapy.	Molecular background of oligodendroglioma : 1p/19q, IDH, TERT, CIC and FUBP1	7 Nov 2015
5.	Observational study	Staedtke V, Dzaye ODA, Holdhoff M. Actionable Molecular Biomarkers in Primary Brain Tumors. Trends Cancer. 2016;2(7):338-49.	Study of actionable biomarkers available in the diagnosis of brain tumours. (i) MGMT promoter methylation as a prognostic and predictive marker in glioblastoma; (ii) codeletion of 1p and 19q differentiating oligodendrogliomas from astrocytomas; (iii) IDH1/2 mutations; and (iv) select pathway-associated mutations.	Actionable Molecular Biomarkers in Primary Brain Tumors	2016
6.	Observational study	Rare Cancers Australia: Just a Little More Time Rare Cancers Update Report. 2016	A review of available cancer data investigating the disparities existing for incidence, mortality and survival across the	Just a Little More Time Rare Cancers Update Report. 2016	2016

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
			cancer spectrum. The study provided a definition for rare cancers, and the burden of disease that rare and less common cancers pose across all ages in Australia		
7.	Health economics study	Sabatini LM, Mathews C, Ptak D, et al: Genomic Sequencing Procedure Microcosting Analysis and Health Economic Cost-Impact Analysis: A Report of the Association for Molecular Pathology. J of Mol Diagn 2016;18:319-328,	US Study by Association for Molecular Pathology on cost and value analysis of specific genomic sequencing procedures (GSPs) gathered from representative laboratories' data. Cost-impact models for three clinical scenarios were generated - advanced non–small-cell lung cancer sensorineural hearing loss, and paediatric neurodevelopmental disorders of unknown genetic aetiology.	Genomic Sequencing Procedure Microcosting Analysis and Health Economic Cost-Impact Analysis: A Report of the Association for Molecular Pathology	2016

Soft Tissue and Bone Tumours

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
1.	Prospective, multicentre, observational study	Italiano A, Di Mauro I, Rapp J, et al: Clinical effect of molecular methods in sarcoma diagnosis (GENSARC): a prospective, multicentre, observational study. Lancet Oncol	A study of 384 patients assessing the clinical effect of systematic implementation of molecular assays to improve sarcoma diagnosis, by the identification of type-specific aberrations. The study concluded that molecular genetic	Clinical effect of molecular methods in sarcoma diagnosis (GENSARC): a prospective, multicentre, observational study	9 Mar 2016

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
		2016;17(4):532-8	testing should be mandatory for diagnostic accuracy and appropriate clinical management of sarcoma.		
2.	Educational publication	Agaimy A, Haller F: CTNNB1 (beta-Catenin)-altered Neoplasia: A Review Focusing on Soft Tissue Neoplasms and Parenchymal Lesions of Uncertain Histogenesis. Adv Anat Pathol 2016;23:1-12.	A review of pathobiology and differential diagnosis of rare beta-catenin-altered neoplasms, highlighting the diagnostic utility of detection of beta catenin mutations in the diagnosis of soft tissue neoplasms.	CTNNB1 (β-Catenin)-altered Neoplasia: A Review Focusing on Soft Tissue Neoplasms and Parenchymal Lesions of Uncertain Histogenesis	10 Dec 2016
3.	Study of diagnostic accuracy	Vargas AC, Selinger C, Satgunaselan L, et al: Atypical Ewing sarcoma breakpoint region 1 fluorescence in-situ hybridization signal patterns in bone and soft tissue tumours: diagnostic experience with 135 cases. Histopathology 2016;69(6):1000-1011	A study in NSW of fluorescence in situ hybridization (FISH) for the EWSR1 gene in the classification and differential diagnosis of bone and soft tissue tumours. The study confirmed that FISH is a sensitive and specific tool in the diagnosis of EWSR1-associated tumours.	Atypical Ewing sarcoma breakpoint region 1 fluorescence in-situ hybridization signal patterns in bone and soft tissue tumours: diagnostic experience with 135 cases	2016
4.	Observational study	Rare Cancers Australia: Just a Little More Time Rare Cancers Update Report. 2016	A review of available cancer data investigating the disparities existing for incidence, mortality and survival across the cancer spectrum. The study provided a definition for rare cancers, and the burden of disease that rare and less common cancers pose across all ages in Australia	: Just a Little More Time Rare Cancers Update Report. 2016	2016
5.	Health economics	Sabatini LM, Mathews C, Ptak D,	US Study by Association for	Genomic Sequencing	2014

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publicati on***
	study	et al: Genomic Sequencing Procedure Microcosting Analysis and Health Economic Cost-Impact Analysis: A Report of the Association for Molecular Pathology. J of Mol Diagn 2016;18:319-328,	Molecular Pathology on cost and value analysis of specific genomic sequencing procedures (GSPs) gathered from representative laboratories' data. Cost-impact models for three clinical scenarios were generated - advanced non–small-cell lung cancer sensorineural hearing loss, and paediatric neurodevelopmental disorders of unknown genetic aetiology.	Procedure Microcosting Analysis and Health Economic Cost-Impact Analysis: A Report of the Association for Molecular Pathology	

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

18. List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):

The Royal College of Pathologists of Australasia
The Royal Australasian College of Physicians
The Royal Australasian College of Surgeons
Pathology Australia
Clinical Oncology Society of Australia (COSA)
Rare Cancer Group
Human Genetics Society of Australia

19. List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):

Not applicable

20. List the relevant consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):

Cancer Voices
Rare Cancers Australia
Cure Brain Cancer Foundation
Leukaemia Foundation
Without a Ribbon
Unicorn Foundation

21. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:

Not applicable

22. Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):

Name of expert 1: Redacted

Telephone number(s): Redacted

Email address: Redacted

Justification of expertise: Redacted

Name of expert 2: Redacted

Telephone number(s): Redacted

Email address: Redacted

Justification of expertise: Redacted

Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INDICATION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

23. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

Specific gene rearrangements, mutations and/or copy number changes are seen in a range of neoplasms and detection of these changes has become best practice to determine diagnosis, prognosis and for the appropriate selection of treatment for CNS tumours.

Effective and affordable health care depends on the availability of accurate, reliable and clinically valid tests. The absence of suitable tests can lead to misdiagnosis with patients potentially receiving unnecessary treatment, experiencing delays in treatment or no treatment when treatment is needed.

These molecular aberrations are particularly characteristic of 'rare' and less common cancers, such as CNS tumours, which have disproportionately higher mortality rates compared to common cancers.

In CNS cancer, the Haarlem guidelines highlight that integration of specific molecular aberrations results in a more precise diagnosis and have formed the basis of the WHO 2016 update on classification of CNS tumours. Patient management, including chemotherapy and radiotherapy choices, are based on the WHO classification, and hence molecular information will be essential in providing accurate diagnoses. This is particularly important in young patients, where timing and dosage of treatment (based on tumour type) impacts on the significant cognitive morbidity associated with treating the brain.
Specific details as follows:

Gilomas
Although a number of different molecular tests may be employed in the accurate diagnosis of glial tumour, this application specifically relates to the detection of co-deletion of 1p/19q chromosome regions as a baseline discriminator between oligodendroglial tumours and other glioma types.

Currently patients are required to self-fund this testing, leading to inequity of access on financial grounds. The presence of chromosome 1p/19q-co-deletion has predictive value for response to chemotherapy in anaplastic oligodendrogliomas. Randomised clinical trials have demonstrated survival advantages for patients treated with combined procarbazine/lomustine/vincristine (PCV) chemotherapy and radiotherapy compared with radiotherapy alone (Touat, 2017).

Touat M, Idbaih A. 1p/19q Co-deletion in Glioma: ESMO Biomarker Factsheet. Lugano, Switzerland: European Society for Medical Oncology; 2017 1p/19q Co-deletion in Glioma: ESMO Biomarker Factsheet.

Stupp R, Brada M, van den Bent MJ, et al. High-grade glioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25 Suppl 3:iii93-101. High-grade glioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.

Glioblastomas
Although a number of different molecular tests may be employed in the accurate diagnosis of glial tumour, this application relates to IDH1/2 mutation and MGMT promoter methylation. IDH-mutated tumours are associated with a more favourable prognosis than for non-mutated grade III astrocytoma indicating important prognostic value of this test. In retrospective analyses, MGMT methylation has been correlated with improved outcomes with alkylating agent chemotherapy. In lower grade IDH-mutated tumours, MGMT methylation indicates a better prognosis overall (Stupp, 2014).

Currently patients are required to self-fund this testing, leading to inequity of access on financial grounds.

Stupp R, Brada M, van den Bent MJ, et al. High-grade glioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25 Suppl 3:iii93-101. High-grade glioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.

Soft Tissue and Bone Tumours

Identification of pathognomonic gene changes is of particular use when diagnosing tumours on limited biopsy material and can impart greater diagnostic certainty without the need for more invasive biopsy and attendant increased costs and risks to the patient. The use of such assays can also decrease the risk of misdiagnosis.

These molecular aberrations are particularly characteristic of "rare" and less common cancers, such as sarcoma, which have disproportionately higher mortality rates compared to common cancers. Rare and less common cancers are the leading cause of death in children under 15 years of age, constitute the fourth most common cause of death in the 20-39 age group and as a group are the leading cause of death in 40-59 year olds accounting for 52% of all cancer deaths, more than double the impact of coronary heart disease alone. In the 60-69 age group, rare and less common cancers as a group are the leading cause of cancer death. As the Australian population continues to age, these numbers are set to increase.

Research using molecular and genomic techniques has and continues to identify somatic changes in genes that are associated with specific types of tumours resulting in more accurate classification and diagnosis, with for example over 53 different translocations now described for specific soft tissue and bone tumours. With increasing numbers of tumour diagnoses made on small tissue and fine needle aspirate biopsies, the detection of a pathognomonic genetic aberration can provide critical information to make the correct diagnosis, without the need for repeat biopsy, more invasive surgical biopsy (and resultant increased risk of complication or morbidity) and ultimately ensure optimal management and the best outcome for patients. For example well-differentiated liposarcoma/atypical lipomatous tumours are frequently located in the retroperitoneum a difficult and risky site to biopsy. It can be problematic to differentiate these sarcomas from benign lipomatous tumours, especially on limited biopsy material.

Immunohistochemistry results are non-specific in several sarcomas types (e.g. Ewing sarcoma and synovial sarcoma) and a confident diagnosis relies on demonstrating the characteristic molecular abnormality. Some rare sarcomas have a broad differential diagnosis (e.g. mesenchymal chondrosarcoma) and while the underlying molecular abnormality is known a FISH probe is not always commercially available. In these cases, a multipanel or NGS approach with the ability to look for multiple possible fusions in a single test would result in a more timely diagnosis and utilise less tissue (decreasing the likelihood of a second biopsy).

MDM2 amplification detected by FISH has been shown to be 100% sensitive and specific on core needle biopsy in comparison to immunohistochemistry which was 65% sensitive and 89% specific, with a false positive rate of 11%.

A recent study on sarcoma diagnosis (GENSARC study Lancet Oncology 2016) 34 showed that the prospective use of molecular analysis for specific gene copy number changes or gene rearrangements resulted in a change in diagnosis in 23% of cases compared to a morphology diagnosis by sarcoma pathology experts. This resulted in a significant change in proposed management in 12% of cases. These authors concluded that molecular testing should be mandatory for diagnostic accuracy of sarcoma and appropriate clinical management.

Somatic tumour gene testing for soft tissue and bone tumours should include:

Atypical lipomatous tumour/dedifferentiated liposarcoma	MDM2
Myxoid/round cell liposarcoma	FUS, DDIT3, EWSR1
Infantile fibrosarcoma	ETV6, NTRK2
Dermatofibrosarcoma protuberans	COL1A1, PDGFB
Ewing sarcoma	EWSR1, FLI1, ERG
Synovial sarcoma	SS18
Alveolar rhadomyosarcoma	FOXO1, PAX3, PAX7

24. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

Patients diagnosed with either CNS glioma or soft and bone cancers at the time of histopathological or morphological review of tumour material would be eligible for this service.

25. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):

The clinical management pathway would be identical to current cancer investigation and treatment:

Patient presentation to general or medical practitioner with evidence of a CNS tumour.
Patient is referred for investigation including radiology and pathology.
Pathology investigation (biopsy, tumour resection etc.) and tentative diagnosis without specific molecular testing.
Treatment based on clinical judgement (for Gilomas and Glioblastomas).

See Appendix A Flowcharts

<u>PART 6b – INFORMATION ABOUT THE INTERVENTION</u>

26. Describe the key components and clinical steps involved in delivering the proposed medical service:

Gilomas

A test of tumour tissue from a patient diagnosed with a CNS glioma to determine the presence of chromosome 1p/19 co-deletion is present. Testing methods include in situ hybridization (ISH), comparative genomic hybridization (CGH) and next generation sequencing (NGS) methodologies among others.

Glioblastomas

A test of tumour tissue from a patient diagnosed with a CNS glioblastoma to determine IDH1/2 mutation and MGMT promoter methylation status. Testing methods include in situ hybridization (ISH), comparative genomic hybridization (CGH) and next generation sequencing (NGS) methodologies among others.

Soft Tissue and Bone Tumours

A test of tumour tissue from a patient diagnosed with soft tissue or bone cancer to detect mutations, changes in gene copy number or structural gene rearrangements in tumour tissue for MDM2, FUS, DDIT3, EWSR1, FLI1, ERG, SS18, FOXO1, PAX3, PAX7, ETV6, NTRK2, COL1A1 and PDGFB. Testing methods include In situ hybridization (ISH), polymerase chain reaction (PCR) and next generation sequencing (NGS) methodologies among others.

27. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

Not applicable

28. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

Not applicable

29. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

Gilomas

Glioblastomas

Testing should be pathologist determinable (able to be requested after a diagnosis of either CNS glioma or CNS Glioblastomas is made) in order to provide definitive diagnosis/classification. Retrospective testing could also be requested by a treating clinician and performed on archival material.

There is no role for repeat testing to monitor disease, however tumour recurrences may be tested to ensure there has been no change in molecular status.

Soft Tissue and Bone Tumours

Testing would be provided as requested by the referring medical practitioner for patients with soft tissue or bone requiring further classification after initial tissue pathology investigation. Further testing may be provided after therapy for monitoring of disease.

30. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

Not applicable

31. If applicable, advise which health professionals will primarily deliver the proposed service:

Approved Pathologists in Accredited Pathology testing laboratories

32. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

Not applicable

33. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

Approved Pathologists in Accredited Pathology testing laboratories

34. If applicable, advise what type of training or qualifications would be required to perform the proposed service as well as any accreditation requirements to support service delivery:

Approved Pathology Practitioners as defined in the MBS for Pathology Items

35. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select all relevant settings):

- ☐ Inpatient private hospital
- ☐ Inpatient public hospital
- ☐ Outpatient clinic
- ☐ Emergency Department
- ☐ Consulting rooms
- ☐ Day surgery centre
- ☐ Residential aged care facility
- ☐ Patient's home
- ☒ Laboratory
- ☐ Other – please specify below

Specify further details here

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

Not applicable

36. Is the proposed medical service intended to be entirely rendered in Australia?

- ☒ Yes
- ☐ No – please specify below

Specify further details here

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

37. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

Gilomas
Glioblastomas
There are no current MBS services for this service. The comparator is therefore tissue pathology investigation of CNS tumours with incomplete classification (i.e. incomplete diagnosis and prognostic assessment of disease).
Soft Tissue and Bone Tumours
There are no current MBS services for this service. The comparator is therefore tissue pathology without complete classification (i.e. incomplete diagnosis and prognostic assessment of disease). Detection of somatic gene rearrangements, copy number aberrations and/or mutations would be required in addition to tissue pathology for soft tissue or bone cancer but without further health care resources for obtaining the tumour tissue (i.e. on the same specimen).

38. Does the medical service that has been nominated as the comparator have an existing MBS item number(s)?

☒ Yes (please provide all relevant MBS item numbers below)
☐ No
Gilomas
Glioblastomas
72830 ; 72846-72850
These codes encompass level 5 tissue biopsy and immunohistochemistry.

Soft Tissue and Bone Tumours
65084; 65087; 72813; 72816; 72817; 72818; 72823; 72824; 72825; 72826; 72827; 72828; 72830; 72836; 72838;

39. Define and summarise the current clinical management pathways that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards including health care resources):

Gilomas
The clinical management pathway after the comparator is the selection of cancer therapy based on histological diagnosis using current methods (routine histology and IHC). There is no IHC assay that can act as a reliable surrogate for chromosome 1p/19q co-deletion by molecular methods.
Molecular subtypes are not identified completely. Selection of therapy is made on incomplete information. Inappropriate treatment may result in patient harm.
Glioblastomas
The clinical management pathway after the comparator is the selection of cancer therapy based on histological diagnosis using current methods (routine histology and IHC). IHC may be useful in identifying IDH1 in [higher grade tumours?]. However, IDH2 mutations and IDH1 [in other cases?] are not identified except by sequencing. MGMT status with IHC lacks standardisation, reproducibility and correlation with clinical outcome (Stupp, 2014).
With the comparator, molecular subtypes are not identified completely. Selection of therapy is made on incomplete information and inappropriate treatment may result in patient harm.
Soft Tissue and Bone Tumours
The clinical management pathway after the comparator is the selection of soft tissue or bone cancer therapy based on histological diagnosis using current methods.
Molecular subtypes are not identified completely. Selection of therapy is made on incomplete information. Inappropriate treatment may be selection resulting in ineffective therapy or patient harm.

See Appendix A Flowcharts

40. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

☒ Yes
☐ No

(b) If yes, please outline the extent of which the current service/comparator is expected to be substituted:

Gilomas
Detection of chromosome 1p/19q co-deletion would be required in addition to current service/comparator.
Glioblastomas
Identification of IDH1/2 mutation and MGMT promoter methylation status in glioblastomas would be required in addition to current service/comparator.
Soft Tissue and Bone Tumours
Detection of somatic gene rearrangements, copy number aberrations and/or mutations for soft tissue or bone cancers would be required in addition to current service/comparator.

41. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service including variation in health care resources (Refer to Question 39 as baseline):

Gilomas
Pathological investigation of CNS glioma tissue will be extended to include identification of chromosome 1p/19q co-deletion to provide further diagnostic and prognostic information. Further therapeutic interventions for the patient via surgery, chemotherapy and/or radiotherapy will be informed by this information.
Glioblastomas
Pathological investigation of CNS glioblastomas for IDH1/2 mutation and MGMT promoter methylation status in to provide further diagnostic and prognostic information.
In lower grade tumours or suspected transformed glioma, IDH1/2 sequencing would be undertaken where IHC is negative for IDH1 with the anti-IDH antibody (R132H mutation).
Gene sequencing is required to determine MGMT promoter methylation status.
Further therapeutic interventions for the patient via surgery, chemotherapy and/or radiotherapy will be informed by this information.
Soft Tissue and Bone Tumours
Pathological investigation of soft tissue or bone tumour tissue will be extended to provide further diagnostic and prognostic information. Therapeutic interventions for the patient by surgery, chemotherapy and/or radiotherapy may be affected by this information depending on the clinical situation.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

42. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

Gilomas

Currently, there is no MBS, other public funding or private health insurance for this medical service. Under international guidelines, histological diagnosis of gliomas requires a layered diagnosis including molecular testing. The detection of co-deletion of 1p/19p chromosome regions is critical to the identification of oligodendroglial tumours. Correct tumour classification is necessary for determining prognosis and predicting response to chemo/radiotherapy

Glioblastomas

Currently, there is no MBS, other public funding or private health insurance for this medical service. Under international guidelines, histological diagnosis of glioblastomas requires a layered diagnosis including molecular testing. The identification of IDH1/2 mutation and MGMT promoter methylation status are critical to the identification of glioblastomas. Correct tumour classification is necessary for determining prognosis and predicting response to chemo/radiotherapy. (Stupp, 2014)

Soft Tissue and Bone Tumours

Currently, there is no MBS, other public funding or private health insurance for this medical service. Tissue pathology (H&E and IHC) and standard haematology testing often require additional molecular investigations for a range of rare and difficult to diagnose cancers. Detection of somatic gene rearrangements, copy number aberrations and/or mutations for MDM2, FUS, DDIT3, EWSR1, FLI1, ERG, SS18, FOXO1, PAX3, PAX7, ETV6, NTRK2, COL1A1 and PDGFB are recommended locally and internationally as best practice for the diagnosis of soft tissue and bone cancer, the appropriate selection of treatment, indicating disease prognosis and monitoring therapeutic outcomes.

The identification of pathognomonic gene changes is of particular use when diagnosing tumours on limited biopsy material and can impart greater diagnostic certainty without the need for more invasive biopsy and other investigation and/or staging tests which may be invasive (e.g. endoscopy) and attendant increased costs and risks to the patient. The use of such assays can also decrease the risk of misdiagnosis and subsequent negative outcomes for the patient undergoing inappropriate treatment.

43. Please advise if the overall clinical claim is for:

☒ Superiority
☐ Non-inferiority

44. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes:

The proposed test involves equivalent safety issues to current tissue pathology investigations.

The absence of suitable testing can lead to misdiagnosis with patients potentially receiving unnecessary treatment, experiencing delays in treatment or no treatment when treatment is needed.

Clinical Effectiveness Outcomes:

Effective and affordable health care depends on the availability of accurate, reliable and clinically valid tests. Providing the right treatment to the right patient at the right time depends on meaningful tests proven to impact clinical decisions, integrated with the most current data relevant to the practice of medicine, and recognized as medically necessary to tailor treatment for the unique biology of a disease. Specific Clinical Effectiveness Outcomes as follows:

Gilomas

In brain cancer, the Haarlem guidelines highlight that integration of specific molecular aberrations results in a more precise diagnosis and are the basis of the WHO 2016 update on classification of CNS. Patient management, including chemotherapy and radiotherapy choices, are based on the WHO classification, and hence molecular information will be essential in providing accurate diagnoses. This is particularly important in young patients, where timing and dosage of treatment (based on tumour type) impacts on the significant cognitive morbidity associated with treating the brain.

Detection of chromosome 1p/19q co-deletion is not the only molecular test which is appropriate and currently utilised for investigation of brain tumours, but is a baseline investigation required for classification of gliomas.

Glioblastomas

In brain cancer, the Haarlem guidelines highlight that integration of specific molecular aberrations results in a more precise diagnosis and are the basis of the WHO 2016 update on classification of CNS. Patient management, including chemotherapy and radiotherapy choices, are based on the WHO classification, and hence molecular information will be essential in providing accurate diagnoses. This is particularly important in young patients, where timing and dosage of treatment (based on tumour type) impacts on the significant cognitive morbidity associated with treating the brain.

The identification of IDH1/2 mutation and MGMT promoter methylation status are not the only molecular tests which are appropriate and currently utilised for investigation of brain tumours. However, they are critical to the identification of glioblastomas. Correct tumour classification is necessary for determining prognosis and predicting response to chemo/radiotherapy.

Soft Tissue and Bone Tumours

These molecular aberrations are particularly characteristic of rare and less common cancers, which have disproportionately higher mortality rates compared to common cancers. Many of these rare cancers occur in younger patients who account for 95% of cancer deaths reported in children under 15 years. Accurate diagnosis of rare cancers is difficult for nonspecialised pathologists and can result in inappropriate medical management. Second opinions are recommended to ensure diagnostic accuracy but can introduce delays in the reporting process. Characterisation of pathognomonic genetic abnormalities would expedite the diagnostic process for many rare cancers.

A recent study on sarcoma diagnosis (GENSARC study Lancet Oncology 2016) showed that the prospective use of molecular analysis for specific gene copy number changes or gene rearrangements resulted in a change in diagnosis in 23% of cases compared to a morphology diagnosis by sarcoma pathology experts. This resulted in a significant change in proposed management in 12% of cases. These authors concluded that molecular testing should be mandatory for diagnostic accuracy of sarcoma and appropriate clinical management.

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

45. Estimate the prevalence and/or incidence of the proposed population:

Gilomas
The prevalence of brain cancer in Australia was. 7.7 per 100,000 with 1724 new cases in 2011. Rates of brain cancer increased from 5.6 per 100,000 in 1982 to 7.7 per 100,000 in 2011. (AIHW 2015 Australian Cancer Incidence and Mortality Book for Brain cancer).
It is estimated that 1855 new cases of brain cancer could be diagnosed in 2017. Approx. 40% of all primary brain tumours are gliomas (Cure Brain Cancer Foundation). Therefore, it is estimated that the population would be 742 new cases per annum.
Glioblastomas
The prevalence of brain cancer in Australia was. 7.7 per 100,000 with 1724 new cases in 2011. Rates of brain cancer increased from 5.6 per 100,000 in 1982 to 7.7 per 100,000 in 2011. (AIHW 2015 Australian Cancer Incidence and Mortality Book for Brain cancer).
It is estimated that 1855 new cases of brain cancer could be diagnosed in 2017. Approx. 12 to 15% of all primary brain tumours are gliobastomas (Brain Tumour Foundation of Canada).
Therefore, it is estimated that the maximum population would be 275 new cases in 2017.
Soft Tissue and Bone Tumours
In Australia, there were 678 new 'other soft tissue cancers' cases and 203 new bone cancer cases in 2013 (an age-standardised incidence rate per 100,000 of 2.7 and 0.8 respectively).
(Australian Cancer Incidence and Mortality (ACIM) books 2017)

46. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

Once

Note: not all cancer patients are treated with surgery, some may have multiple surgeries, but most would not have surgery once per year, therefore once per year is a reasonable average estimate.

47. How many years would the proposed medical service(s) be required for the patient?

Gilomas
Glioblastomas
One each
A tumour recurrence may require re-testing to determine if the tumour status has changed.
Unfortunately, mortality rates in brain cancer are high (1241 deaths in 2012). Therefore, an estimate of one year would be reasonable.

Soft Tissue and Bone Tumours
Five
Note: not all cancer patients are treated with surgery, some may have multiple surgeries, but most would not have surgery every year for five years therefore five years is a reasonable maximum estimate.

48. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

Gilomas - 742
Glioblastomas - 275
Soft Tissue and Bone Tumours - 880

49. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

Gilomas
Glioblastomas

Uptake in the next three years will result in all of the at-risk population receiving testing as part of the initial diagnosis/classification process.
Rates of brain cancer have risen from 5.6 per 100,000 in 1982 to 7.7 per 100,000 in 2011 (AIHW). Therefore, it is reasonable to estimate a 1% increase per year indicating that the projected number of patients with gliomas would remain at less than 800 in three years' time whilst patients with glioblastomas would remain at less than 300 in three years' time.
Leakage to populations not targeted by the service will be constrained by the MBS item number descriptors to ensure testing is applied only where clinically indicated. Leakage to populations not targeted by the service will be constrained by the MBS item number descriptors to ensure testing is applied only where clinically indicated.

Soft Tissue and Bone Tumours

Uptake in the next three years will result in all of the at risk population using the test in diagnosis.
AIHW statistics indicate that rates of soft tissue and bone cancers are relatively stable. Therefore, the projected number of patients will remain at less than 1000 per year for the next three years.
Leakage to populations not targeted by the service would be restricted by the item descriptor.

PART 8 – COST INFORMATION

50. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

Equipment and resources	Gilomas	Glioblastomas	Soft Tissue and Bone Tumours
FISH kit, probes, reagents, ancillary reagents	$350.00	$350.00	$450.00
Labour medical (consultant pathologist)	$50.00	$50.00	$75.00
Labour scientific	$40.00	$40.00	$60.00
Labour on costs	$14.00	$14.00	$15.00
Total costs per Test	**$454.00**	**$454.00**	**$600.00**

51. Specify how long the proposed medical service typically takes to perform:

7 -10 working days

52. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Category 6 –Genetics P7
Proposed item descriptor Detection of chromosome co-deletion 1p/19q in the assessment of CNS tumours (gliomas and glioneuronal tumours) Fee: $454 **OR** In the assessment of CNS gliomas, identification of: • IDH1/2 mutation status if IDH1 (R132H) IHC is negative **AND/OR** • MGMT promoter methylation status in the assessment of glioblastomas. Fee: $454 (for each) **OR** In the assessment of Soft Tissue and Bone Tumours, identification of MDM2, FUS, DDIT3, EWSR1, ETV6, NTRK2, COL1A1 and PDGF rearrangement or copy number changes Fee: $1,200 (as a panel) **OR** $454 (for each)

PART 9 – FEEDBACK

The Department is interested in your feedback.

53. How long did it take to complete the Application Form?

Insert approximate duration here

54. (a) Was the Application Form clear and easy to complete?

☐ Yes
☐ No

(b) If no, provide areas of concern:

Describe areas of concern here

55. (a) Are the associated Guidelines to the Application Form useful?

☐ Yes
☐ No

(b) If no, what areas did you find not to be useful?

Insert feedback here

56. (a) Is there any information that the Department should consider in the future relating to the questions within the Application Form that is not contained in the Application Form?

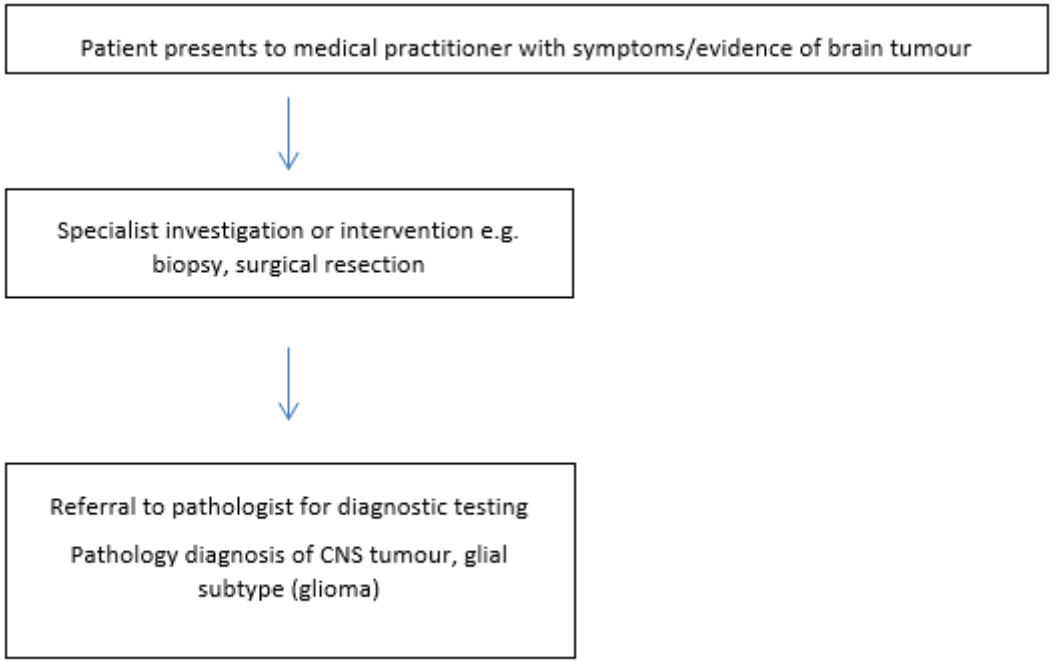
☐ Yes
☐ No

(b) If yes, please advise:

Insert feedback here

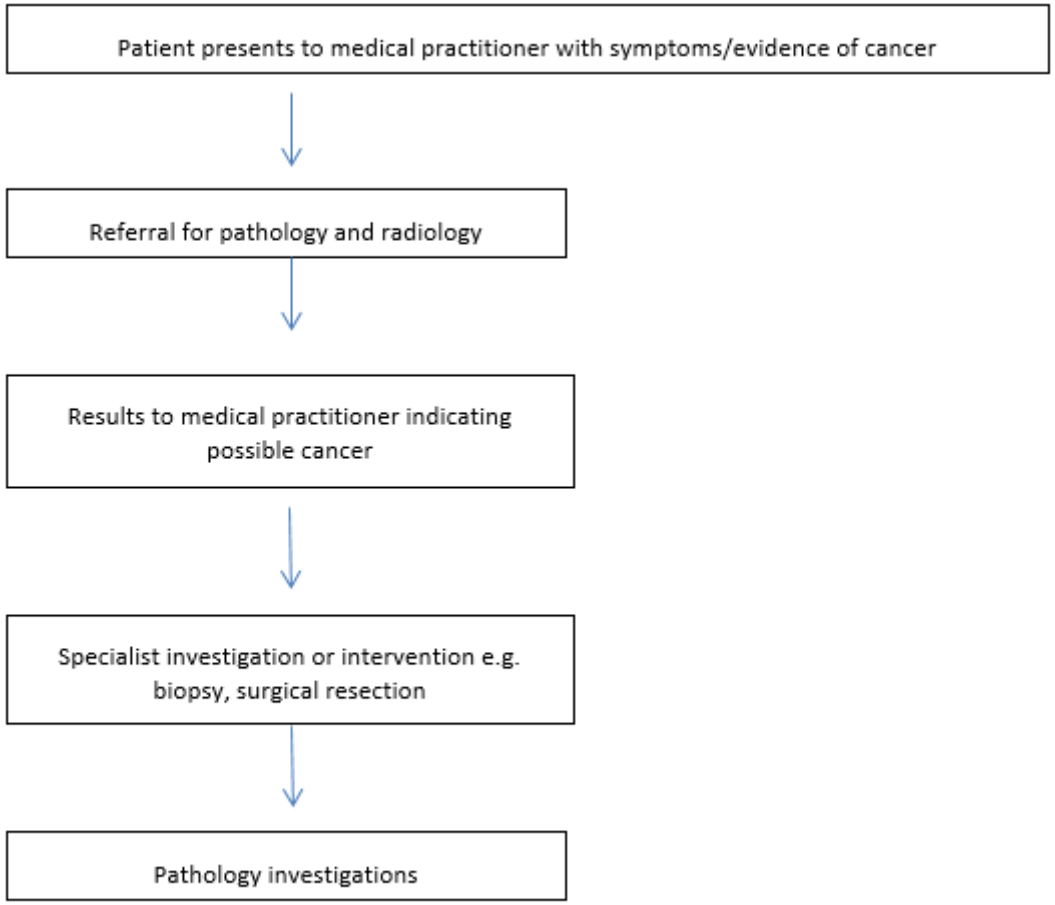
Appendix A Flowcharts

Q26 Clinical pathway before intervention

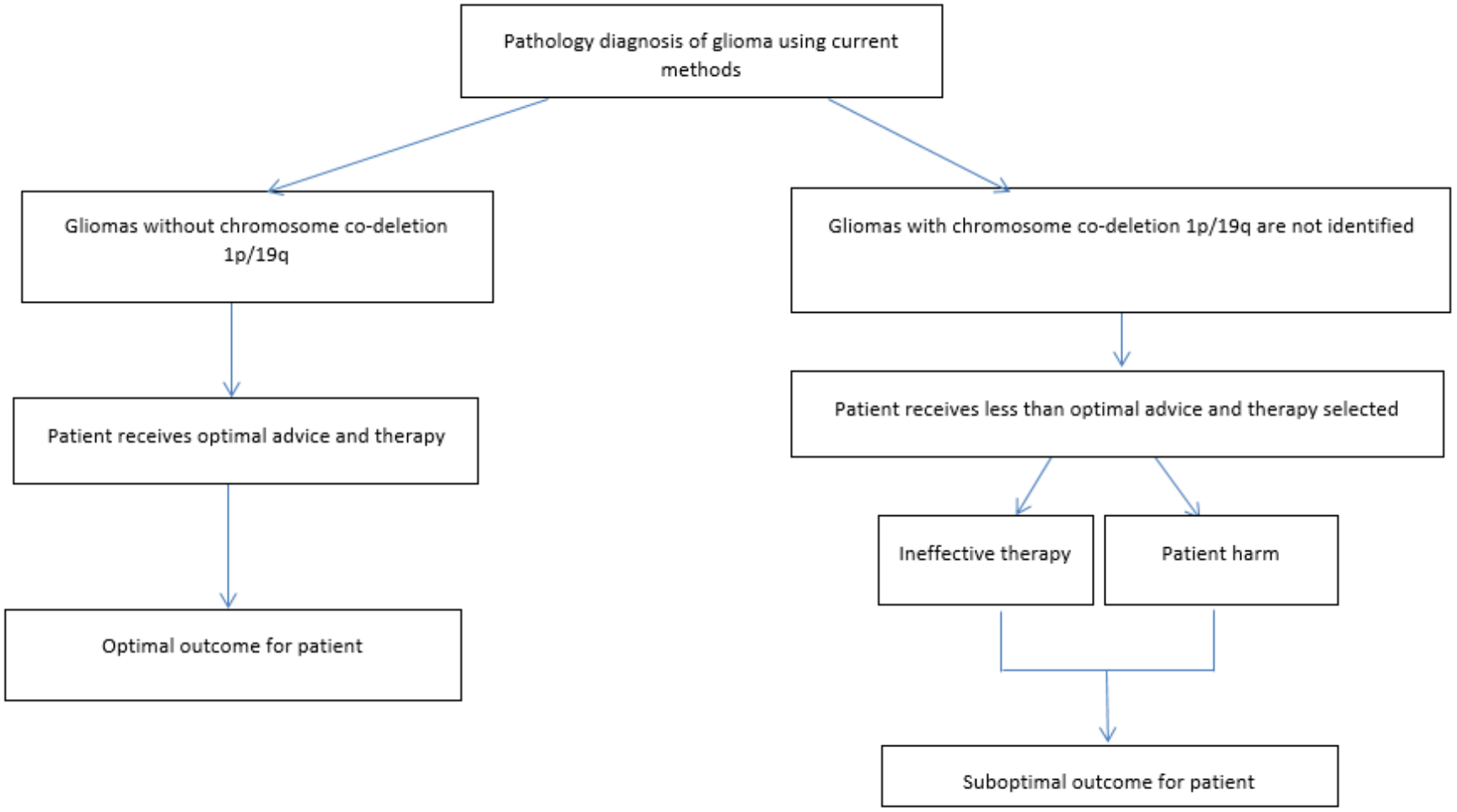


Appendix A Flowcharts

Q26 Clinical pathway before intervention



Q40 Clinical pathway after comparator (current)



Q40 Clinical pathway after comparator (current)