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 renal cell carcinoma, hydatidiform moles, granulosa cell ovarian tumour, salivary gland tumours, and secretory carcinoma of the breast

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)

Renal cell carcinoma (RCC); hydatidiform moles; granulosa cell ovarian tumour; salivary gland tumours; and secretory carcinoma of the breast.

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)

Characterisation of VHL, TP53, RB1 status, TFE3 / Xp11.1 translocation and detection of chromosome 3 (chr3) monosomy for the diagnosis of RCC; characterisation of ploidy status for the diagnosis and classification of patients with hydatidiform moles; classification of mutation in FOXL2 (402C>G) for the diagnosis of granulosa cell ovarian tumour; detection of somatic gene rearrangements for the diagnosis of salivary gland tumours including mammary analogue secretory carcinoma, hyalinising clear cell carcinoma, mucoepidermoid and NUT midline carcinomas; and characterisation of somatic tumour gene rearrangements for the diagnosis of secretory carcinoma of the breast.

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:

Not applicable

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

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):

Insert description of 'other' amendment here

(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:

Not applicable

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?

Not applicable

☐ Yes
☐ No

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

Not applicable

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

Not applicable

☐ 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?

Not applicable

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

Not applicable

☐ Yes
☐ No

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

Not applicable

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

Not applicable

☐ 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?

Not applicable

☐ Yes
☐ No

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

Not applicable

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

Single use consumables:

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).
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

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?

Not applicable

☐ 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?

Not applicable

☐ Yes (please provide details below)
☐ No

Estimated date of submission to TGA: Insert date of submission here
Proposed indication(s), if applicable: If applicable, insert description of proposed indication(s)
Proposed purpose(s), if applicable: If applicable, insert description of proposed purpose(s) here

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.

Renal Cell Carnicoma

	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	Ljungberg B, Bensalah K, Canfield S, et al: EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol 67:913-24, 2015	European clinical practice guidelines on the classification of renal cell carcinoma providing levels of evidence for the recommendations (adhering to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines).	EAU guidelines on renal cell carcinoma: 2014 update	27 Jan 2015
2.	Literature review	Koul H, Huh J-S, Rove KO, et al. Molecular aspects of renal cell carcinoma: a review. American Journal of Cancer Research. 2011;1(2):240-54.	Literature review of current epidemiology, pathophysiology, evaluation, treatment, and future research directions of RCC.	Molecular aspects of renal cell carcinoma: a review	2011
3.	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	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 ***
			provided a definition for rare cancers, and the burden of disease that rare and less common cancers pose across all ages in Australia		
4.	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 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	2014

Hydatidiform Moles

	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.	Study of diagnostic accuracy	Furtado LV, Paxton CN, Jama MA, et al: Diagnostic utility of microsatellite genotyping for molar pregnancy testing. Arch Pathol Lab Med 137:55-63, 2013	A study of molecular genotyping for diagnosing and classifying hydatidiform mole to distinguish differences in risk for persistent gestational trophoblastic disease. Data on 102 cases were presented; 48 were classified as	Diagnostic Utility of Microsatellite Genotyping for Molar Pregnancy Testing	2 Jan 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***
			hydatidiform mole (31 complete hydatidiform mole; 17 partial hydatidiform mole) demonstrating the utility of microsatellite genotyping for accurate classification of hydatidiform mole.		
2.	Study of diagnostic accuracy	LeGallo RD, Stelow EB, Ramirez NC, Atkins KA. Diagnosis of hydatidiform moles using p57 immunohistochemistry and HER2 fluorescent in situ hybridization. Am J Clin Pathol. 2008;129(5):749-55.	A study of HER2 FISH for the diagnosis and classification of 54 cases of hydatidiform moles (HM) demonstrating the utility of HER2 FISH and IHC for p57 in the evaluation of HM, especially when triploid content is seen.	Diagnosis of Hydatidiform Moles Using p57 Immunohistochemistry and HER2 Fluorescent In Situ Hybridization	2008

Granulosa Cell Ovarian Tumour

	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.	Study of diagnostic accuracy	Rosario R, Cohen PA, Shelling AN: The role of FOXL2 in the pathogenesis of adult ovarian granulosa cell tumours. Gynecol Oncol 2016;33:382-7, 2014	A review of 52 research papers, nine of which investigated the pathogenic effect of FOXL2 allele. The evidence of these studies demonstrated the role of FOXL2 402C>G mutation in the development of adult ovarian granulosa cell tumours.	The role of FOXL2 in the pathogenesis of adult ovarian granulosa cell tumours	May 2016
2.	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	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***
			definition for rare cancers, and the burden of disease that rare and less common cancers pose across all ages in Australia		
3.	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 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	2014

Salivary Gland 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.	Educational publication	Stenner M, Klussmann JP. Current update on established and novel biomarkers in salivary gland carcinoma pathology and the molecular pathways involved. Eur Arch Otorhinolaryngol. 2009;266(3):333-41.	Review of new information on the molecular pathology of salivary gland tumours	Current update on established and novel biomarkers in salivary gland carcinoma pathology and the molecular pathways involved	2009
3.	Educational	Simons SA, Bridge	US review of diagnosis	Sinonasal small	21 Nov

	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***
	publication	JA, Leon ME: Sinonasal small round blue cell tumors: An approach to diagnosis. Semin Diagn Pathol 33:91-103, 2016	the difficulties of sinonasal tumours diagnosis and the requirement for immunohistochemical and molecular studies in non-specific cases.	round blue cell tumors: An approach to diagnosis	2015
3.	Study of diagnostic accuracy	Clauditz TS, Gontarewicz A, Wang C-J, et al. 11q21 Rearrangement is a Frequent and Highly Specific Genetic Alteration in Mucoepidermoid Carcinoma. Diagnostic Molecular Pathology. 2012;21(3):134-7.	Study of 1200 salivary gland adenomas and carcinomas for translocation t(11;19)(q21;p13) involving the MECT1 and MAML2 genes demonstrating the utility of testing to diagnose MEC.	11q21 Rearrangement is a Frequent and Highly Specific Genetic Alteration in Mucoepidermoid Carcinoma	2012
4.	Study of diagnostic accuracy	Martins C, Cavaco B, Tonon G, et al. A Study of MECT1-MAML2 in Mucoepidermoid Carcinoma and Warthin's Tumor of Salivary Glands. The Journal of molecular diagnostics : JMD. 2004;6(3):205-10.	Study of 10 primary MEC and 7 primary Warthin's tumours for the MECT-MAML2 fusion gene demonstrating the utility of testing to diagnose MEC.	Mucoepidermoid Carcinoma and Warthin's Tumor of Salivary Glands.	
5.	Educational publication	Gupta R, Balasubramanian D, Clark JR: Salivary gland lesions: recent advances and evolving concepts. Oral Surg Oral Med Oral Pathol Oral Radiol 119:661-74, 2015	Australian review of changes to the diagnosis of salivary gland lesions and implications for patient management highlighting the importance of molecular testing.	Salivary gland lesions: recent advances and evolving concepts	5 May 2015
6.	Observational study	Sethi R, Kozin E, Remenschneider A, et al. Mammary analogue secretory carcinoma: update on a new diagnosis	Review of diagnosis of mammary secretory carcinoma	Mammary analogue secretory carcinoma: Update on a New Diagnosis of	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 publication***
		of salivary gland malignancy. Laryngoscope. 2014;124(1):188-95.		Salivary Gland Malignancy	
7.	Observational study	Bishop JA. Unmasking MASC: Bringing to Light the Unique Morphologic, Immunohistochemical and Genetic Features of the Newly Recognized Mammary Analogue Secretory Carcinoma of Salivary Glands. Head and Neck Pathology. 2013;7(1):35-9.	Review of diagnosis of mammary secretory carcinoma	Unmasking MASC: Bringing to Light the Unique Morphologic, Immunohistochemical and Genetic Features of the Newly Recognized Mammary Analogue Secretory Carcinoma of Salivary Glands	2013
8.	Observational study	French CA. NUT Midline Carcinoma. Cancer genetics and cytogenetics. 2010;203(1):16-20.	Study of the molecular cytogenetics of NUT midline carcinoma (NMC) demonstrating the presence of abnormality t(15;19)(q14;p13.1), BRD4-NUT fusion, and NUT-variants where the partner genes is BRD3 or other uncharacterised genes. The study indicated that the histological features of NMC are not diagnostic and the commonly undiagnosed or misdiagnosed and that the true frequency of NMC is yet to be determined.	NUT Midline Carcinoma.	2010
9.	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	: 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***
			definition for rare cancers, and the burden of disease that rare and less common cancers pose across all ages in Australia		
10.		Chau NG, Hurwitz S, Mitchell CM, et al. Intensive treatment and survival outcomes in NUT midline carcinoma of the head and neck. Cancer. 2016;122(23):3632-40.	A retrospective review of all known cases of HNNMC in the International NUT Midline Carcinoma Registry as of December 31, 2014, was performed. 48 consecutive patients were treated from 1993 to 2014, and clinicopathologic variables and outcomes for 40 patients were available for analyses for overall survival (OS) and progression-free survival (PFS) were analyzed. The study found that HNNMC has a poor prognosis. Chemotherapy or radiation alone is often inadequate therapy but aggressive initial surgical resection with or without postoperative chemoradiation or radiation is associated with significantly enhanced survival.	Intensive treatment and survival outcomes in NUT midline carcinoma of the head and neck	2016

Secretory Carcinoma of the Breast

	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.	Observational study	Vasudev P, Onuma K. Secretory Breast Carcinoma: Unique,	A review of the features of this rare breast cancer sub-type.	Secretory Breast Carcinoma: Unique, Triple-	2011

	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***
		Triple-Negative Carcinoma With a Favorable Prognosis and Characteristic Molecular Expression. Archives of Pathology & Laboratory Medicine. 2011;135(12):1606-10.		Negative Carcinoma With a Favorable Prognosis and Characteristic Molecular Expression	
2.	Study of diagnostic accuracy	Lae M, Freneaux P, Sastre-Garau X, et al. Secretory breast carcinomas with ETV6-NTRK3 fusion gene belong to the basal-like carcinoma spectrum. Mod Pathol. 2009;22(2):291-8.	A study of six cases to determine the phenotypic class (ie luminal A/B, ERBB2, basal-like) of secretory breast carcinoma. The ETV6 rearrangement was confirmed in all cases by FISH. These results demonstrated that secretory breast carcinomas have immunohistochemical and genetic features that distinguish them from other basal-like tumours of the breast.	Secretory breast carcinomas with ETV6-NTRK3 fusion gene belong to the basal-like carcinoma spectrum.	2009
3.	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
4.	Study of diagnostic accuracy	Sturm D, Witt H, Hovestadt V, et al: Hotspot mutations in H3F3A and IDH1 define distinct epigenetic and	A study demonstrating subgroups of glioblastomas (GBM) that can be identified by specific molecular markers (H3F3A and	Hotspot Mutations in H3F3A and IDH1 Define Distinct Epigenetic and Biological Subgroups of	16 Oct 2012

	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***
		biological subgroups of glioblastoma. Cancer Cell 22:425-37, 2012	IDH1 mutations).	Glioblastoma	
5.	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 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	2014

18. **Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

N/A

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***

	Type of study design*	**Title of research (including any trial identifier if relevant)**	**Short description of research (max 50 words)****	**Website link to research (if available)**	**Date*****
1.	For yet to be published research that may have results relevant to your application, insert the type of study design in this column and columns below	For yet to be published research that may have results relevant to your application, insert the title of research (including any trial identifier if relevant) in this column and columns below	For yet to be published research that may have results relevant to your application, insert a short description of research (max 50 words) in this column and columns below	For yet to be published research that may have results relevant to your application, insert a website link to this research (if available) in this column and columns below	For yet to be published research that may have results relevant to your application, insert date in this column and columns below
2.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
3.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
4.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
5.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
6.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
7.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
8.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. 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
Clinical Oncology Society of Australia (COSA) Rare Cancer Group
Clinical Oncology Society of Australia (COSA)

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

The Royal College of Pathologists of Australasia is the provider of the comparator service. Other organisations that might request the medical service are:
The Royal Australasian College of Physicians
The Royal Australasian College of Surgeons
COSA (Clinical Oncology Society of Australia (COSA)
Pathology Australia
Public Pathology Australia
Human Genetics Society of Australia

21. 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
Leukaemia Foundation
Without a Ribbon
Unicorn Foundation

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

Not applicable

23. 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

24. 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 VHL, TP53, RB1 status, TFE3/Xp11.1 translocation , chromosome 3 (chr3) monosomy, secretory carcinoma and characterisation of ploidy status by STR genotyping or FISH of these changes has become best practice to determine diagnosis, prognosis and for the appropriate selection of treatment of RCC.

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.

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 RCC, 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 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.

Salivary Gland Tumours

Malignant salivary gland tumours are rare diseases. This application is relevant to mammary analogue secretory carcinoma, hyalinising clear cell carcinoma, mucoepidermoid and NUT midline carcinomas that all require genetic characterisation of the tumour tissue for accurate diagnosis and selection of therapy.

Mammary analogue secretory carcinoma (MASC) is an unusual and rare malignant salivary gland tumour first described in 2010.

Mucoepidermoid carcinoma (MEC) is more common, found in 50% of malignant salivary gland tumours. Hyalinizing clear cell carcinoma (HCCC) is uncommon occurring in only about 1% of all intra-oral salivary gland tumours.

NUT midline carcinoma is a rare and aggressive subtype of squamous cell carcinoma, frequently arising from the head and neck, and mediastinum, that can only be diagnosed with genetic characterisation of the tumour tissue. As these carcinomas have a poor prognosis, aggressive intervention is required to enhance survival. Therefore, accurate and early diagnosis is vital in the care of these patients.

Molecular aberrations are particularly characteristic of “rare” and less common cancers 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.

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.

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.

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.

25. 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:

Renal Cell Carcinoma
Patients diagnosed with these diseases at the time of histopathological or morphological review of tumour material would be eligible for this service.

Hydatidiform Moles
Patients diagnosed with hydatidiform moles at the time of histopathological or morphological review of tumour material would be eligible for this service.

Granulosa Cell Ovarian Tumour
Patients diagnosed with granulosa cell ovarian tumour at the time of histopathological or morphological review of tumour material would be eligible for this service.

Salivary Gland Tumours
Patients diagnosed with midline carcinomas at the time of histopathological or morphological review of tumour material would be eligible for this service.

Secretory Carcinoma of the Breast and Mammary analogue secretory carcinoma (MASC) of salivary glands
Patients diagnosed with secretory carcinoma of the breast or MASC of salivary glands at the time of histopathological or morphological review of tumour material would be eligible for this service.

26. 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 or symptoms suggestive of RCC/ hydatidiform mole/ granulosa cell ovarian tumour/midline carcinoma/cancer.
- Patient is referred for investigation including radiology and pathology.
- Pathology investigation (biopsy, tumour resection etc.)

See Appendix A Flowcharts

PART 6b – INFORMATION ABOUT THE INTERVENTION

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

Renal Cell Carnicoma
Hydatidiform Moles
Salivary Gland Tumours
A test of tumour tissue from a patient diagnosed with RCC/cancer/ midline carcinomas to detect mutations, changes in gene copy number or structural gene rearrangements in tumour tissue or bone marrow or blood in the case of haematological malignancies. Testing methods include In situ hybridization (ISH), polymerase chain reaction (PCR) and next generation sequencing (NGS) methodologies among others. FISH would be the most commonly used method

Granulosa Cell Ovarian Tumour
A test of tumour tissue from a patient diagnosed with ovarian cancer to detect FOXL2 402C>G gene aberrations. Testing methods include In situ hybridization (ISH), polymerase chain reaction (PCR) and next generation sequencing (NGS) methodologies among others.

Secretory Carcinoma of the Breast or MASC of the salivary gland
A test of tumour tissue from a patient diagnosed with triple negative breast cancer to detect ETV6-NTRK3 translocation. Testing methods include In situ hybridization (ISH), polymerase chain reaction (PCR) and next generation sequencing (NGS) methodologies among others.

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

    Not applicable

29. **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

30. **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):**

    Testing would be provided as requested by the referring medical practitioner for patients with RCC/ neoplastic disease/midline carcinomas/triple negative breast cancer requiring further classification after initial tissue pathology.

31. **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

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

    Approved Pathologists in Accredited Pathology testing laboratories

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

    Not applicable

34. **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

35. **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

36. **(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

37. 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)

38. 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):

There are no current MBS services for this service. The comparator is therefore tissue pathology or haematological investigation without complete classification (i.e. incomplete diagnosis and prognostic assessment of disease and ineffective assessment of minimal residual disease). Detection of somatic gene rearrangements, copy number aberrations and/or mutations would be required in addition to tissue pathology and/or haematological investigations but without further health care resources for obtaining the tumour tissue (i.e. on the same specimen).

39. 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

65084; 65087; 72813; 72816; 72817; 72818; 72823; 72824; 72825; 72826; 72827; 72828; 72830; 72836; 72838

40. 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):

The clinical management pathway after the comparator is the selection of 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

41. (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:

Detection of somatic gene rearrangements, copy number aberrations and/or mutations would be required in addition to current service/comparator.

42. 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):

Renal Cell Carnicoma
Hydatidiform Moles
Granulosa Cell Ovarian Tumour
Secretory Carcinoma of the Breast
Pathological investigation of 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.

Salivary Gland Tumours
Pathological investigation of tumour tissue will be extended to provide further diagnostic and prognostic information on malignant salivary gland tumours; MASC, MEC, HCCC and NUT.

Therapeutic interventions will be affected by this information.

In NUT midline carcinomas, chemotherapy or radiation alone is often inadequate. More aggressive initial surgery, with or without postoperative chemoradiation or radiation is associated with significantly enhanced survival (Chau, 2016).

Chau NG, Hurwitz S, Mitchell CM, et al. Intensive treatment and survival outcomes in NUT midline carcinoma of the head and neck. Cancer. 2016;122(23):3632-40. Intensive treatment and survival outcomes in NUT midline carcinoma of the head and neck.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. 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):

Currently, there is no MBS, other public funding or private health insurance for this medical service. Tissue pathology (H&E and IHC) 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 are recommended locally and internationally as best practice for the diagnosis, 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

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

☒ Superiority
☐ Non-inferiority

45. 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 tests can lead to misdiagnosis with patients potentially receiving unnecessary treatment, experiencing delays in treatment or no treatment when treatment is needed.

Clinical Effectiveness Outcomes:

Renal Cell Carcinoma
Hydatidiform Moles
Granulosa Cell Ovarian Tumour
Secretory Carcinoma of the Breast
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.

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.

Salivary Gland Tumours
Treatment of NUT midline carcinomas with chemotherapy or radiation alone is often inadequate. More aggressive initial surgery, with or without postoperative chemoradiation or radiation is associated with significantly enhanced survival.

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.

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.

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

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

Renal Cell Carcinoma
The prevalence of RCC in Australia is 11.9 cases per 100,000 with 3,059 new cases diagnosed in 2013 (AIHW). Only a subset of these cases would need FISH for gene rearrangements in TFE3 or TFEB – estimated 10% of cases based on age (younger patients are more likely to have a translocation RCC) or microscopic appearances of the tumour.

Hydatidiform Moles
The prevalence of molar pregnancy is 1 per 1,000 pregnancies. In Australia, there were 305,377 births in 2015 (ABS). It is estimated that there are approx. 300 cases of hydatidiform mole per year.

Granulosa Cell Ovarian Tumour
This prevalence of ovarian cancer is 10.6 per 100,000 women in Australia with 1394 new cases in 2013 (AIHW). Granulosa cell tumours are a rare subset occurring in approx. 5% of ovarian cancers. Therefore, a likely population is 70.

Salivary Gland Tumours
The incidence of all head and neck cancer, excluding lip, was 13.1 per 100,000 in Australia, with 3,362 new cases diagnosed in 2013. Only 9 were found in children under the age of 15 and another 13 cases in the 20- to 29-year age group. Another 105 cases occurred in the 25- to 39-year age group.

Salivary gland tumours account for 6% of these cancers, approx. 202 per year. MEC is estimated to occur in 50% an estimated population of 101 per year. MASC, HCCC and NUT are rare and can be estimated to occur in less than 1% of cases.

Therefore, the total population could be estimated as 150.

Secretory Carcinoma of the Breast
Secretory carcinoma is a rare subtype of breast carcinoma occurring in less than 0.15% of all breast cancers.

It is estimated that 17,586 new cases of breast cancers will occur in 2017. Therefore, the incidence of secretory carcinoma of the breast is likely to be <30.

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

Renal Cell Carcinoma
Once for diagnosis

Hydatidiform Moles
Once for diagnosis

Granulosa Cell Ovarian Tumour
Once for diagnosis
On average once per year expected for minimal residual disease assessment in some haematological cases (pathologist-determinable).
Note: not all cancer patients are treated with surgery, some may have multiple surgeries, but most would not have surgery once per year and only a minority of patients with lymphoma may require minimal residual disease using genetic investigations, therefore once per year is a reasonable average estimate

Salivary Gland Tumours
One

Secretory Carcinoma of the Breast
Once for diagnosis

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

Renal Cell Carcinoma
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**.**

Hydatidiform Moles
Five

Granulosa Cell Ovarian Tumour
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.

Salivary Gland Tumours
One
A tumour recurrence may require re-testing to determine if the tumour status has changed. Unfortunately, prognosis is poor and an estimate of one year would be reasonable.

Secretory Carcinoma of the Breast
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.

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

Renal Cell Carcinoma
3,000

Hydatidiform Moles
300

Granulosa Cell Ovarian Tumour
70

Salivary Gland Tumours
Not all patients with a malignant head and neck will require the test. The projected number of patients is likely to be less than 150 in the first year.

Secretory Carcinoma of the Breast
Test required generally once only for diagnosis. In the cases of recurrence a second test may be required.

50. 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:

Renal Cell Carcinoma
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.
AIHW statistics indicate an average 3% increase per year in the number of new cases of RCC. Therefore, it is reasonable to estimate that the projected number of new patients with RCC would remain at less than 4,000 in three years' time. Testing for TFE3 or TFEB is estimated to be required in approximately 10% of

cases – the test would more often be ordered in younger patients or patients with particular microscopic changes in the tumour.

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. It is important to recognise that knowledge in this field is advancing rapidly with new diagnostic genetic aberrations increasingly reported. It is difficult to predict numbers of additional patients who may benefit from future advances in knowledge of molecular aberrations in these cancers. To date, these aberrations seem particularly characteristic of rare and less common cancers.

Hydatidiform Moles
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.

The projected number of patients is estimated to remain at less than 500 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. It is important to recognise that knowledge in this field is advancing rapidly with new diagnostic genetic aberrations increasingly reported. It is difficult to predict numbers of additional patients who may benefit from future advances in knowledge of molecular aberrations in these cancers. To date, these aberrations seem particularly characteristic of rare and less common cancers.

Granulosa Cell Ovarian Tumour
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.

AIHW estimates that there has been an average increase of 2% per year for these cancers, indicating that the projected number of patients will remain at less than 100 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.

Salivary Gland Tumours
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. The total is likely to remain at less than 150 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.

Secretory Carcinoma of the Breast
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.

Secretory carcinoma of the breast is rare and it is likely that the projected number of patients will remain at less than 50 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. It is important to recognise that knowledge in this field is advancing rapidly with new diagnostic genetic aberrations increasingly reported. It is difficult to predict numbers of additional patients who may benefit from future advances in knowledge of molecular aberrations in these cancers. To date, these aberrations seem particularly characteristic of rare and less common cancers.

PART 8 – COST INFORMATION

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

Equipment and Resources	Renal Cell Carnicoma	Hydatidiform Moles	Granulosa Cell Ovarian Tumour	Salivary Gland Tumours	Secretory Carcinoma of the Breast
FISH kit, probes, reagents, ancillary reagents	$500.00	$350.00	$350.00	$350.00	$350.00
Labour medical (consultant pathologist)	$50.00	$50.00	$50.00	$50.00	$50.00
Labour scientific	$40.00	$40.00	$40.00	$40.00	$40.00
Labour on costs	$14.00	$14.00	$14.00	$14.00	$14.00
Total per test	**$604.00**	**$454.00**	**$454.00**	**$454.00**	**$454.00**

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

7-10 working days

53. 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

Characterisation of ploidy status by STR genotyping or FISH in the assessment of hydatidiform moles.
OR
Identification of FOXL2 402C>G status in the assessment of granulosa cell ovarian tumours.
OR
Identification of NUT gene status at 15q14 in a patient with a malignant head and neck or midline carcinoma for the diagnosis of NUT midline carcinomas.
OR
Identification of ETV6-NTRK3 gene status in a patient with secretory carcinoma of the breast or mammary analogue secretory carcinoma (MASC) of salivary glands.
Fee: $454 each
OR
In the assessment of malignant salivary gland tumours, identification of:

- MALM2 gene status for the diagnosis of mucoepidermoid carcinoma **AND/OR**
- ETV6-NTRK3 gene status for the diagnosis of analogue secretory carcinoma **AND/OR**
- EWSR1 gene status for the diagnosis of hyalinising clear cell carcinoma.

Fee: $454 (for each)
OR
Identification of TFE3 or TFEB gene rearrangement in the assessment of renal cell carcinoma.
Fee: $454 (for each)

PART 9 – FEEDBACK

The Department is interested in your feedback.

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

Insert approximate duration here

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

☐ Yes
☐ No

(b) If no, provide areas of concern:

Describe areas of concern here

56. (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

57. (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?

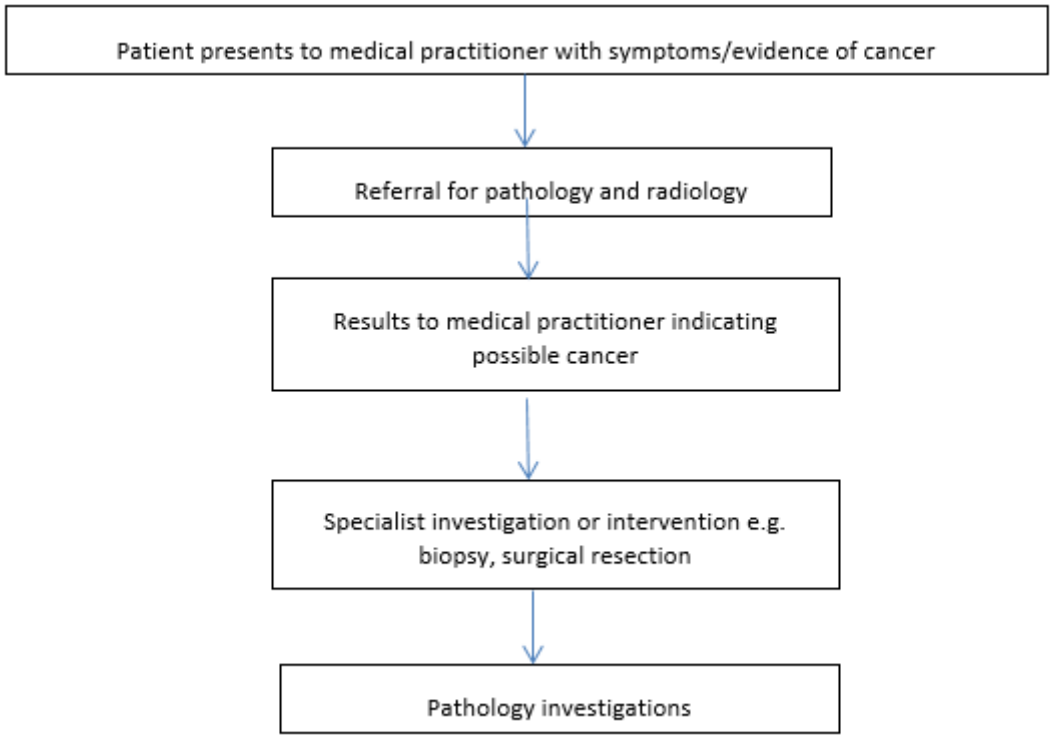
☐ Yes
☐ No

(b) If yes, please advise:

Insert feedback here

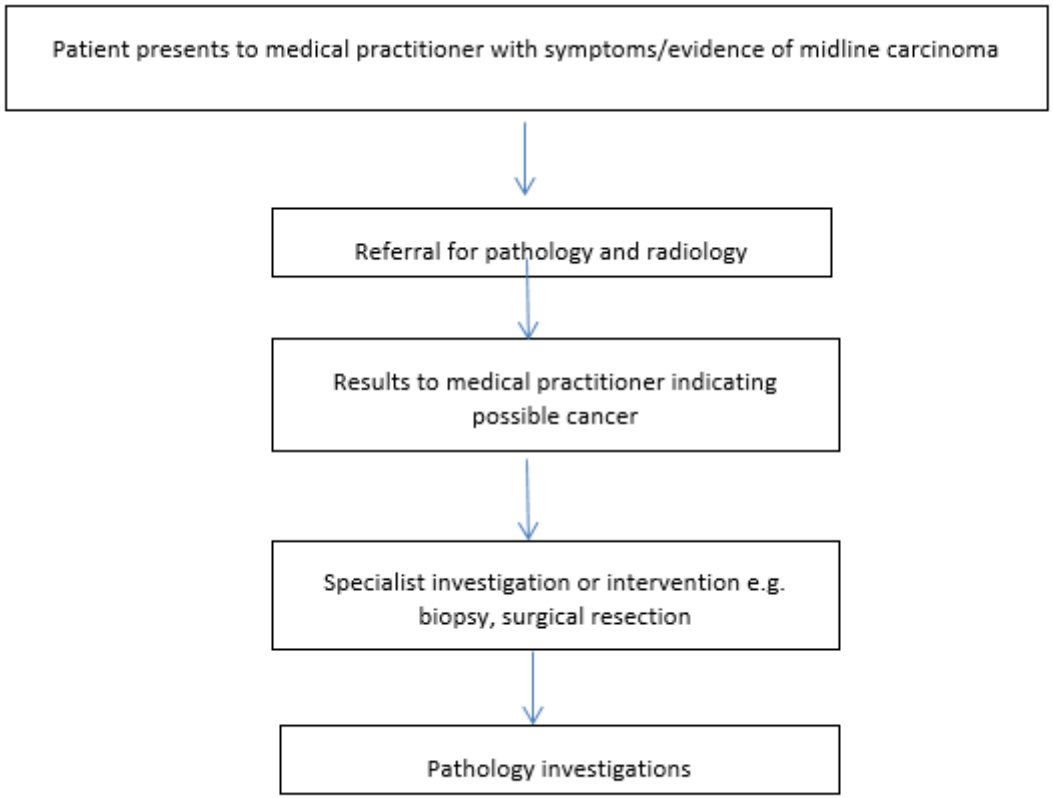
Appendix A Flowcharts

Q26 Clinical pathway before intervention

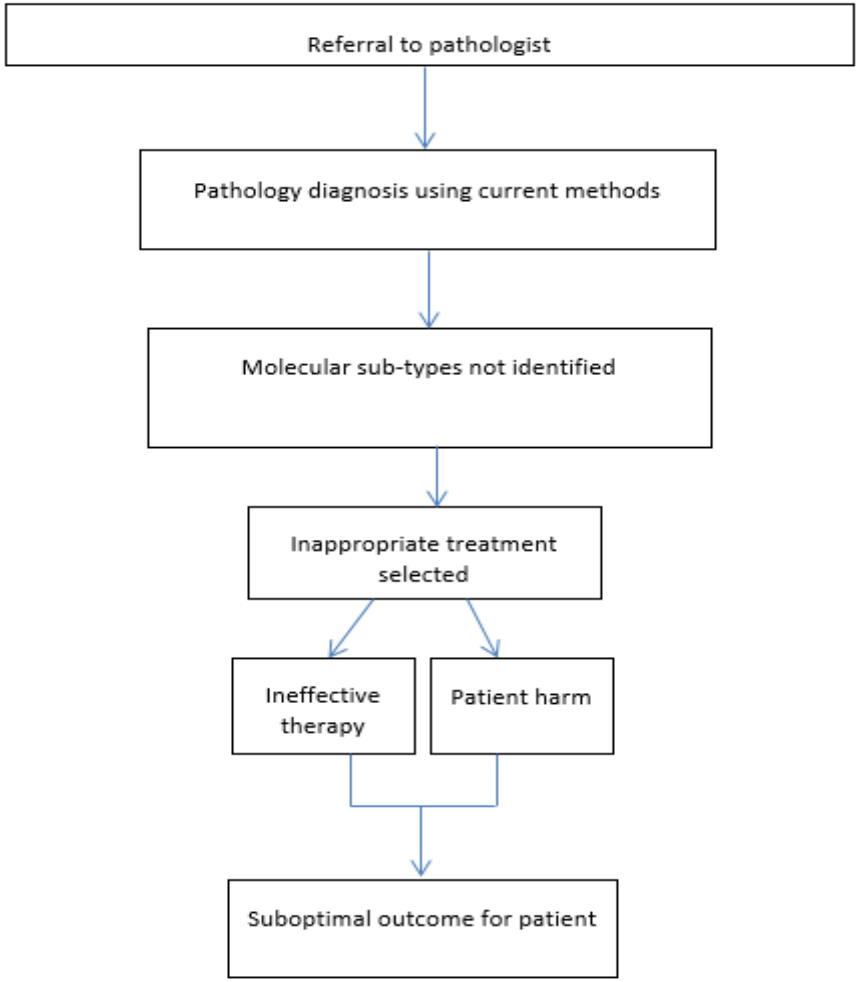


Appendix A Flowcharts

Q26 Clinical pathway before intervention



Clinical pathway after comparator (current)



Q40 Clinical pathway after comparator (current)