Submission to the Public Consultation on the *Pharmaceutical Benefits Advisory Committee (PBAC) Guidelines Review*

14 September, 2015

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Introduction

Medicines Australia welcomes the commencement of the Pharmaceutical Benefits Advisory Committee (PBAC) Guidelines Review (hereafter the review). The review is an opportunity to ensure the PBAC Guidelines meet world's best practices, incorporate new and updated methodological approaches and more generally incorporate improvements to PBAC assessment processes.

Medicines Australia also welcomes public consultation on the "items to be included in the review" and encourages regular opportunities for all stakeholders to engage with the review through consultation such as this and visibility of, and engagement with, the review milestones.

Medicines Australia is the peak organisation representing the research-based pharmaceutical industry in Australia. Our members comprise over 80% of the prescription medicines market by value and play an integral role in delivering better health outcomes for Australians. Medicines Australia's members include the vast majority of sponsors who seek to make their medicines available to Australian patients via the Pharmaceutical Benefits Scheme (PBS) via a submission to the PBAC.

To support the early work of the PBAC Guidelines Review Steering Committee (GRSC) and to ensure that industry's concerns were appropriately represented, Medicines Australia prepared a summary paper of issues in July 2015. For completeness this document is attached as appendix 1. Medicines Australia does not seek to repeat in depth these issues, therefore the purpose of this submission will be to make three additional overarching recommendations to ensure the realization of world's best practice guidelines.

Medicines Australia recommends that the review:

1. Consider key methodological guidance issues for updating or addition to the guidelines;
2. Consider process issues for updating during, or in parallel to, the review; and
3. Follow a robust and transparent process with input from all relevant stakeholders and experts.

PBAC Guidelines Overview

The PBAC Guidelines provide detailed instructions for sponsor companies on what information is required by the PBAC and its subcommittees to assist them in making a recommendation to the Government to list a medicine on the PBS.

The volume and depth of information provided by pharmaceutical companies to the PBAC is large and complex. As new technologies are developed and drug discovery and research becomes more intricate and more able to be targeted to specific genetic variations, it is vital to regularly review the guidelines that govern the system. Regularly updating, streamlining and incorporating the latest HTA methodological advances into the guidelines will ensure they remain fit for purpose.

Medicines Australia welcomes its appointment to the GRSC, whose membership includes experts in Health Technology Assessment (HTA). Medicines Australia notes that considerable work has already been undertaken by this group, in partnership with Adelaide Health Technology Assessment (AHTA).

Recommendations

As principal users of the guidelines, sponsor companies have a unique and valuable insight into the relevance and practicality of the existing version of the PBAC Guidelines and the issues that need examination, evaluation and modernization. Consequently, Medicines Australia has periodically and again, more recently sought feedback from member

companies as to potential areas within the Guidelines that need review and/or drafting of new guidance.

These have been detailed in the sections below and Medicines Australia proposes that the GRSC and AHTA incorporate these as part of the review.

1. **Consider key methodological guidance issues for updating or addition to the guidelines;**

The most recent survey of the Medicines Australia membership confirmed the need to address issues already raised in the primary submission at appendix 1. In particular, further guidance is essential on such issues as the choice of comparators, adaptive clinical trial design, indirect comparisons, surrogate to final outcomes and patient cross over in clinical trials. These issues are consistently and repeatedly raised and are yet to be resolved.

In addition, industry and many other stakeholders have called for the establishment of methods to enable the inclusion of broader societal costs and benefits and how these may be considered by the PBAC. In particular, contemporary guidance on the inclusion of assessments relating to the full economic and fiscal impact of a new medicine. i.e the consideration of non-health benefits and costs, including productivity gains, reductions in welfare dependence and disability payments.

Through this recent survey Medicines Australia also identified additional issues not outlined in appendix 1 which should also be addressed through this review. These include:

- Guidance on the evidentiary requirements for biosimilar medicines, in particular the evidence reviewed by the TGA and evidence considered by the PBAC in determining biosimilarity versus substitutability and appropriate prescribing advice. Consideration should be given to instances where biosimilars may need to follow the major submission pathway depending on the clinical assessment necessary for the purpose of substitution and prescribing directions;
- Vaccines specific evidentiary requirements and guidance, in particular:
    - Discount rates
    - Dynamic transmission modelling
    - Time horizon expectations for modelling vaccines outcomes
    - Indirect costs and benefits for society relating to vaccines
    - Quality of life estimates and methods for short term diseases in young children (and their carers);
- Evidentiary requirements and methods to deal with the paucity of data, for treatments for rare diseases and agreement on the definition and criteria for determining a rare disease;
- Incorporation of the quality of life of carers in economic analyses; and
- Use of discrete choice experiments and other methods (e.g., patient value mapping) to understand how patients value an intervention.

2. **Consider process issues for updating during, or in parallel to, the review**

Whilst the focus of the review is on updating technical and methodological guidance, Medicines Australia encourages consideration of strong sponsor feedback that clarity with respect to pre and post- PBAC processes is required. These include, but are not limited to:

- Early engagement and specialist advice in therapy areas prior to the PBAC meeting, and in collaboration with the sponsor. i.e specialist subcommittee(s) for rare diseases, or particular conditions similar to the Australia Technical Advisory Group on Immunisation (ATAGI);

- Earlier patient involvement into the decision making process. Learnings can be taken from other countries such as Canada, the Netherlands and the UK. Each county utilises the voice or view of the patient in slightly different ways; however all are consistent in making it a form of standard practice occurring throughout the assessment process;
- Establish a process for tiering of submissions with the intention of streamlining the overall PBS application process. This includes streamlining of simpler minor or cost-minimisation submissions, or submissions for rare diseases with low budget impact to allow more time for consideration of complex cost-effectiveness or cost-minimisation submissions;
- Implementation of an online portal for the provision of PBAC submissions and correspondence during the process between the PBAC secretariat and the sponsor;
- Reviewing the current process for the assessment of co-dependent technologies to address the substantially longer evaluation process for targeted therapies than non-targeted therapies;
- Reviewing the current process for PBAC hearings for sponsors and the inclusion of consumer hearings to ensure most value for the PBAC during the decision making process. Innovative delivery methods for hearings could be considered, including via video link or teleconference; and
- Regular monitoring and reporting of how the PBAC Guidelines are being used in practice going forward and rolling updates to ensure they remain consistent with the updated literature and remain world's best practice. Medicines Australia understands the approach taken by the UK's National Institute for Health and Care Excellence (NICE) Decision Support Unit, enables methodologies to be updated easily outside of the guidelines document itself. Adopting this type of approach would reduce red tape and ensure the guidelines remain contemporary.

A comprehensive outline of other process issues identified by Medicines Australia for review including specific recommendations is outlined in appendix 1.

Medicines Australia notes that while PBAC processes are outside the scope of the current review, the Department of Health has made a commitment to also review and update PBAC processes to reflect current practice. Medicines Australia calls for this process review to be undertaken in parallel with the Guidelines review, and in doing so offers support to assist with this.

3. Follow a robust and transparent process with input from all relevant stakeholders and experts.

Process and timelines

Medicines Australia encourages the Department to ensure that the review follow a robust, reliable, predictable and transparent format such as the structure and key procedural steps that were recently enshrined in a revised Post Market Review Framework. To provide clarity of process and predictability for engagement, the post market review framework defines specific steps that include; public consultation on terms of reference, stakeholder forums, public submissions, and publication of a draft report for further consultation. For the Guidelines review a similar approach would require; public consultation on the issues for consideration (underway), publication of and consultation on the resulting issues papers, transparency of the PBAC's consideration of the issues and the submissions, and a final consultation on the proposed revised guidelines in their entirety.

Medicines Australia acknowledges that the review is intended to be completed by 30 June 2016 with new guidelines to be published in that timeframe or shortly after. Whilst Medicines Australia encourages a timely review and update of the guidelines, this should not be at the expense of an in-depth and wide ranging review to ensure they are aligned with world's best practice. To that end, should particular methodological issues be identified that require further or more detailed scrutiny, discussion or consultation, Medicines Australia calls for these to be carved out from the review to be dealt with by a separate and dedicated subgroup to ensure the issues are sufficiently addressed.

Medicines Australia acknowledges the expertise of the membership of the GRSC including local and international experts in HTA. However, this should not preclude the GRSC or AHTA seeking advice from, or including, other experts in their respective fields during the review in the development and review of issues papers. A wide ranging review that seeks to include a broad church of stakeholders including all relevant local and international technical experts will be better able to deliver world's best practice guidelines.

To this end Medicines Australia also calls for the methodological issues identified for review to date, and during this consultation process, to be published and consulted upon further. Medicines Australia also welcomes further public consultation on the issues papers once drafted.

Implementation of new guidelines

Medicines Australia expects that updated guidelines will be welcomed by its membership and the broader industry if they live up to the promised expectations. That is to incorporate a 'world's best practice' approach to methodological progress and improved collaboration on understanding the full value of medicines.

As with previous policy changes, Medicines Australia recommends that considerable education will be necessary following the release of the new guidelines. This could include a roadshow to workshop the new guidelines or any associated process changes. Medicines Australia would be happy to assist the Department of Health in conducting such activities and welcomes further dialogue on this.

Such educational activities would be of benefit to not just the industry, but the evaluators, PBAC and subcommittee members and service providers within the industry. Ensuring a common understanding and interpretation of the guidelines, including their intersection with the PBAC remit as outlined in Section 101 of the National Health Act (1953) is imperative.

Summary:

Medicines Australia acknowledges that a review of this nature is multifaceted and complex, and that the issues raised in this submission may not be exhaustive. Medicines Australia looks forward to the opportunity to raise other issues during the review as necessary, either through the GRSC or further public consultation.

Timely access to new, safe and effective medicines is a shared goal of the government, the PBAC, patients and the industry Central to this goal is a predictable and robust PBAC process underpinned by world's best practice methods and guidelines. Medicines Australia again welcomes the commencement of the review and encourages the development of high-quality and fit-for-purpose guidelines that incorporate new, updated and proven methodological approaches.

Appendix 1: Submission to the Guidelines Review Steering Committee Review of the PBAC Guidelines – 27 July 2015

APPENDIX 1

MEDICINES Australia

Submission to the Guidelines Review Steering Committee

Review of the PBAC Guidelines

July 27, 2015

APPENDIX 1

BACKGROUND:

Announcement of the PBAC Guidelines Review

The Minister for Health, Sussan Ley announced (on April 25th) a review of the PBAC submission Guidelines. Ms Ley said the Guidelines are used by the pharmaceutical industry to prepare submissions to the PBAC so it can assess whether a product should be included on the Pharmaceutical Benefits Scheme (PBS).

"This review demonstrates a proactive approach from the Pharmaceutical Benefits Advisory Committee to ensure the guidelines remain appropriate," Ms Ley said. *"It is particularly timely given emerging technologies and international calls for Governments to subsidise drugs based on changing evidence, as is the case with cancer drugs."*

Ms Ley said the PBAC guidelines were regularly reviewed to make sure the submission and assessment process remains consistent and transparent, while incorporating international best practice and removing any unnecessary regulatory burden on the pharmaceutical industry.

"The PBAC Guidelines help ensure Australians have access to safe, clinically proven and cost-effective medicines as soon as possible," Ms Ley said. *"The Guidelines incorporate international best practice and remove any unnecessary regulatory burden on the pharmaceutical industry while safeguarding the sustainability of the PBS so it can benefit future generations. We welcome the PBAC's decision to review the Guidelines and maintain Australia's standing as a world leader in health technology assessment."*

The Review will address technical methods issues raised by the PBAC and stakeholders since the last substantial revision. The Review will develop a methods guidance replacing Parts II and III and some of the appendices of the current Guidelines as well as revising the overall procedures for lodging submissions.

An external contractor has been appointed (South Australian Group) and will develop the methods guidance with the support of the Guidelines Review Steering Committee (GRSC). The GRSC consists of Australian and international experts to ensure that the Guidelines are of the highest quality and that they continue to reflect best international practice.

Medicines Australia's Response

In a media release April 27th 2015, Medicines Australia (MA) welcomed the announcement of a review of the PBAC Guidelines.

"*We are pleased that the Government has announced that a review of the PBAC Guidelines will be undertaken,"* MA's CEO, Tim James, said. *"Any opportunity that we can have to improve the quality of our health technology system in Australia must be taken, for Australia to keep pace with the rest of the world."*

The volume and depth of information provided by pharmaceutical companies to the PBAC in health technology submissions is large and growing. As new technologies are developed and drug discovery and research becomes more complex and targeted to specific genetic variations, it is critical to continuously review the guidelines that underpin the system.

"Medicines Australia is committed to good, high quality health technology assessment in Australia and is always ready to work with the government to ensure this is achieved," Mr James said. *"Medicines Australia would also welcome regular monitoring and reporting of how the guidelines are being used in practice. This would help to establish whether*

improving the guidelines leads to improved access to medicines for Australian patients. Further, this provides a perfect time to review health technology assessment methods and a timely consideration of how to better capture the full value that medicines provide to the population, as well as to the participation and productivity of Australians.

"The Pharmaceutical Industry is always ready to work with Government to ensure the goals of the National Medicines Policy are supported and advanced. We have already demonstrated our commitment to ensuring a sustainable Pharmaceutical Benefits Scheme and we will continue to support measures that recognise the value of innovation through best practice health technology assessment."

MA's Thoughts on Potential Areas for Review

The PBAC Guidelines are viewed by MA's member companies as an integral component of the HTA-based medicines reimbursement system we have in Australia. As such, MA supports the PBAC Guidelines Review project and believes this initiative is a great opportunity to update, streamline and incorporate the latest HTA methodological thinking within the PBAC Guidelines.

MA notes that in order to help define issues for potential work-up into version 5.0 of the PBAC Guidelines, evaluators and members of the ESC, DUSC and PBAC were surveyed. MA believes that valuable insight into the relevance and practicality of the current version of the PBAC Guidelines can also be garnered from sponsor companies. As such, MA sought feedback from member companies as to potential areas within the Guidelines that need review &/or drafting of new guidance – with the overall intent being to provide a summary paper to the GRSC and contractor responsible for producing version 5.0 of the PBAC Guidelines.

The feedback from MA sponsor companies has been summarised under the following 3 headings:

- **Guidance specific to pre and post PBAC processes,**
- **Guidance specific to Sections A-F of PBAC Guidelines, and**
- **Processes & guidance from other HTA & reimbursement systems that may enhance PBAC decision making.**

It may be that some of the proposals for consideration fall outside the scope of the current review (e.g. category 3). However it was deemed an opportune time to collate the current views of MA sponsor companies in relation to HTA guidance both locally and more broadly.

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MA RECOMMENDATIONS FOR THE GUIDELINES REVIEW:

Guidance Specific to Pre and Post PBAC Processes

RECOMMENDATION # 1

MA proposes that aspects within the current version of the PBAC Guidelines related to pre PBAC processes (i.e within the *Introduction* and *General Information* Sub-sections) be:

- updated to reflect process changes since the last revision,
- expanded to include post PBAC processes, and
- carved off as a document/ resource/ portal to be used in conjunction with the core PBAC Guidelines – thereby assisting with the objective of streamlining the PBAC Guidelines specific to technical/ methodological guidance.

Understanding pre and post PBAC processes is an integral part of the sponsor's role in partnering with the Department to list medicines on the PBS. While some aspects of the pre PBS listing process are captured within the current version of the PBAC Guidelines, there are significant gaps, as well as recent changes to PBAC processes that need to be captured in a more fulsome processes document.

MA proposes that a separate workstream be initiated to draft a PBS processes document/ resource/ portal that can be used in conjunction with version 5.0 of the PBAC Guidelines. MA details below the pre and post PBAC processes that it proposes be covered in the PBS processes reference document/ resource/ portal.

Pre-PBAC Processes:

Pre-PBAC submission meetings: These meetings are an important part of the submission process as not only do they enable the sponsor to seek guidance from the Department of Health (DoH) on particular issues the sponsor sees as associated with the intended drug, but they also provide a form of horizon scanning for DoH. Guidance required includes i) to whom the request is to be sent, ii) a link to the briefing template, iii) guidance on DoH's objectives for these meetings, iv) timing of pre-PBAC submission meetings.

17 week PBAC process: Documentation of this to be continued in the PBS processes reference, BUT to also work in cross-reference and a flow chart specific to the co-dependent process.

PES commentary & ESC Advice: Guidance on timing, process and focus to be provided. In addition, sponsors see the need for the system to formally provide acknowledgement of which issues have been answered adequately by sponsors in their pre-ESC / DUSC Responses.

Parallel process & Delegate's Overview: Clarity around the cut-off for the timing of the TGA Delegate's Overview is required.

PBAC Hearings: Guidance on timing, process and focus to be provided along with link to MA guidance on PBAC Hearings. Currently, the timeframe for requesting a PBAC hearing and receiving a date and time is problematic with respect to engaging a relevant expert to present at the PBAC hearing. It may be that timing could be improved if sponsor companies requested a listing the Thursday post receipt of the ESC/DUSC advice and the Department provided a PBAC hearing date and time on the Friday.

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Post-PBAC Processes:

The objective of formally including this section within a processes reference document/ resource/ portal is to provide sponsors with guidance for the Post-PBAC period. Regardless of whether a sponsor receives a positive or a negative PBAC recommendation, there are activities which must be initiated. The need for post-PBAC process advice is particularly relevant for sponsors receiving a positive recommendation, as the situation is unclear since the abolition of the Pharmaceutical Benefits Pricing Authority (PBPA) in April 2014 (although references to the PBPA remain on the current Dept. of Health website). MA notes that the absence of clear guidance on post-PBAC requirements & a framework creates uncertainty and promotes inefficiency, which is contrary to the Govt / Dept.'s stated objective of achieving timely listings and minimising red tape (noted to be a key reason for abolishing the PBPA[1]). MA proposes that a flowchart (specific to both rejected and approved PBAC outcomes) be drafted to assist sponsor companies navigate through both the post-PBAC processes.

Potential PBAC Process Improvements:

As an adjunct to the above recommendation for a pre and post PBAC processes reference document/ resource/ portal, MA also wishes to provide feedback from sponsor companies as to potential ways that have been mooted to improve the PBAC process and untimately deliver timely access to new medicines via the PBS**.**

i) Early multi-stakeholder meetings. With the increasing complexity of many medicines, it is apparent that expert advice is required early in the process, and ideally well in advance of the development of the submission to the PBAC. An early multi-stakeholder meeting would be expected to overcome many of the problems currently seen during the evaluation of complex medicines and is likely to reduce 'submission churn'. This approach is successfully undertaken in other jurisdictions (e.g. the NICE in the UK reviews the drug and therapeutic area and agrees the decision problem to be addressed by the sponsor in its submission).

ii) Tiered or fit-for-purpose submissions. As recently proposed by other stakeholders (e.g. the Cancer Drugs Alliance), a fit-for-purpose PBAC system may lead to efficiency gains. For example, a system that has a more comprehensive evaluation for complex applications that are often associated with higher budget impact and therapeutic value, while a less comprehensive evaluation is proposed for treatments associated with a low budget impact, treatments for rare diseases and those with a comparable clinical benefit and cost to existing therapies.

iii) Minor submissions and parallel process. Currently, minor submissions are unable to be considered via the TGA/ PBAC parallel process system. Minor submissions are potentially ideally suited for parallel assessment and should be able to proceed down this pathway.

iv) Co-dependent process: While the co-dependent process leads to improved access timings compared o some MSAC decisions of the past (>5 years), there are still efficiencies that can be gained and should be investigated. Drug-test pairings should not be penalised by greater complexity and longer timeframe to patient access than their non co-dependent counterparts.

[1] http://www.pbs.gov.au/info/news/2014/03/streamlined-pbs-pricing

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Guidance Specific to Sections A-F of PBAC Guidelines (Technical/ Methodological)

RECOMMENDATION # 2

MA proposes that:

- edits identified in the table below be directly incorporated into V 5.0 of the PBAC Guidelines,
- suggested changes to the Guidelines in the table below be considered by the GRSC &/or contractor, and
- potential issues papers identified in the table below also be considered by the GRSC & contractor - alongside the issues papers identified in i) the Schedule of work, and ii) from the survey of evaluation groups, ESC, DUSC and PBAC.

RECOMMENDATION # 3

MA proposes that:

- working groups be established per each issues paper to assist with the planning and initial drafting of potential guidance.

MA, academia, the Department and the PBAC have had a long history of working collaboratively to ensure the PBAC Guidelines are a "living-document", relevant for sponsor companies, evaluators and the PBAC. Working groups specific to i) indirect comparisons, ii) surrogate to final outcomes and iii) compliance to medicines were the last examples where MA, the Department and the PBAC worked together to construct issues papers delivering appropriate guidance. Unfortunately, competing priorities over the last 2 years has meant that this guidance has not been formally included in the current PBAC Guidelines. As such, MA supports the current review's proposal to update these previously drafted papers for inclusion in version 5.0 of the Guidelines.

While MA believes that consolidation of this guidance within the upcoming revision is an obvious first step, it also believes the current review provides an opportunity to identify other technical/ methodological matters not previously raised or discussed. In an attempt to help identify potential topics for new issues papers, member companies were asked to provide areas of the PBAC guidelines where they felt additional information &/or clarification was needed. The table below consolidates the feedback so far from member companies and is separated into minor edits (•), suggested changes to the PBAC Guidelines (#), and potential issues papers for drafting and inclusion in the Guidelines (@).

MA notes that the evaluation groups, ESC, DUSC and PBAC were recently surveyed in an attempt to identify potential issues papers for future work-up. MA also notes that once selected, the contractor will draft the first version of the GRSC approved issues papers. MA requests that the potential issues papers identified in the table below also be included in the GRSC discussions specific to future work and that the GRSC give serious consideration to having a broader group assist with the planning and drafting of the identified issues papers. This approach has worked well previously and may save time by reducing feedback via the public consultation process.

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PBAC Submission subsection	Required Edit &/or Suggested Change to Guidelines
Contents/ About these Guidelines	• **Page v – address for correspondence:** PBAC submission address has changed. • **Page xv – abbreviations:** a number of abbreviations need to be added/ deleted (e.g. MAP, SPA added; PBPA deleted). • **Page xvii – what are the PBAC guidelines?:** URL needs to be added. • **Page xxii – part III additional information requests for specific types of products:** URL needs to be added. • **Page xxiv – associated documents:** URL needs to be added. **# Page xxiv – associated documents:** Manual of Resource Items - Needs updating as current version dated December 2009; updating in area of oncology esp needed - suggest include links to any oncology / haem Guidelines, such as NSW EviQ, etc. **# Page xxiv – associated documents:** Sources of Epidemiological Data – update and involve input from MOGA & COSA as to what sites they would recommend for onc/haem disease. • **Page xxv – submission forms:** URL needs to be added. --- # **Page xxii – part III additional information requests for specific types of products:** amend process to allow parallel process for vaccines. # **Page xxiv – associated documents:** add co-dependent process document; add pricing toolbox developed by MA; add Managed Access Program document; update Manual of Resource Items
General Information	• **Page 3 - 1.3.1:** "y" missing off efficacy. • **Page 5 - Box 1.2:** "t" missing off not (in printed version). • **Page 6 – 1.3.5:** end letters missing off words "the, use, the, with" on printed document. • **Page 7 – 1.4.2:** change PBAC minutes provided **"**within 20 working days of a meeting" to "within 25 working days of a meeting". • **Page 7 – 1.4.2:** delete reference to PBPA. • **Page 8 – flowchart 3:** amend timing of receipt of PBAC minutes from "3 weeks after" to "5 weeks after". • **Page 9 – 2:** add "but" between "submissions" and "might" within resubmissions bullet point. • **Page 39 – 5.1:** remove fullstop after submissions; remove fullstop after below; add fullstop after checklist. • **Page 41 – 5.1:** remove fullstop after available; remove fullstop after format. • **Page 44 – 5.3:** add y to end of "identified b"; correct "different". --- # **Page 1-44 – Significant updates and additions needed to Part 1 of the PBAC Guidelines.** Could this General Information on pre, during & post PBAC processes be separated from the PBAC Guidelines as a document/ link to be read in conjunction with the PBAC Guidelines? This would assist in delivering a streamlined technical document. # **Page 6 – 1.4 Processing submissions:** currently outlines ability for parallel process and 2 opportunities for written pre-PBAC consultation documents for sponsors. Information specific to the opportunity for a pre-PBAC submission meeting, a PBAC hearing and a post PBAC rejection meeting (along with links to pre-PBAC submission template & MA guidance on PBAC hearings) would add significantly to this sub-section. # **Page 7 – 1.4.1 Sources of advice:** Information specific to the process for provision of consumer &/or professional body advice (e.g. 10 weeks prior to PBAC meeting) along with a link to the PBAC form/ template would add significantly to this sub-section. # **Page 8 – Flowchart 3:**Depending upon where co-dependent submissions are discussed, design a similar flowchart specific to the co-dependent process. # **Page 35 – 3.4:** Within this uncertainty section reference to SPAs and MAPs as potential tools to manage remaining/ key uncertainties – along with link to these documents. # **Page 40 – Key Documents:** costs data for PB11 not usually available at time of submission. # **Page 44 – 5.3:** include requirement that the TGA delegate's overview is required 1 week

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	before the PBAC meeting for a recommendation to be made.
Section A	**# Disease area overview –** often used by sponsors to provide context upfront. Formalise a sub-section within Section A to cater for presentation of the disease area overview. **# A.1 – Requested PBS and pharmacological class and action:** **# A.2 – Indications and requested restriction:** include criteria for streamlined authority and authority only restrictions. **# A.4 – Main comparator:** Swap Main Comparator section (A.4) with Treament Algorithm section (A.5). Presentation of the current treatment algorithm will then be able to flow into determination of the appropriate Main Comparator. **@ A.4 – Main comparator:** Develop an Issues Paper that provides greater clarity and guidance around when to use i) a single comparator, ii) multiple comparators, ii) a non PBS but TGA listed comparator, iii) a non PBS non TGA listed comparator, & iv) a potential future comparator/s. **# A.5 – Clinical management algorithms:** Swap to before Main Comparator section. **# A.6 – Differences between the proposed medicine and the main comparator:** Delete as is essentially a copy and paste of label information from Product Information sheets.
Section B	# Using **CONSORT** or **PRISMA** statements as a guideline for how to present evidence may assist with reducing length of Section B. **# B.4 – Characteristics of the included clinical trials:** address applicability of trial design and patient characteristics here rather than Section C. **# B.5 – Outcome measures of the included clinical trials:** following review and update, include summary and reference/ link to i) methods for indirect comparisons from the Indirect Comparisons Working Group, & ii) methods for dealing with patient cross-over from the DoH paper (e.g. website or appendix to Guidelines). **@ B.5 – Outcome measures of the included clinical trials:** Develop issues papers specific to i) network meta-analysis, ii) MCID, iii) superiority claims in the absence of H2H data, iv) comparative effectiveness using subgroup analyses, and v) Bayesian methodologies. Include summary and reference/ link to papers (e.g. website or appendix to Guidelines). **# B.7 – Extended assessment of comparative harms:** Delete as post marketing safety is primarily remit of TGA.
Section C	**# C.1-C.4** - Re-align order of Section C so that each issue is dealt with in a sequential fashion **# C.2 – Focused analytical plan:** following review and update, include summary and reference/ link to i) surrogate to final outcomes from the STFO WG (e.g. website or appendix to Guidelines).
Section D	**# D.5 – Results of economic evaluation:** emphasise that the stepped approach is not there as a means to revert back to the trial-based analysis, but to see the impact of changes at each step. **@ D.6 – Sensitivity analyses:** Develop issues paper specific to i) probabilistic sensitivity analyses and reference/ link to paper (e.g. website or appendix to Guidelines).
Section E	**# Section E - Spreadsheets:** i) removal of duplication across worksheets will make them more user friendly ii) improve consistency between Minor & Major submission section E spreadsheets or just have one template for both types of submission **# Section E - General**: align guidance with excel spreadsheets requirement for estimates over six years; and split PBS, RPBS and effective and list prices as per spreadsheets. **# Section E.1- Justification of data sources:** provide guidance on acceptable data sources for an epidemiological approach in very small indications (e.g. utilising Compassionate Use Program data) to estimate patient numbers **# Section E.6- Identification of uncertainty:** provide guidance on when and how to use univariate or multivariate analyses.

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Section F	**# F.2 – Risk Share Arrangements:** include summary and reference/ link to Managed Access Program Framework considered at the March 2015 PBAC meeting (e.g. website or appendix to Guidelines). **# F.3 – Other Information:** include potential for non-randomised trials information/ data to be described here.
Appendices	• **Page v – address for correspondence:** PBAC submission address has changed. • **Page xv – abbreviations:** a number of abbreviations need to be added/ deleted (e.g. MAP, SPA added; PBPA deleted). • **Page xvii – what are the PBAC guidelines?:** URL needs to be added. • **Page xxii – part III additional information requests for specific types of products:** URL needs to be added. • **Page xxiv – associated documents:** URL needs to be added. • **Page xxv – submission forms:** URL needs to be added. # **Appendix 1:** update second half of appendix 1 to refer to the current review process, PBAC Guidelines Steering Committee, and potential topics for consideration in future reviews of the guidelines. # **Appendix 3:** remove references to PBPA; review and edit text in light of PBAC's review of restrictions. # **Appendix 6:** update to reflect latest literature on MCID. # **Appendix 7:** complement with link to currently validated/ accepted utility values by disease area. # **Appendix 10:** provide link to Section E spreadsheet # **Potential Additional Appendices** - summary of co-dependent process - summary of Managed Access Program requirements - summary of consumer input process (& link to submission template) - summary of Indirect Comparison Guidance - summary of STFO Guidance - summary of Compliance to Medicines Guidance - summary of patient cross-over in clinical trial guidance - summary of PBAC views on WTP, societal input, etc - summary of Fixed Dose Combination requirements (refer to PSD from naproxen-esomeprazole FDC independent review 2013) (If the above aren't included within Main body of PBAC Guidelines, then include as appendices or reference and provide links)
Other	**# Create a portal or portals to document processes & methodologies that have been accepted.** - similar to the NICE DSU publications. Allows flexibility with no need to update guidelines each time a process/ method has been accepted.

• Edit **#** Suggested Change **@** Potential Issues Paper

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Processes & Guidance from other HTA & Reimbursement Systems that may Enhance PBAC Decision Making:

RECOMMENDATION # 4

MA proposes that overseas HTA 'best practices' and HTA research initiatives outlined below be discussed by the GRSC for potential inclusion:

- within PBAC processes and/or within version 5.0 of the PBAC Guidelines, or
- as future issues papers examining ways to improve subsidised access to medicines in Australia.

MA notes the extensive public discussion from non-industry stakeholders in regard to PBAC decision-making in recent times, particularly in regard to the differences between the approaches to reimbursement decision-making in Australia compared to the rest of the world. In fact, the availability, or not, of subsidised access to medicines in Australia compared to other similarly developed jurisdictions has been the subject of a number of recent papers & reports. The reasons for the disparity is a matter for concern, with a suggestion that this could be due to the Australian system 'lagging behind' other jurisdictions where Health Technology Assessment (HTA) principles are also used to determine public funding of health technologies, such as medicines.

MA therefore believes that the upcoming PBAC Guidelines Review is an opportune time to also review current best-practice from other HTA-based jurisdictions. MA applauds the appointment of Andy Briggs to the GRSC, as well as the engagement of Professor John Karnon, Professor Mark Schulper, Professor Michael Drummond, Professor Elizabeth Roughead, Dr Hossein Afzali & Mr Thomas Sullivan as methodological consultants. The opportunity to tap into the academic insight and broad knowledge of other HTA reimbursement systems will be crucial to ensuring version 5.0 of the PBAC Guidelines is state of the art.

To assist with identification of potential HTA 'best practices' from overseas that are worth considering in the context of this PBAC Guidelines Review, MA has collated examples provided from sponsor companies specific to the UK, Scotland and Canadian systems (see below). In addition, HTA based initiatives currently being undertaken by specialist bodies such as EUnetHTA and HTAi have been provided in Table 1 for consideration by the GRSC.

United Kingdom (NICE – Decision Support Unit); Web: http://www.nicedsu.org.uk/

The Decision Support Unit (DSU) is commissioned by the National Institute for Health and Care Excellence (NICE) to provide a research and training resource to support the Institute's Technology Appraisal Programme. The DSU is a collaboration between the Universities of Sheffield, York and Leicester. It also has members at the University of Bristol, London School of Hygiene and Tropical Medicine and Brunel University.

NICE's Decision Support Unit (DSU) provides a variety of services which support the formal NICE evaluation process. The sections under the DSU umbrella include:

- Methods Development: these provide guidance on methodological issues associated with different topics such as End-of-Life, mapping of EQ-5D (i.e., estimation of health utilities from clinical outcomes), adjusting for survival where cross-over has occurred in a trial,

effects of treatment on Quality of Life (QoL) in oncology, weighting of QALYs, etc. Other topics recently explored include accounting for the value of innovation and software review.

- Appraisal Specific Projects: these provide guidance on a technology in a specific clinical area or a therapeutic area in general, for example, cetuximab in colorectal cancer and Crohn's disease, respectively.
- Technical Support Documents: these provide guidance on specific topics relevant to HTA, including the synthesis of evidence, utilities, how to review the parameters in an economic model, survival analysis, patient level simulation, accounting for switching between treatments and the use of observational data.

The public availability of this information (which is an academically rigorous synthesis of the agreed position for each topic) is invaluable as it provides clarity and certainty to all parties involved in developing and evaluating a reimbursement application.

The DSU also provides training on behalf of NICE, which is available to the NICE technical team, appraisal committee members and those submitting evidence, including industry, consultancies and academic groups. The training covers general issues around technology assessment and appraisals, the application of specific methods in areas such as evidence synthesis and the use of software for decision modelling.

The adoption of a DSU-like approach in Australia would be of great value to all stakeholders involved in developing submissions to the PBAC. Not only would it enable efficiencies by providing a means whereby all stakeholders could access agreed positions on particular issues, it would enable a dialogue between the stakeholders, including the evaluation centres. By all following an accepted methodology, it would also assist with reducing submission churn. This also provides flexibility, as there would be no need to continually update the Guidelines each time a process/method has been accepted.

Scotland (Scottish Medicines Consortium [SMC]); Web:
https://www.scottishmedicines.org.uk/About_SMC/What_we_do/index

The SMC is a committee of clinicians, board representatives from the National Health Service (NHS), the pharmaceutical industry and the public, all of whom have a vote. Most of the clinicians have a direct role in patient care, while the three volunteer public partners ensure the views of patients and carers are taken into account during decision-making. This wide mixture of backgrounds helps ensure decisions are made from a broad perspective. SMC meetings are open to the public.

The SMC process actively involves pharmaceutical industry, not only by it having representatives on the Committee itself, but via the SMC User Group Forum, which first met in August 2002. Since the SMC established its systems and processes, the SMC has worked collaboratively in building positive relationships with the Association of British Pharmaceutical Industry (ABPI), meaning representatives of ABPI have been involved with the SMC and its processes from an early stage. SMC and ABPI have fostered a strong relationship and ABPI continues to offer unfailing commitment to the process with representation on both the New Drugs Committee (NDC) and SMC.

There are several notable features of the SMC process that potentially improve the decision-making for the funding of new technologies, including:

APPENDIX 1

1. The SMC User Group Forum
2. Capturing the Patient and Care Voice
3. Patient and Clinician Engagement (PACE)

1. The SMC User Group Forum (SMC UGF)[2]

The SMC UGF comprises representatives of the pharmaceutical industry - people with hands on experience of handling Health Technology issues for companies – who meet quarterly, with those from the SMC, including representatives of the SMC Executive, the NDC, pharmacy and health economic assessors and the Secretariat. The aim of the group is to identify, address and resolve process issues relating to the work of the SMC.

Their priorities for 2014 include:

- Review of orphan and 'End of Life' (EoL) medicines - finalisation of the detailed methods and process.
- Meetings in public - ensuring confidentiality is handled appropriately
- Ensuring companies fully understand the changes and support maintaining the efficiency of the SMC processes. The immediate focus will be on educating companies on the changes related to orphan and EoL medicines

The SMC UGF also aims to increase the involvement, support and education of companies, in particular those who infrequently make submissions to the SMC, with the aim of improving the quality of their submissions.

2. Capturing the patient and Carer voice

SMC actively engages with the Health Technology Assessment international (HTAi), the global scientific and professional society for all those who produce, use, or encounter HTA. The HTAi interest sub-group for patient involvement in HTA has developed values and quality standards for patient involvement in HTAs. By adopting the principles laid out by the HTAi's sub-group, the SMC has committed to achieving the HTAi's vision that patient and citizen perspectives improve HTA. As such, the SMC works in partnership with patient groups to gather the perspectives of the patients and their carers.

3. Patient and Clinician Engagement (PACE)

Following an extensive review, the SMC has changed the way it evaluates end of life medicines and medicines to treat very rare conditions. From May 2014 pharmaceutical companies have been able to request that SMC convenes a PACE group to review their medicine following the issue of the draft report from the formal SMC process.

The PACE process gives patient groups and clinicians a stronger voice in SMC decision making. In addition, the assessment process for ultra-orphan medicines will involve a broad decision-making framework. Because the benefits of a medicine, including how it can impact the quality of a patient's life, may not always be fully captured within the conventional assessment process, the main purpose of PACE is to gather detailed information which will allow an informed discussion on this topic.

[2] Source: https://www.scottishmedicines.org.uk/About_SMC/What_we_do/Industry_Involvement

APPENDIX 1

Since the new process was introduced SMC has received an increased number of submissions for these medicines. The submissions received in May and June 2014 have been prioritised for assessment on the basis of feedback from Area Drug and Therapeutics Committees and Regional Cancer Networks on patient need. The SMC agreed with the service and ABPI that from July 2014:

- The monthly submission dates that SMC generally works to will be removed for medicines for end of life /orphan conditions
- Submissions for these medicines will be scheduled for assessment in order of date and time received
- For medicines where there is exceptionally high patient need, e.g. no other treatment available, SMC may schedule the submission earlier

Canada (Canadian Agency for Drugs and Technologies in Health [CADTH]); Web: https://www.cadth.ca/

Via CADTH, under the heading Collaboration and Outreach[3], the Canadian approach to HTA involves a commitment to sharing of best practices and partnerships between Government, specialist HTA bodies such as HTAi and EUnetHTA, academia & industry.

CADTH also provides a variety of resources that enables sponsors to find, produce, interpret, and implement evidence. These include software applications, search tools, customized Excel spreadsheets, and more. Examples of these 'support' resources are the tools provided under the topic 'Finding the Evidence: Literature Searching Tools in Support of Systematic Reviews'.

CADTH has two review processes: the CADTH pan-Canadian Oncology Drug Review (pCODR), which deals specifically with cancer drugs, and the CADTH Common Drug Review (CDR), which deals with other drugs. Both pCODR and CDR are designed to bring consistency and clarity to the assessment of drugs in Canada by reviewing clinical, economic, and patient evidence, and using this information to make non-binding recommendations to Canada's public drug plans to support their drug funding decisions. Similar to the Scottish and UK systems, both review processes enable the patient perspective to be comprehensively incorporated into the HTA decision-making process.

CADTH also offers pharmaceutical companies advice on their early drug development plans from a health technology assessment perspective via the CADTH Scientific Advice Program[4].

[3] https://www.cadth.ca/collaboration-and-outreach/partnerships-and-linkages
[4] See at CADTH Scientific Advice Program.

APPENDIX 1

Table 1. HTAi/EUnetHTA supported initiatives

Topic	Country	Outline of approach	Benefits to stakeholders
Formal stakeholder engagement and explicit stakeholder input into listing decisions	UK, Netherlands, Sweden, Canada, Scottish Medicines Consortium (SMC) Also endorsed by HTAi interest subgroup for patient and citizen involvement in HTA.	All major stakeholders actively participate in and own the approval process for new technologies. In Canada, patient evidence is provided as part of the submission from the beginning of the process.	High. Allows inclusion of additional, relevant voices and more informed decision making. Increased transparency.
Simplified rapid HTA process	Netherlands, Sweden, SMC, EUnetHTA	Tiering of submissions based on complexity, unmet need, clinical benefit, rarity and budget impact. Opportunity for early engagement with multiple stakeholders. Ability to focus assessment resources where they are most needed, and simply and speed up items where they are not. Ideal in an environment of resource constraints.	Reduces bureaucratic and sponsor resources upfront. Reduces resubmissions by addressing issues early. In SMC, submissions for rare diseases and end of life medicines may be submitted at any time, not just certain times during the year, and may be reviewed earlier.
Wider societal benefits explicit, broader definition of value	Netherlands, Sweden, Germany, EUNETHTA core domains	Incorporates productivity gains, caregiver benefits, welfare costs, organizational issues (ie. admin efficiencies), and ethical issues Could be assessed using Multi-Criteria Decision Analysis	True value of medicines realized. Takes a broader perspective therefore highlights importance of medicines beyond health and health budget.