Australian Government

Department of Health

# Consultation Survey on MSAC Application 1671

## Targeted carrier testing for severe monogenic conditions

This feedback survey relates to the application form and Population, Intervention, Comparator and Outcome (PICO) Confirmation for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)).

Please use this template, to prepare your feedback on the application form and/or the PICO Confirmation. You are welcome to provide feedback from either a personal or group perspective for consideration by the Department of Health when the application is being reviewed.

The data collected will be used to inform the Medical Services Advisory Committee (MSAC) process to ensure that when proposed healthcare interventions are assessed for public funding in Australia, they are patient focused and seek to achieve best value.

This feedback survey should take approximately 15 minutes to complete.

You may also wish to supplement your responses with further documentation or diagrams or other information to assist the Department in considering your feedback.

Thank you for taking the time to provide valuable feedback.

**Responses may be provided to the MSAC, its subcommittees, a health technology assessment group and the applicant. Should you require de-identification please contact the Consumer Evidence and Engagement Unit (details below).**

While stakeholder feedback is used to inform the application process, you should be aware that your feedback may be used more broadly by the applicant.

**Please reply to the Consumer Evidence and Engagement Unit:**

**Email:** commentsMSAC@health.gov.au

**Postal: MDP 910 GPO 9848 ACT 2601**

# PART 1 – PERSONAL AND ORGANISATIONAL INFORMATION

**1. Respondent details**

Name: Matilda Haas

Email: matilda.haas@mcri.edu.au

Phone No: 0403287727

**2. Is the feedback being provided on an individual basis or by a collective group?**

☐ Individual
☒ Collective Group

**If individual, specify the name of the organisation you work for**

| |
|---|
| |

**If collective group, specify the name of the group**

| |
|---|
| Australian Genomics |

**3. How would you best identify yourself?**

☐ General Practitioner
☐ Specialist
☒ Researcher
☐ Consumer
☐ Care giver
☒ Other

**If other, please specify**

| |
|---|
| Research Projects and Partnerships Manager submitting on behalf of Australian Genomics in consultation with lead researchers. |

# PART 2 – CLINICAL NEED AND PUBLIC HEALTH SIGNIFICANCE

**4. Describe your experience with the medical condition (disease) and/or proposed intervention and/or service relating to the application form**

Australian Genomics is an Australian Government initiative supporting genomic research and its translation into clinical practice. Through broad engagement and a national collaborative approach, it achieves two key objectives: to improve efficiency, reach and timeliness of genomic research projects, and to support Commonwealth State and Territory health departments in the implementation of genomics research outcomes by refining and communicating evidence to inform policy development.

Australian Genomics engages with current and emerging government policy and priorities to identify gaps and opportunities, to support policy and action for integrating genomic technologies into the health system. By interfacing with consumers, governments, industry and global genomics initiatives, Australian Genomics drives change and growth in the sector.

As part of its portfolio of project management, Australian Genomics administers the Mackenzie's Mission Australian Reproductive Carrier Screening Project, which will determine the feasibility of providing free carrier screening to every Australian couple that wants it. The project will test thousands of couples for about 750 recessive and X-linked genetic conditions. Clinical utility evidence will be supported by research on cost-effectiveness, implementation and translation, ethical and social considerations, and psychosocial factors associated with expanded reproductive carrier screening.

**5. What do you see as the benefit(s) of the proposed medical service, in particular for the person involved and/or their family and carers?**

The aim of reproductive carrier screening is to give couples more reproductive decision-making options, which has the follow-on benefit of increasing their chance of having a healthy child.

Specific to this application, benefits to individuals and their families and carers could potentially include that targeting specific communities/populations may increase awareness of the availability of the carrier screening testing within those communities and with GPs and other health professionals working in those communities. However, as we note in response to later questions, our stance is that it is more equitable to offer expanded carrier screening to all people regardless of ethnic background.

In drawing comparisons with the approach of the Mackenzie's Mission Reproductive Carrier Screening study (the subject of MSAC application 1637), this kind of testing may be suited to individuals and couples who, for ethical, social or other reasons, want to limit carrier testing to a more discrete panel of genes where genetic variants which lead to a higher risk of genetic conditions are known to be concentrated in their ethnic heritage.

It may also be considered an advantage that because an individual undergoes testing, the test can be sought over a broader time within the life span and may mean more of the community participate in testing.

**6. What do you see as the disadvantage(s) of the proposed medical service, in particular for the person involved and/or their family and carers?**

Some identified disadvantages associated with this testing intervention are expanded upon in response to other questions. These include:

The population and expected utilisation of the test are not correctly defined (referring to the appendix – expanded on in Q6a).
Application of carrier testing to an exemplar population does not promote equitable access to testing and limits the generalisability of the conclusions drawn.
A couples-based approach has many advantages over the proposed model in this application, especially when testing happens in the ante-natal period.
There are no limitations or expectations set on laboratories on how they would select and update their gene lists.
Cost-effectiveness and uptake data in the AJ population have not been correctly estimated and are not transferable to other settings (expanded upon in Q6a).
Testing under this framework relies upon a person having good knowledge of their family history (to be able to determine >10% risk as a criterion for accessing testing).

**7. What other benefits can you see from having this intervention publically funded on the Medicare Benefits Schedule (MBS)?**

Reproductive carrier screening has powerful potential to ensure the birth of healthy children, unaffected by autosomal and X-linked genetic conditions, for couples who want to engage in this kind of genetic testing. This will also save health system dollars. Carrier testing is currently only available in Australia on a user pays basis, and so MSAC should seek to fund testing through the MBS. There is more than one application concurrently being considered by MSAC (1671, 1637), which outline different approaches to reproductive carrier screening. The question then becomes about the best approach, in terms of feasibility, community acceptance, clinical and personal utility, ethical, economic, and social factors.

It is our opinion that the intervention outlined in this application does not maximise clinical utility, would not promote equitable delivery of reproductive carrier screening, and is less likely of the two applications currently under consideration to be the most cost-effective option.

**8. What other services do you believe need to be delivered before or after this intervention, eg Dietician, Pathology etc?**

Pre-testing educational services by appropriately trained health care professionals
Genetic counselling services
IVF and PGD services (pre-conception)
Amniocentesis or CVS (antenatal)
The roles of all these services have been identified and discussed in the application.

# PART 3 – INDICATION(S) FOR THE PROPOSED MEDICAL SERVICE AND CLINICAL CLAIM

**9. Do you agree or disagree with the proposed population(s) for the proposed medical service as specified in Part 6a of the application form?**

- ☐ Strongly Agree
- ☐ Agree
- ☐ Disagree
- ☒ Strongly Disagree

**Specify why or why not:**

Demonstrating that an individual has a greater than 10% chance of being found to be a carrier of one of a number of autosomal and X-linked recessive conditions will be very difficult for many ethnicities due to lack of published data. Using expanded reproductive carrier screening for all individuals overcomes this inequity. This approach is the subject of Application 1637. That is, if all individuals have access to reproductive carrier screening for multiple genes that does not require ethnicity as an entry point to having screening, then all individuals have the option for screening that gives them the highest chance of being found to be at risk of having a child with an autosomal recessive or X-linked recessive condition.

For some time now recommendations have been to not perform ethnically targeted carrier screening. As one example, the recently published revised American College of Medical Genetics and Genomics (ACMG) guidelines on carrier screening[1] states: "Restricting carrier screening by using socially defined ethnic constructs or by self-identified ancestry is both inequitable and scientifically flawed."

Data provided on page 11 of in the Application itself reinforces this. Under "Importance of expanded carrier screening in the Ashkenazi Jewish population" – the number of carriers identified in an Ashkenazi student population using non-targeted expanded carrier screening was 25% higher than using screening targeted at 14 AJ conditions.

From a modelling point of view, it is not appropriate to use the AJ population as an exemplar for this test, where the incidence of being a carrier for a genetic condition is higher than the rest of the population. Therefore, any economic inferences related to the predicted annual uptake in the Ashkenazi Jewish population cannot be generalisable to the wider Australian population.

It is also unclear why the female is tested first, and the male test is dependent on the outcome of the female's result. No economic arguments have been presented as to why this diagnostic strategy may provide better health or economic consequences compared with the strategy of testing both genetic contributors at the same time. It is very likely that the diagnostic, clinical, and economic benefits of assessing both parents at the same time (and providing risk for the couple combined) could outweigh the additional cost of screening.

The calculations presented from page 54 onwards on the simulation of anticipated annual uptake are crude and not sufficiently justified. Reference #75 that the applicants cite in support of the simulation of anticipated uptake is a conference proceeding from 2017, which is not publicly available. While the applicants note that expected uptake, for example in Model 1, would be in the range of 40-70%, they have assumed perfect (100%) uptake, significantly inflating calculations upwards.

[1]Gregg, A. R., M. Aarabi, S. Klugman, N. T. Leach, M. T. Bashford, T. Goldwaser, E. Chen, T. N. Sparks, H. V. Reddi, A. Rajkovic, J. S. Dungan, Acmg Professional Practice, and Committee Guidelines. 2021. 'Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: a practice resource of the American College of Medical Genetics and Genomics (ACMG)', Genetics in medicine.

**10. Have all the associated interventions been adequately captured in Part 6b of the application form?**

☐ Yes
☒ No

**Please explain:**

It is also unclear what service is offered by whom to assess the individual as at >10% personal risk of being a heterozygous carrier. This may be considered another associated intervention that is not captured in this section or the accompanying figure.

**11. Do you agree or disagree that the comparator(s) to the proposed medical service as specified in Part 6c of the application form?**

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

**Please explain:**

The overarching comparator is no testing, while the comparator for the AJ exemplar population is enzyme testing for Tay Sachs disease. These are appropriate comparators when considered in relation to the status of available carrier screening tests.

**12. Do you agree or disagree with the clinical claim made for the proposed medical service as specified in Part 6d of the application form?**

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

**Specify why or why not:**

The clinical claims are well-defined and relate to carrier screening programs more broadly, rather the focussing on the test proposed as part of this application.

# PART 4 – COST INFORMATION FOR THE PROPOSED MEDICAL SERVICE

**13. Do you agree with the proposed MBS item descriptor, as specified in Question 53 of the application form?**

- ☐ Strongly Agree
- ☐ Agree
- ☒ Disagree
- ☐ Strongly Disagree

**Specify why or why not:**

The requirement to be asymptomatic should be removed. A person who has cystic fibrosis should not be excluded from having carrier screening for example.

Is item AAAA missing the number "3" in relation to the statement *"…in addition to at least other genes relevant to the ancestry of that individual…"*?

In item AAAA, how is a>10% personal risk of being a genetic carrier assessed?

What incentive will there be for laboratories to add additional genes to the panel for the same test cost, when the workload associated with variant interpretation and curation will increase?

Under CCCC (and DDDD) the requirement for the test to be only ordered by specialists and consultant physicians should be changed to any medical practitioner. It is critical that general practitioners can order all reproductive carrier screening to enable the broadest range of individuals to have access to such screening.

Under CCCC it states that a male at any risk should be tested at the same time as his female partner if the female is at greater than 10% risk of having a child with one of the conditions for which screening is offered. The opposite should also be available. That is, if a male is at greater than 10% risk then his female partner at any risk should also be able to be tested.

Item EEEE, a reanalysis item number, is an important inclusion. Managing re-contact in the case of a changed result would be an important consideration and would require input from genetic counselling and clinical genetics services.

**14. Do you agree or disagree with the proposed MBS fee, as specified in Question 53 of the application form?**

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

**Specify why or why not:**

However, one could speculate about the value gained from a $600 test for a panel of around 9 genes, in comparison with the cost of Whole Exome Sequencing, which can facilitate

analysis of hundreds to thousands of genes. More comprehensive technologies such as Next Generation Whole Exome Sequencing would also offer greater flexibility for reanalysis.

# PART 5 – ADDITIONAL COMMENTS

**15. Do you have any additional comments on the proposed intervention and/or medical condition (disease) relating to the proposed medical service?**

**16. Do you have any comments on this feedback survey? Please provide comments or suggestions on how this process could be improved.**

While the introduction of MBS funded reproductive carrier screening testing in Australia is important to pursue, the best model should be achieved first. This model will be evidence based and will consider all of the factors discussed here, and factors additional to our response. These include clinical and personal utility, cost-effectiveness, equity of access, community perceptions, and other social and ethical issues.

**Again, thank you for taking the time to provide valuable feedback.**