Recommended screening policy for the Australasian newborn bloodspot screening programs was developed by a joint subcommittee of the Human Genetics Society of Australasia and the Division of Paediatrics of the Royal Australasian College of Physicians and this policy follows. However, the New Zealand programme has had a policy since 2011 ([https://www.nsu.govt.nz/system/files/page/newborn_metabolic_screening_programme_policy_framework_june_2011.pdf](https://www.nsu.govt.nz/system/files/page/newborn_metabolic_screening_programme_policy_framework_june_2011.pdf) and a National Framework is currently being developed for the Australian programmes (White CA, Lister K, Newborn Bloodspot Screening: Developing the Australian national policy agenda. Med J Aust, 2014 201 577). When finalised this framework and the NZ policy will replace this document.

Program policies and which disorders are included are decided by each jurisdiction (individual States in Australia, and New Zealand). Newborn screening services for Australia are coordinated from the five centralised screening laboratories (New South Wales, Queensland, South Australia, Victoria and Western Australia). There is a single laboratory service for New Zealand, funded by the New Zealand Ministry of Health. All Australasian programs are voluntary and fully publically funded.

Newborn bloodspot screening for inborn errors of metabolism is a public health activity aimed at the early identification of infants affected by certain congenital disorders. Timely intervention in these disorders significantly reduces morbidity, mortality and associated disabilities. Newborn screening is an accepted part of neonatal healthcare in all developed countries, established in Australasia since the late 1960’s.

1 General Recommendations
Newborn screening is recommended provided that:
1.1 There is benefit to the baby from early diagnosis (benefit to the family may also benefit the baby).
1.2 The benefit is reasonably balanced against financial and other costs.
1.3 There is a reliable test suitable for newborn screening.
1.4 There is a satisfactory system available to deal with diagnostic testing, counselling, treatment and follow-up of patients identified by the test.

2 Organisation of Programs

2.1 The screening program comprises the sum of the operations necessary to ensure that all babies are offered testing, all necessary follow-up is done, all cases found are adequately treated and there are appropriate quality management and program evaluation processes in place.
2.2 The current policy of public funding for newborn screening programs should be retained. They should be organised and controlled within the public health sector.
2.1 Screening programs should facilitate development and implementation of nationally recognised newborn screening standards, policies and guidelines. They should take advice about the general operation of the screening program from multidisciplinary expert sources.
2.4 Screening programs should provide a seamless system of care that coordinates and involves community and hospital based providers, tertiary care centres and paediatric sub-speciality clinics.
2.5 Health professionals and the public should be kept well informed about screening programs. Specifically, written information and the opportunity for discussion must be provided for parents before testing, and health professionals should be provided with comprehensive guidelines describing all aspects of the screening program including correct sample collection procedure.
2.6 Healthcare authorities have a responsibility to ensure tests are available to all babies born in their region.
2.7 For each baby born, an individual or individuals must be identified as responsible for providing information about the test, offering the test, obtaining appropriate consent, collecting the sample and completing any requested follow-up.
2.8 A system should be in place to ensure that community- and hospital-based providers know which samples have been received by the screening laboratory. Special care must be taken to ensure that a sample is collected from each baby or refusal of testing is documented and notified to the screening laboratory. An acceptable way of achieving this is for the empty screening test card (with demographic information but no blood sample) to be returned to the laboratory with the documented refusal.
2.9 Programs should regularly assess the screened disorders with the aim of stopping screening for conditions where blood spot screening no longer has clinical utility, and adding new disorders. A framework for assessment of disorders is given in Appendix 1.
2.10 Regular assessments of screening program performance should be undertaken and must include sensitivity, specificity, positive predictive value, timeliness of reporting and outcome of diagnosed patients. Outcome assessment should include short and long term evaluation and may be based on surrogate measures in disorders that are well understood.

3 Laboratory Services

3.1 Screening tests should be carried out in large centralised laboratories, so that costs can be kept low, expertise rapidly gained and kept, and for low prevalence disorders, sufficient data are available for assessment of assay performance.
3.2 Laboratories must contribute to an Australasian data set (see appendix 3).
3.3 Laboratories must have appropriate accreditation. External assessors should review programs to ensure that suitable tests, quality assurance, cut-off points, follow-up procedures and screening audit processes are in operation.
3.4 The HGSA should ensure that quality control programs are available Australasia-wide for each test employed on a routine service basis.
3.5 The screening laboratory director is responsible for ensuring the correct performance and interpretation of the tests, ensuring that the baby’s doctor, treating midwife or parents are informed of any abnormal result and of the appropriate action to be taken. The director should ensure that responsibility for further action is formally handed over to an appropriate healthcare professional.

4 Legal and Ethical Considerations
4.1 Participation in a newborn screening program should not be mandatory. Parents should be informed of the availability of testing. If after discussion the parents refuse to have their newborn tested, they should sign a statement that they are fully informed about the test and the consequences of not testing.
4.2 The screening program should have appropriate policies and procedures to ensure that the privacy and confidentiality of the patient and family are carefully protected.
4.3 If a newborn screening test is investigational or being developed and the benefits and risks are yet to be demonstrated, separate consent and/or more detailed information may be required and this should be discussed with appropriate ethics and advisory committees.
4.4 A separate HGSA policy covers the storage and use of residual material on newborn screening cards. All programs should develop their own detailed policy based on the instructions in the HGSA policy, and include the following:
   i After completion of newborn screening testing, cards should be stored securely for such period of time as is determined by the screening program, taking into account legal requirements and local pathology service guidelines for samples.
   ii Further use of the stored samples for purposes other than screening program audit requires either written permission from the individual, the parents or guardian, or a legally binding directive, or appropriate ethics committee approval for research studies. Such studies would generally involve de-identified samples.
   iii The written information for parents should include information about the storage and potential uses of residual samples.

5 Research and Audit
5.1 Screening programs should support collaborative research, particularly that related to current and potential newborn screening. Such research should be conducted in line with local ethics and advisory committee recommendations and should consider the benefit to families which can arise from non-anonymised studies and what permission might be required for such studies.
5.2 Pilot studies may be required to demonstrate the safety, effectiveness validity and clinical utility of tests for additional disorders and new testing technologies.
5.3 Screening programs must facilitate program audit against agreed standards covering all program aspects including short and long-term follow-up.
5.4 Programs must contribute to Australasian data sharing and benchmarking of quality indicators.
5.5 Programs are encouraged to contribute to appropriate international collaborative efforts.
Appendix 1
Framework for Assessment of Current and Potential Disorders

Within Australia, there is an urgent need for the development of a national evidence-based process to evaluate proposals for changes to the conditions covered by newborn screening programs. There are several published criteria for judging if a condition is suitable for newborn screening. The best known discussion of screening in general, and which has stood the test of time, is the Wilson and Jungner paper, which incorporates ten major criteria, not all entirely applicable to newborn screening. More recently there have been attempts to systematise the consideration of new disorders from the United States and the United Kingdom.

There are many problems in devising a useful assessment tool. A major one is that disorders suited to newborn screening have so far been very rare, with little evidence of the highest quality to demonstrate the efficacy of early, pre-symptomatic, diagnosis and treatment. Also, some tests either current or proposed are multiplex tests: for a negligible up-front cost a new disorder can be added. This may lead to a less rigorous consideration of potential harms.

The possible advantages of early detection by newborn screening are not only reduction in mortality and morbidity but may be simply the ability to make a definitive diagnosis in an untreatable condition where such a diagnosis may be missed clinically. The possible disadvantages are the over-diagnosis of mild disease, resulting in unnecessary medicalisation, and the costs of testing, diagnosis and early management.

Different issues arise for different conditions. For some conditions cost and availability of treatment is the most important consideration, for others, the brief time-frame available for effective management. The Human Genetics Society of Australasia, through its joint Newborn Screening Committee, has attempted to produce a common framework for presenting new disorders for consideration by jurisdictions, taking ideas from the USA, UK, and from the Wilson and Jungner WHO paper. The form presented here asks for published evidence in three domains: the condition proposed, the screening test, and the treatment available and its efficacy. The evidence should be graded according to a modification of that proposed by Harbour and Miller, outlined below.

**THE CONDITION:** The condition should be an important health problem potentially leading to significant morbidity or mortality, and for which early identification appears likely to be of benefit to the infant. In some disorders able to be included in a multiplex test, a benefit for the family may be important, where the condition is untreatable and may lead to early mortality, but where a definitive diagnosis might be aided by the performance of the screening test.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Supporting Evidence (with references)</th>
<th>Grade of evidence*</th>
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<tbody>
<tr>
<td>Incidence:</td>
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<tr>
<td>How determined:</td>
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<tr>
<td>(screening/clinical)</td>
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<tr>
<td>Timing of clinical onset: (when condition would usually be detected clinically)</td>
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<td>Severity:</td>
<td></td>
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<tr>
<td>Morbidity, disability</td>
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<tr>
<td>Mortality</td>
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<tr>
<td>Spectrum of disease</td>
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<tr>
<td>Likely or known health gains from early diagnosis and treatment.</td>
<td></td>
<td></td>
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<tr>
<td>Possible harms from screening / early diagnosis</td>
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</table>
**THE TEST:**

<table>
<thead>
<tr>
<th>Proposed test:</th>
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<tbody>
<tr>
<td>Sample</td>
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<tr>
<td>Test</td>
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<tr>
<td>Clinical validation</td>
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<td>Laboratory performance</td>
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<td>• Sensitivity</td>
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<td>• False +ve rate</td>
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<td></td>
<td>• PPV</td>
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</table>

Is it multiplex?  
What else may be detected?  

<table>
<thead>
<tr>
<th>Confirmatory testing:</th>
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<tbody>
<tr>
<td></td>
<td>• Availability</td>
<td></td>
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<tr>
<td></td>
<td>• Reliability</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Laboratory performance</td>
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</tbody>
</table>

DNA analysis: If proposed.  
Which mutations to be included?  
Laboratory performance  
Reason for inclusion:  
(Confirmatory testing; part of screening; prediction of severity?)  

Possible harms as a direct result of proposed tests:  

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**THE TREATMENT:**

<table>
<thead>
<tr>
<th>Established interventions:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Which patients need a treatment/intervention?</td>
<td></td>
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</table>

Efficacy:  

Urgency:  
Evidence for benefit or likely benefit from neonatal diagnosis and treatment  

Availability:  

Costs: (direct and infrastructure)  

Possible harms from treatment:  

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Newborn bloodspot screening  
2017PL01  
August 2017
GRADINGS OF EVIDENCE:

A: At least one high-quality meta-analysis, systematic review, or RCT directly applicable to the target population or a systematic review of RCTs or a body of evidence consisting principally of well-conducted studies directly applicable to the target population and demonstrating overall consistency of results.

B: A body of evidence including high-quality case-control or cohort studies with a very low risk of confounding, bias or chance, a high probability that the relationship is causal, directly applicable to the target population and demonstrating overall consistency of results.

C: A body of evidence including well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal, directly applicable to the target population and demonstrating overall consistency of results.

D: Non-analytical studies, cohort or case-control studies with a significant risk of confounding, bias or chance, case reports, or case series. Expert opinion.

E: No evidence available.
