Development of the Criteria for the clinical use of IVIg in Australia
(Second Edition)

National IVIg Criteria Review Working Group
A National IVIg Criteria Review Working Group (NICRWG) was established to oversee the 2010–11 Criteria Review process.

The NICRWG comprised representatives from both clinical and government sectors and individual experts who were engaged in the initial review.

Terms of reference
The NICRWG was responsible for:

- calling for submissions from governments, and members of the clinical community — individuals or groups, including clinical colleges and societies;
- assessing submissions and determining whether a systematic review was required to address the submission;
- determining and agreeing on the Criteria wording in response to submissions that did not require systematic review;
- facilitating and supporting the procurement process to engage a systematic reviewer;
- conducting a consensus process for recommendations that had lower than level IV evidence to facilitate agreement on the recommended wording for the revised Criteria;
- ensuring appropriate clinical and public consultation processes were conducted;
- producing an exposure draft of the revised Criteria;
- conducting a cost analysis of the proposed changes to the Criteria; and
- providing the Jurisdictional Blood Committee (JBC) with recommendations for consideration, on the basis of the systematic review, clinical consultation and cost analysis.

NICRWG representative members were also responsible for seeking and consolidating input from represented organisations as appropriate throughout the systematic review and drafting process.

Membership
- JBC Representatives (Ms Joan Bedford and Ms Carolyn Duck)
- National Blood Authority (NBA) Representative (Principal Medical Officer — Dr Chris Hogan)
Chair

JBC appointed Ms Joan Bedford as the chair of the NICRWG for the duration of the review.

Individual experts

The clinicians who chaired the discipline specific subgroups during the development of the first edition of the Criteria were invited to participate as individual experts on the NICRWG. These experts were:

- Associate Professor Andrew Kornberg — neurology
- Associate Professor John Gibson — haematology
- Associate Professor Sean Riminton — clinical immunology

Secretariat support

- Ms Jennifer Roberts — Project Director
- Ms Julie Bland — Project Manager (to August 2011)
- Ms Sandra Russell — Project Manager (from August 2011)
- Ms Donna Cassoni — Project Officer

Additional expert advice

The following colleges and societies provided additional expert advice;

- Australasian College of Dermatologists
- Australian & New Zealand Intensive Care Society
- Bone Marrow Transplant Society of Australia and New Zealand National Asthma Council Australia
- Perinatal Society of Australia and New Zealand
- Thoracic Society of Australia and New Zealand

Many other clinical experts gave generously of their time and expertise. All contributions are gratefully acknowledged.

Formal submission process

In preparation for the 2010–11 Criteria Review, clinical stakeholders were advised about the 2010–11 Criteria Review in mid-2009 in order to gauge interest from the clinical community, and gain insight into the type of, and number of formal submissions that the NBA expected to receive.
Individuals, organisations and representative bodies who had indicated they would make a submission and those who had sought clarification were notified directly of the formal submission process. Members of IVIg user groups and clinicians ordering IVIg were informed of the submission process and timetable.

Formal submissions from the clinical community were accepted from December 2009 to February 2010 for:

- removal of an existing condition;
- a change to the documented content of an existing condition; and a new condition.

As part of the formal submission process, the clinical community was asked to provide supporting documentation, including:

- journal articles;
- case reports (published or unpublished);
- support from relevant clinical society/college; and other relevant information.

**Review of submissions**

All formal submissions were provided to the NICRWG for consideration and to determine what approach would be used to assess each submission. Based on the information provided with the formal submissions and expert opinion, the NICRWG decided the process of consideration for each submission:

- a systematic review;
- a consensus process without systematic review, due to limited availability of published evidence;
- minor wording adjustments followed by a consensus process; or
- no action.

**Systematic review**

The NBA engaged Biotext Pty Ltd to conduct a systematic review of the literature on IVIg for a number of specific conditions identified by the formal submission process and subsequent NICRWG discussions.

The literature review focused on four areas:

- pyoderma gangrenosum;
- diabetic amyotrophy;
- autoimmune encephalopathies and neuropathies (a total of 10 indications); and
- sepsis (a total of nine indications).

The reviews followed the methods described in the National Health and Medical Research Council (NHMRC) handbook, *How to review the evidence: systematic review and assessment of the scientific literature* (NHMRC 2000) and the Evidence-based practice workbook published by BMJ Books (Glasziou et al 2007). Reviews were restricted to studies
published since 2004 (the date of the last major systematic literature review conducted on the indications for IVIg use), and aimed to:

- identify and critically appraise the scientific literature regarding the efficacy and risks of IVIg therapy;
- analyse scientific publications (including existing guidelines) that identify the key therapeutic issues in IVIg therapy; and
- include studies comparing IVIg with other treatments, including immunoglobulin administered by other routes, when such other treatments have been studied in comparison with intravenous administration.

Biotext Pty Ltd worked closely with the NICRWG to develop review questions based on the ‘PICO’ method (population/problem, indication, comparator, and outcome) for each condition included in the review.

An evidence statement was developed for each clinical question using the NHMRC Evidence Statement Form as described in Additional levels of evidence and grades for recommendations for guideline developers (NHMRC 2008).

For each systematic review undertaken, an evidence report was prepared. The evidence reports included specific details of the review methods and search terms used for that particular condition.

As this was a partial review of the Criteria, and to ensure consistency in any revised edition, each evidence report includes an assessment of the alignment of the literature against the categories previously used in the Criteria, outlined in Table 1.

As many of the systematically reviewed conditions are rare and there is limited published clinical evidence, this approach also assisted the consensus process.
### Table 1 Level of evidence categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Studies</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High-quality randomised controlled trials (RCTs)</td>
<td>Clear evidence of benefit</td>
</tr>
<tr>
<td>2a</td>
<td>Some RCTs and/or case studies</td>
<td>Evidence of probable benefit – more research needed</td>
</tr>
<tr>
<td>2b</td>
<td>Some RCTs and/or case studies</td>
<td>Evidence of no probable benefit – more research needed</td>
</tr>
<tr>
<td>2c</td>
<td>High-quality RCTs with conflicting results</td>
<td>Conflicting evidence of benefit</td>
</tr>
<tr>
<td>3</td>
<td>High-quality RCTs</td>
<td>Clear evidence of no benefit</td>
</tr>
<tr>
<td>4a</td>
<td>Small case studies only</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>4b</td>
<td>No included studies</td>
<td>-</td>
</tr>
</tbody>
</table>

**Development of revised wording**

For each condition, the NICRWG agreed required amendments or a new indication being considered for inclusion, draft wording or amendments to existing wording were prepared, by either:

- NICRWG clinical experts;
- a NICRWG member representing an appropriate college or society; or
- a clinical expert from a relevant college or society not represented on the NICRWG.

**Consensus process**
For many rare and complex conditions, there is insufficient high-quality data in the clinical literature to produce evidence-based recommendations. Therefore, there is a role for expert opinion and consensus in the development of materials to guide clinical use.

For the 2010–11 Criteria Review, the consensus process consisted of informal and formal consensus processes. Where consensus could not be reached, no amendments to the previously published content were made.

**Informal consensus process**

Where necessary, advice on proposed wording was sought from a relevant college or society. Proposed wording, along with any other advice received from relevant colleges and societies was considered by the NICRWG. This usually occurred during meetings of the NICRWG or via electronic correspondence.

Consensus was reached when all members either strongly agreed or agreed to the proposed new wording or amendments. For some amendments, this was an iterative process, but where consensus was not reached, the formal consensus process was implemented.

**Formal consensus process**

The formal consensus process allowed participants to discuss the issue of concerns face to face. The structured process facilitated contributions from all members, recognised relevant expertise, and limited the capacity of any one member to dominate. The formal consensus process was based on an agreed set of guiding principles and values.

The consensus process was facilitated by the Chair of the NICRWG and consisted of:

- **A pre-meeting process** — where members had access to all materials relating to the proposed change, including advice from experts outside the NICRWG and evidence reports.
- **A consensus meeting** — where each item requiring consensus followed an agreed process:
  - overview of the recommendation
  - open discussion — where members could clarify the recommendation and then each member had the opportunity to highlight or state any concerns they had with the proposed recommendation
  - a summary of concerns — where all concerns were summarised and an opportunity was provided for the concern to be resolved through modification to the recommendation or proposed wording

- Finalisation — if all concerns have been resolved the Chair called for consensus. However, if concerns had been discussed but remained unresolved and consensus was not reached, consideration was given to the formal consensus guiding principles and values, before another call for consensus was made. If consensus could not be reached this second time, the recommendation was not accepted and no amendments were proposed.
Public consultation

Various stakeholders were consulted to help inform the discussions and decisions of the NICRWG. In particular, advice was obtained from a range of colleges and societies to inform the decisions around changes and proposed wording amendments.

Once agreement on the proposed amendments was reached, an exposure draft outlining these changes was developed. Public consultation, seeking feedback on the proposed amendments to the *Criteria*, was undertaken for an eight-week period from 25 June to 19 August 2011.

Stakeholders were advised of the public consultation process through:

- a national newspaper advertisement;
- a direct email to specific colleges and societies;
- a direct email to stakeholders who registered their interest in participating via the NBA’s website;
- a direct email to stakeholders involved in the clarification processes; and
- materials on the NBA’s website

Comments on the proposed amendments to the *Criteria* contained in the 31 submissions provided during the public consultation process were considered by the NICRWG.

The consensus processes outlined above were used to develop additional amendments or to confirm the drafted entry. A number of additional changes were agreed primarily to clarify and improve consistency in understanding of the entry.

Finalisation and approval

The NICWWRG completed their terms of reference in October 2011 by providing JBC with recommendations for consideration, on the basis of the systematic review, clinical consultation and cost analysis. The finalised Criteria document was endorsed by the Jurisdictional Blood Committee in December 2012. This led to the second edition of the *Criteria* being approved by Health Ministers.