Submission to Australian Government
Review of Health Technology Assessment (HTA) in
Australia

May 2009
Executive Summary

Health Technology Assessment (HTA) is becoming an increasingly important and sophisticated tool that has the potential to assist governments and other payers to allocate scarce healthcare resources where they are most effective and needed within a health system. A well managed, best practice HTA system has the potential to assist payers in making informed decisions about allocating such resources in the health system. An HTA system that is not well managed or does not align with best practice operating principles runs the risk of inefficiently allocating resources, failing to meet health outcomes, sending distorted signals to medical technology providers and denying patients appropriate access to medical technologies.

There are a number of key principles that Medicines Australia (MA) believes should underpin any HTA based system to ensure that such a system is achieving its policy objectives. These are derived from the collected experience of the pharmaceutical industry in Australia and supported by international scholarly literature. These include:

- maintaining the separation of the registration and reimbursement processes;
- a preference for HTA to be conducted from a broad societal perspective rather than a narrower “payer’s” perspective;
- HTA, as a technical analysis, to be one input into the decision to reimburse a technology, along with other considerations including clinical need, prevalence of disease, ethical and equity issues, and incentives to drive technology innovation;
- appropriate transparency around the assessment, appraisal and decision making processes, including the criteria used to make a recommendation;
- ensuring that there is appropriate separation of powers between payers, policy-makers, program administrators, evaluators and decision-makers;
- wide stakeholder input into the HTA appraisal and decision making, including from consumers and consumer organisations, health professionals and industry;
- public disclosure of decisions and reasons for recommendations to reimburse or not reimburse a technology, and
- appropriate accountability measures, including an appeals procedure, quality assurance programs/audits of evaluations, and the publication of system performance indicators.

In addition to these principles, a number of issues concerning the technical application of HTA are presented for debate by the Review. These cover issues such as:

- the need for clear guidelines
- the need to include all costs and benefits regardless of to whom they accrue
- choice of comparator
- the appropriate use of evidence, and
- methodologies of economic evaluation.

MA welcomes the opportunity to contribute to the Australian Government’s HTA Review. The Review’s objective is to “recommend options for improving the process efficiency and reducing the regulatory burden for Commonwealth HTA processes to
facilitate medical innovation without compromising timely and affordable patient access
to medical services and devices”.

MA has worked closely with the Australian Government over the years to refine and
improve the HTA framework within which the Pharmaceutical Benefits Advisory
Committee (PBAC), the key pharmaceutical HTA evaluation body in Australia, operates.
The PBAC advises the Australian Government on listing medicines for reimbursement
on the Pharmaceutical Benefits Scheme (PBS).

MA continues to be an active partner with the Government and other stakeholders in the
evolution of the PBS listing process. This partnership has led to gradual improvements
over time to the processes and frameworks for assessing the relative clinical-
effectiveness, safety and cost-effectiveness of pharmaceuticals for the purposes of
listing on the PBS. However, it is important to note that this remains a dynamic and
demanding area that requires ongoing engagement by all stakeholders, including
industry. While pharmaceuticals, arguably, have the most rigorous and structured HTA
system compared with other areas of Government health funding in Australia, there are
still a range of issues in that system that require review, analysis and dialogue between
industry, government, consumers and other stakeholders.

1. **Introduction**

Medicines Australia (MA) represents the innovative medicines industry in Australia. Its
member companies comprise more than 80 percent of the value of sales of prescription
pharmaceuticals in Australia and are engaged in the research, development,
manufacture, supply and export of prescription medicines.

MA notes that Health Technology Assessment (HTA) is becoming an increasingly
important and sophisticated tool that has the potential to assist governments and other
payers to allocate scarce healthcare resources to where they are most effective and
needed within a health system. Australia has embraced HTA for pharmaceuticals but
other areas of healthcare have not adopted HTA to the same extent. As such MA
welcomes the opportunity to contribute a submission to the Australian Government’s
Review of Health Technology Assessment in Australia (HTA Review). The objective of
this Review is to “recommend options for improving the process efficiency and reducing
the regulatory burden for Commonwealth HTA processes to facilitate medical innovation
without compromising timely and affordable patient access to medical services and
devices”.

Although, the Review’s Terms of Reference deal only obliquely with pharmaceuticals
(recognising already the sophisticated role of the PBAC and the PBS listing process) in
relation to hybrid and co-dependent technologies, MA believes that the industry has
much to contribute to any discussions on expanding/enhancing the role of HTA in other
areas of the Australian health system. The pharmaceutical industry, both in Australia
Medicines Australia - Submission to Australian Government Review of Health Technology Assessment (HTA) in Australia

and internationally, has extensive and growing experience in working within health systems that incorporate HTA as a key component of their health insurance provisions. MA welcomes the opportunity to share its learning in this area. As possibly the most experienced external stakeholder familiar with engaging with Australia’s complex and rigorous HTA system as it applies to pharmaceuticals, MA is uniquely placed to provide an informed external perspective on how HTA operates in Australia and how such systems should be designed in the Australian context. The Australian pharmaceutical industry’s experience with the development of the PBAC processes for HTA in Australia suggest that designing or reforming an HTA system from a set of guiding principles that in consultation with industry helps to ensure consistency and best practice HTA.

MA has long worked closely with the Australian Government to refine and improve the HTA based framework within which the PBAC operates and MA continues to be an active policy partner in the ongoing evolution of the PBS listing process. This partnership can be seen, amongst other things, in the current work of the Access to Medicines Working Group (AMWG), the ongoing development of the Guidelines for preparing submissions to the PBAC, the biennial MA-Department of Health and Ageing (DoHA) Joint Medicines Policy Conference, and the work developing and implementing the recommendations of the Post-PBAC Review. MA has also contributed substantially to a number of independent reviews relevant to the reimbursement of pharmaceuticals in Australia, most notably the 2005 Productivity Commission report into the Impacts of Advances in Medical Technology in Australia. This partnership has led to gradual improvements over time to the processes and frameworks for assessing the relative clinical-effectiveness, safety and cost-effectiveness of pharmaceuticals for the purposes of listing on the PBS, but it is important to note that this remains a dynamic and demanding area that requires ongoing engagement by all stakeholders.

2. **Scope of the MA Submission as it Relates to the HTA Review TOR**

In addition to addressing the specific Terms of Reference and related questions, this submission also presents what it believes to be a set of guiding principles that should underpin any expanded or better coordinated HTA system in Australia.

The submission pays particular attention to separating the evaluation, appraisal and decision making elements of a HTA-based system. It also notes the importance of maintaining adequate separation between payers and decision-makers, as well as policy-setters, program administrators, and evaluators.

Importantly, the submission also emphasises that formal HTA (understood as cost-effectiveness analysis) should be only one, albeit an important, input into decisions around reimbursement. Decisions need to reflect the values of the community to whom they are relevant and include considerations of the various social, legal and ethical dimensions pertinent to a health technology. Decisions to reimburse can also have an
impact on the broader economy in the sense that health technology adoption can result in improved productivity, as well as generate employment in local industry.\(^1\)

This has implications for the importance of wider stakeholder input to the process, the criteria used for reimbursement decisions based on HTA and the technical assessment itself. The broad scope of HTA and the importance of wide stakeholder input are highlighted throughout this submission.

In providing its guiding principles, MA recognises that the existing HTA processes for pharmaceuticals in Australia may not automatically translate to other health technology areas, such as medical devices. For example, the life cycle of a specific type or variation of a device is shorter (12-24 months) than a medicine as development is characterised by a constant flow of incremental product improvements. Too early an assessment of a technology might ignore both the learning curve phenomenon and the fact that the process of innovation in medical devices is one of continuous, often small incremental, improvements in close interaction with the users (physician or surgeon) of the technology. In addition, the clinical trial evidence available and relevant for a medical device will often not be the double-blind randomised clinical trial (RCT) as is often the case for pharmaceuticals. While focusing on lessons from the pharmaceutical experience, this submission points out key differences between medical devices and medicines in answering the key questions associated with each of the Review’s terms of reference.

There are important reasons for maintaining a clear separation between the registration and reimbursement processes and decision-making. The inclusion of the Therapeutic Goods Administration (TGA) within the terms of reference for the Review as an explicit HTA agency is curious. The TGA, Australia’s regulatory agency, evaluates health technologies for the purposes of permitting a health technology to be marketed in Australia. Its decision-making is concerned with assessing the risk-benefit balance of allowing a product to be purchased for use by consumers in the Australian market. HTA concerns the assessment of the relative clinical, safety and cost-effectiveness of a health technology for the purposes of allocating scarce taxpayer (or other insurance derived) resources. The decision-making “frame” for these regulatory and reimbursement evaluations are qualitatively different and it would be an error to conflate them.

Whilst the TGA should not be considered an HTA agency, MA does agree that there may be scope for further streamlining, coordinating or overlapping the evaluation processes of both the TGA and PBS processes to ensure the timely access to health technology for Australian consumers. This submission will limit itself on this issue noting that the current discussions between the TGA and the Access to Medicines Working Group (AMWG) on streamlining the regulatory and reimbursement systems in terms of overlapping timelines are highly pertinent to the HTA Review.
3. **Guiding Principles for a Good HTA System**

In presenting a set of principles that underpin a best practice HTA system, this submission draws on a growing number of scholarly papers in the published literature, as well as its own experience in working with the Department of Health and Ageing and the PBAC over many years. The submission divides the principles into policy level considerations relating to a HTA-based system, and those related to technical aspects of HTA itself.

**Broad Policy Principles**

- **HTA is a necessary but insufficient input to decision-making:** HTA, as a technical assessment of the clinical safety, effectiveness and cost-effectiveness of health technologies should be only one of a number of inputs into deciding whether to reimburse a health technology. Decisions need to reflect the values of the community to whom they are relevant (including its “willingness-to-pay”) and include considerations of the various social, legal and ethical dimensions pertinent to a health technology. These will include, but not be limited to, clinical need, disease prevalence, equity of access, equity of outcomes and the consideration of the health needs of future generations by the provision of incentives for ongoing research and development (see 4 below). MA believes that there is significant merit in clearly articulating the additional factors involved in HTA decision-making in Australia, similar to the Social Values Statement the United Kingdom’s National Institute of Health and Clinical Excellence (NICE) has produced.

- **The value of a health technology is most appropriately calculated from the “societal” rather than a narrow “health-system” perspective:** The issue of perspective is an important policy-level issue that needs to be made explicit and prioritised for debate in the review. The PBAC currently takes a minimalist perspective when determining the cost-effectiveness of a medicine. It considers almost exclusively the costs and benefits that accrue to the health-care system and recipient of care. When considering the “value” of a medicine, the PBAC takes little consideration to the benefits that may accrue to family members, carers, or to society in general (e.g. through increases in economic productivity). The failure to take a “societal perspective” when assessing a medicine risks introducing inefficiencies into the funding of the taxpayer funded health care system by distorting the understanding of the relative value of different health care interventions in the broader community and economy. The distorting effects of taking such a minimalist perspective were noted by the OECD in its recent report in global pharmaceutical pricing policies.\(^1\) MA’s position on counting both

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\(^1\) “In a free and unsubsidised market, the willingness and ability to pay of individual consumers would define price elasticity, suggesting that the payer perspective results in a better approximation of market outcomes. However, to the extent that there are externalities associated with pharmaceutical consumption (e.g., health improvements resulting in increased worker productivity), markets would
direct and indirect benefits of health technology is also supported by the Productivity Commission’s report into Medical Technology which found that “The extent to which PBAC takes into account potential indirect benefits of medicines, such as hospital or aged care cost savings or the ability of patients to return to work, is unclear. While a lack of hard and relevant data and methodological issues complicate measurement of these impacts, *discounting them on the grounds that unrealised savings should not be counted (because freed up hospital beds are used for other patients), or that any individual can be withdrawn from and replaced in the workforce without cost, is misconceived.*” (Emphasis added)²

Likewise, as the benefits generated by the adoption of a technology accrue across the whole of society, the opportunity costs generated by the funding of new health technologies should be considered across the whole of government and the whole economy. Health technology evaluations should not be constrained simply to an evaluation simply within the health system or, even worse, as pharmaceuticals or devices in isolation.

- **Broad stakeholder input is required so that decisions reflect societal values:** HTA is a complex and heavily value laden process. Despite the rigour often contained in HTA, like many areas of economic assessment, value judgements often play a role in framing the decision and assessment of an economic outcome. It is important that decisions reflect actual societal values and preferences. In order to facilitate this, a number of mechanisms are required to ensure that stakeholders (consumers, HCOs, health professionals, etc) can provide meaningful input into the decision-making process, whilst respecting confidentiality requirements. MA believes that the Government and PBAC have taken positive steps in this direction by having a consumer representative on PBAC, permitting public comments on individual agenda items, as well as piloting systems for the procurement of formal Consumer and Clinical Impact Statements from the Consumer’s Health Forum of Australia and the Royal Australasian College of Physicians respectively. In addition, further improvement in this direction could be made. Consideration should be given to the establishment of a new PBAC Social Values Sub-committee, parallel to the PBAC’s Economic Subcommittee (ESC) and Drug Utilisation Subcommittee (DUSC), to provide advice on general community values as they apply to individual medical technologies being assessed. At a higher level, consideration should also be given to the establishment of a Citizens Council. This Council would deliberate

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on more contentious broader ethical and policy matters as they apply in the HTA context (e.g. “fair-innings” arguments).

- **HTA should be used as a tool to generate incentives for innovation to meet future health needs:** To the extent that HTA informs the price of a medicine and through that the rate of a return to the sponsor, through an assessment of cost-effectiveness, a question arises about maximising short-run (static) vs. long-run (dynamic) efficiency. An HTA system concerned principally with static efficiency would seek to maximise the health of today’s population for as little cost as possible while de-valuing the return on investment of the developers of health technology. Such an approach pays no attention to the potential for HTA to generate incentives to encourage or direct research and development into interventions that will serve the health needs of future generations. Australia’s National Medicines Policy recognises this tension but current practice is dominated by concerns for “static efficiency” alone. Recent developments in pricing policy, such as the cessation of valuing Australian domestic industry activity in pricing (through Factor (f) in pricing decisions), are consistent with the view that reimbursement should not be used as a policy tool to encourage or prioritise research and development to meet the needs of future generations. An HTA system focussed on the more long run priority of dynamic efficiency puts greater emphasis on the fact that what payers will pay for a technology will have long run impacts on investment in future health technologies. MA believes that a short-sighted ‘static efficiency’ approach ignores the complex dynamic between price setting, return on investment and R&D activity, a point again recently explored by the aforementioned OECD report.‡

‡ “Pharmaceutical pricing and reimbursement policies stand to affect innovation through multiple channels, influencing both the incentives to invest in private R&D and the costs of investment. The main channel of prospective influence is the impact of pricing and reimbursement policies on the expected return on investment in R&D. Such policies also serve as one of several types of determinants of the funds available for investment in R&D, most directly via their role in influencing manufacturers’ sales revenues from national markets. They can also have an indirect impact, to the extent that they influence the prices and consumption of medicines in other countries, thereby further influencing the global sales revenue that serves as an important source of funding for private R&D” (emphasis added) (OECD (2008) Pharmaceutical Pricing Policies in a Global Market, Paris, p.192).

and


and

“To the extent pricing schemes reduce the level of sales revenue accruing from global sales of pharmaceuticals sold by research-based firms, they effectively reduce the low-cost capital available for investment in R&D, thereby increasing investment costs. Firms will
Indeed, The Australian Government’s Productivity Commission has also identified that R&D investment in medical technology “is influenced by funding and insurance arrangements and regulation”. While Australia has historically had a relatively small market for medical technology, including pharmaceuticals, in a global context, the fact that Australia is becoming more of a reference country in other markets suggests that Australia’s reimbursement decisions will contribute to global market incentives for future investment in medical technologies like pharmaceuticals.

- **Flexible decision making to account for changes over time:** HTA is mostly undertaken once the regulatory or marketing approval has been granted. There must be the recognition by the HTA agency that not all information about the costs and benefits of a technology will be available at this time. Decision making processes must be flexible enough to handle such uncertainty and decisions to reimburse technologies should be driven by good judgment. Interim reimbursement should be granted where appropriate and a risk-share arrangement established between the government and the sponsor which may involve post-launch collection of clinical, economic and financial data. The AMWG is currently considering under what conditions such Coverage with Evidence Development may be workable in Australia.

- **Avoiding inefficiency through unnecessary regulatory burden:** As HTA is always an approximation of the use of health technology in actual clinical practice, decisions to reimburse will always be taken with necessarily imperfect information and thus with varying degrees of uncertainty. Over time such “decision-making under uncertainty” has a natural tendency to result in increased informational, data or methodological demands. PBAC submissions now regularly run into thousands of pages and cost many hundreds of thousands of dollars to prepare. Recent developments would suggest that in the future both the informational requirements and the administrative costs will increase substantially. MA argues that HTA agencies need to be more conscious of the growing regulatory burden being placed on sponsors, and in particular that the relationship between additional information/data and the reduction of uncertainty for decision-making is characterised as one of diminishing returns. It is often preferable to find flexible approaches to manage uncertainty rather than increase the regulatory burden.

- **HTA decisions and related technical assessments are NOT transferable across jurisdictions:** While HTA agencies in Australia need to be mindful of

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continue to invest when expected returns on investment exceed expected costs, but R&D investment levels will be lower due to the higher financing costs associated with an increased reliance on outside funding sources when present sales revenues are reduced.” (OECD (2008) *Pharmaceutical Pricing Policies in a Global Market*, Paris, p.194.)
international decisions, local HTA assessments will need to be undertaken taking into account local perspectives and stakeholder inputs. While most clinical trials are multi-national and the results can be adjusted to reflect local populations, economic analyses are less transferable from international settings and will be highly sensitive to local variables including clinical practice, choice of comparator and health system costs. Also, the overarching perspective, health system funding and financial incentives to health professional may significantly differ between countries.

- **Decision-making frameworks for pharmaceuticals do not automatically translate to other areas:** While it is important to recognise that the experience and expertise gained with pharmaceuticals is important, there are aspects that are not automatically applicable to medical devices. For example, the life cycle of a specific type or variation of a device is shorter than a medicine as development is characterised by a constant flow of incremental product improvements in close interaction with the users (physician or surgeon) of the technology.

- **The registration and reimbursement processes must remain separate:** The processes for evaluating a medical technology for regulatory and reimbursement purposes need to remain separate. The regulatory process provides approval for a medicine to be marketed in a country and is designed to ensure that medical technologies that are sold in a market place are safe and do what they are purported to do. The reimbursement process is designed to evaluate for a payer, either public or private, whether a medical technology provides enough value for money when compared to existing technologies, to justify the payer reimbursing part or all of the cost of that technology in the market. The decision-making “frame” for these evaluations is qualitatively different and it would be an error to conflate them.

- **Principles of sound administrative governance should be respected:** HTA systems should uphold principles of good governance to avoid conflicts of interest. This means that a clear separation of the assessment, evaluation, appraisal and decision making functions. It also means that, there should be separation between policy makers, program administrators, evaluators and decision-makers. The Productivity Commission pointed to the obvious tension that lack of appropriate separation creates, when it found that: “Where HTA is undertaken by organisations that also have expenditure responsibilities, this may lead to tensions between different objectives: that is, between facilitating optimal use medical technology and controlling health expenditure.”

For example, the Department of Health and Ageing, the agency that manages, influences and funds the PBAC evaluation process, also manages the control of PBS expenditure. While PBAC evaluations of company submissions are conducted by external universities for the PBAC, DoHA can play an influential
role in reviewing these submissions and their external evaluations. The potential exists that the HTA evaluation could be influenced by broader policy and budgetary issues in addition to straight HTA issues.

- **Transparency of the process and decisions:** There should be appropriate transparency of the HTA processes and decisions. It is important that the sponsors of health technology can be confident of the business environment in which they operate and are provided with a clear understanding of the criteria (both HTA and other contributing factors) that are to be met to achieve reimbursement through a HTA-based system. Reasons for decisions should also be published in a form that respects commercial-in-confidence material. For example, a public summary document explaining in detail why a technology has been accepted or rejected may aid the transparency of the decision-making process. The report(s) needs to be accessible for a range of stakeholders including industry, clinicians, and patients. It is therefore recommended that a technical summary as well as a summary that is understandable by the general population be provided.

- **Defined timelines and processes:** To provide greater certainty to applicants for reimbursement, it is recommended that the HTA process have structured and set timelines for each part of the assessment, appraisal, and decision-making process. It is important that these timelines are consistently met. While accepting that different types of products will require different levels of assessment and appraisal time, it should be possible to establish time-frames for various “tiers” of products.

- **Accountability of decision-making:** An appeals procedure is essential to ensure accountability of decision-making processes. There should be clearly defined criteria for a decision to go to an appeal which adjudicates in disputes over interpretations of the technical (HTA) evidence and/or procedural and process issues. The appeals body should be different and independent from the initial appraisal body, and principles of good governance should be upheld.

- **Quality assurance mechanisms:** Given the importance of the technical evaluations, it is important that quality assurance mechanisms are in place to ensure that the analysis and advice that informs the decision-makers is fair, balanced, accurate, consistent, and up to date. Quality and excellence in HTA is an important goal for any HTA system. MA recommends that a representative sample of evaluation reports is regularly audited for quality by an independent party and a system of indicators should be developed to ensure that HTA evaluations are conducted in a timely, accurate, and impartial manner.

- **Capacity development and professional support:** HTA is a complex, multidisciplinary area requiring investment in the education and skills of a workforce capable of meeting both the policy and technical demands of such a
system. There is currently a significant shortfall in trained HTA professionals across government, academia and industry. This needs to be addressed simply to meet the demands of the existing HTA systems in Australia. Expanding HTA to other areas of the health system will exacerbate this and significant resources will be required to meet future capacity requirements. There is scope for a substantial collaborative exercise between government, industry and academia to develop the supply of HTA skills and expertise in Australia.

**Principles relating to technical aspects of HTA**

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<th>Issue</th>
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<tr>
<td>HTA Guidelines</td>
<td>Guidelines should be explicit, methodologically sound and up-to-date and reflect international best practice. They should be sufficiently flexible to take into account unique aspects of the new technology and available data rather than be prescriptive (i.e. reflect “should do” rather than “must do”). All relevant stakeholders should be involved in the development of HTA guidelines including Government, academics, industry and clinicians. Guidelines should be viewed as a “dynamic” document and should be periodically updated to reflect updated technical methodology and experience from past submission assessments.</td>
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<td>Perspective</td>
<td>The perspective should be societal with a focus on measuring costs and benefits (outcomes) to whomever they accrue. The use of a narrow perspective will undervalue the community benefit of some interventions compared to others. For example, certain conditions have an important impact not just on the patient but on the carer, family and the wider community (e.g. schizophrenia).</td>
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<td>Choice of comparator</td>
<td>The definition of the comparator should be that intervention that the new technology is likely to replace in clinical practice. The proxy for this is usually current standard of care or usual practice or most commonly used treatment. It should be recognised that clinical practice will vary across the world and multi-national clinical trials may not be always against the comparator that would be the most likely to be replaced in clinical practice in Australia – this has implications for types and preferences for the evidence used in the HTA.</td>
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<td>Costs</td>
<td>Both direct and indirect (production) costs should be included within a societal perspective. Guidelines should encourage the inclusion of a wide range of costs that are impacted by the introduction of the new technology, and should not just reflect the budget impact in one area of health spending.</td>
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<td>Outcomes (benefits)</td>
<td>HTA should recognise all potential benefits of a new intervention and could include clinical measures as well as final measures (survival) where appropriate. It should include a wide range of evidence and</td>
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Practitioners of HTA should recognise that not all benefits of a new technology will be reflected in clinical or final outcome measures, but may be important to the patient and the healthcare system, such as interventions that improve convenience and the process of care.

While recognising the importance of quality of life improvements to a patient, HTA assessments should recognise that existing utility instruments may not be very sensitive or address issues of quality of life that are important to a specific intervention and/or disease. Different utility instruments will produce different QALY estimates which will have a flow-on effect to the resultant cost-effectiveness result.

The appropriate evidence to demonstrate clinical efficacy/effectiveness of an intervention should be provided. Randomised clinical trials (RCTs) are often considered the best form of evidence. However, RCTs, while having high internal validity (results relevant for people who have intervention under ideal conditions), have lower external validity (results that are less applicable under real world conditions).

It should be recognised that in some cases head-to-head RCTs may not be available against the appropriate comparator from multi-national trials. In these cases additional data sources such as indirect comparisons of RCTs and observational data should be considered appropriate evidence for HTA.

The choice of economic evaluation technique should be based on the objective of the HTA and the therapeutic and economic benefit of a technology. An HTA system should allow the full range of economic evaluation techniques to be presented including cost-minimisation analysis, cost-benefit analysis, cost-effectiveness analysis and cost-utility analysis.

While incremental cost-effectiveness ratios (ICERs) may provide some value in determining the value of one healthcare intervention over another, the arbitrary use of a single ICER threshold (or league table approach where ICERs of different health technologies are simply ranked in order) should be viewed with caution. The use of the ICER in making a decision to reject or accept an application should be made explicit, along with the basis for the decision and the ICERs importance relative to other factors.

While there is no internationally accepted method for determining what an acceptable ICER might be, it should reflect society’s willingness to pay. It should be recognised that the community may value more highly interventions for some disease areas (e.g. oncology) and this therefore infers a range of ICER acceptability. Thus decision making and ICER considerations adjustable to reflect these community values.
Dealing with clinical and economic uncertainty

Uncertainty in clinical, economic and financial data should be addressed in an environment of partnership and finding a solution between the HTA agency, sponsor and any other stakeholder that may be affected by or influence uncertainty, such as clinicians and patients. Where there is an important clinical need for the product but data is not available at the time of launch, rather than deny patient access to the intervention flexibility in approaches should be considered. This might for example take the form of an arrangement or commitment, agreed between the government and the sponsor, which may involve post-launch collection of clinical, economic and financial data (e.g., coverage with evidence development, utilisation review).

4. Terms of Reference Key Questions

Term of Reference 1

Simplification and better co-ordination between all Commonwealth health technology assessments

- consideration of a single entry point and tracking system for applications for market registration and funding
- making time to affordable access as short as possible for new technologies while maintaining or improving the rigour of evaluation processes
- examination of the feasibility of conducting concurrent assessment for market registration and funding and coverage purposes, noting work in this area

Key Questions

1. How can the interaction between the different HTA agencies (i.e. TGA, MSAC and PDC) and their processes for the registration and approval for market entry and public and private health funding of new medical services and devices be improved?
2. How could the administrative processes of each individual HTA agency (i.e. TGA, MSAC and PDC) be simplified without compromising the scientific rigour underpinning the HTA process?
3. How can HTA undertaken by other countries be used in the Australian context? What are the limitations, risks and opportunities that would need to be considered?
4. How can assessment of cost effectiveness be improved to ensure HTA can inform government decisions in a timely manner?

There is much scope to simplify, improve efficiency, and reduce time-lines to reimbursement and patient access for both pharmaceutical and medical devices.
Process improvements include streamlining the TGA and HTA processes, improving efficiency of the assessment process by prioritising applications, horizon scanning and enhanced dialogue throughout the assessment and appraisal of a new technology. It will be argued that there are limitations in HTA adapting decisions from other countries and applying to the Australian context. A further initiative that will reduce time to reimbursement in some instances is allowing reimbursement in situations of clinical and economic uncertainty. This will be addressed under Term of Reference 3.

Streamlining the TGA and HTA Processes
While there is scope for simultaneous and mutually informed evaluations, a key principle is that the processes for evaluating a medical technology for regulatory and reimbursement purposes need to remain separate. The regulatory process provides approval for a medicine to be marketed in a country and this is appropriately based on a single, non-comparative assessment of a technology’s safety, efficacy and effectiveness. In simple terms, it is designed to ensure that medical technologies that are sold in a market place are safe and do what they are purported to do. This is quite different from an assessment for the reimbursement process which is designed to evaluate for a payer, either public or private, whether a medical technology provides enough value for money compared against other technologies, to justify the payer reimbursing part or all of the cost of that technology in the market.

While the two processes must remain separate because they have fundamentally different purposes, there is scope for improving administrative efficiencies in both processes, some of which may involve greater interchange between the two. Currently in most instances for both pharmaceuticals and devices in Australia and internationally, a sponsor cannot apply for HTA assessment or reimbursement until the regulatory approval has been granted (or for medicines in Australia, a company has received a positive TGA delegate’s recommendation). A process improvement that has the potential to improve the timelines to patient access for a new technology is to streamline the regulatory and reimbursement processes so that they run concurrently rather than consecutively. While the two processes make separate decisions and while there may be some practical impediments, there is little in principle that prevents an HTA being conducted while regulatory approval is still being finalised.

As part of the AMWG discussions between the Department of Health and Ageing and MA on identifying ways to improve PBS processes, the AMWG has met with the TGA to discuss the various ways in which the TGA and the PBAC can increase the efficiency of the regulatory and reimbursement processes by streamlining and coordinating their respective processes to reduce the time it takes to list a medicine on the Pharmaceutical Benefits Scheme (PBS). These discussions have included aligning the medicine registration and PBS listing processes to allow parts of these areas to run concurrently. Note that these discussions have principally focused on adjusting the PBAC processes to better connect or integrate with the TGA processes. There is no attempt to alter the TGA’s regulatory assessment process to fit the PBAC process. This is appropriate.
Several pilot projects are about to commence to test earlier commencement of PBAC evaluation whilst TGA assessment is still being conducted. The proposal effectively allows for an extended evaluation of complex-submissions by adding an additional evaluation cycle before the beginning of the current system (which would be broadly concurrent to the TGA evaluation). There is scope to extend this pilot to less complex applications.

A number of areas have been identified where efficiencies in the registration of new medicines by the TGA can be made. TGA has now embarked on a business improvement process which will significantly decrease the time to have new medicines registered on the Australian Register of Therapeutic Goods, while maintaining the integrity of the regulatory process.

There appears to be scope to apply the experience from the streamlining pilot project to medical devices sector which would result in earlier patient access to important medical procedures. In addition, increased collaboration between reimbursement and regulatory agencies should include benefit risk assessments where the regulatory agency is collecting post marketing data and where there is a need to collect evidence for reimbursement purposes as a condition of listing.

**HTA Application Timelines**

One limitation to the current MSAC process is that timelines for the assessment, appraisal and decision making process are not clearly defined. The time taken for an application to move through each stage of the process will depend on the completeness of the application form, the quality of the available evidence and the complexity of the service. There is no specific cut-off date for lodging an application and MSAC meets at least four times per year. A significant delay in the timeline may be due to MSAC commissioning a systematic review of the evidence including economic evaluation evidence. Given the life cycle of a specific type or variation of a medical device is (12-24 months) this may significantly impact on the commercial viability of the product in addition to delaying patient access to the technology.

This situation contrasts with the PBAC evaluation process used for pharmaceuticals. While not perfect, each round of the PBAC process is quite predictable and transparent. Each PBAC cycle runs over 17 weeks, from lodgement of a submission by a company to PBAC decision. There are three cut-off dates per year with three PBAC meetings. Companies making submissions usually know where in the process their submission is, how long each step will take, and when they will be required to provide inputs into the process. This makes the process more predictable and holds the administrative timeliness of the PBAC and its processes to account.

The PBAC defined timelines are achievable due to the onus on industry to provide an assessment of the clinical, economic and financial evidence in line with the PBAC Guidelines. The evidence in this submission is then evaluated by an academic body. As
discussed earlier, in some instances MSAC outsource the assessment to an external body to compile the evidence. This may result in extended timelines for the reimbursement application process.

To provide greater certainty to applicants for reimbursement of medical devices, it is recommended that MSAC develop a more defined process that includes structured and set timelines for each part of the assessment, appraisal and decision making process. While accepting that different types of products will require different levels of assessment and appraisal time, it should be possible to establish time-frames for various “tiers” of products. Adapting a model similar to the PBS listing process may be beneficial. There are defined cut-off dates for applications, and set dates for each part of the assessment process. To achieve more defined timelines, consideration should be given to have the sponsor present the evidence in the submission and the academic body review the evidence, as per the PBS reimbursement process. The goal is to ensure predictability and transparency in the process without the process itself unduly lengthening the time required for review.

Improving HTA Efficiency by Tiering Technology Applications

Resources and expertise to undertake HTA in Australia are limited. The resources used for HTA should be used in a cost-effective manner. The technology assessment and appraisal process should spend more time and resources on products and services that either have the most clinical need, the highest potential budget impact and/or where the data assessment is the most complex rather than spending similar resources on products that will have neutral impact on budgets or are requesting same price due to similar efficacy and safety.

MSAC does apply criteria for prioritising assessment based on for example clinical need, disease prevalence/incidence, likely utilisation, cost of the technology – this could be extended to include tiering product based on complexity of the technology so as to enable a more efficient use of time and resources.

For example, the current process for assessing submissions in the PBS listing process acknowledges that submissions require differential levels of evaluation and assessment on the basis of complexity. As such submissions are routinely tiered as major (considered by PBAC following full independent evaluation and sub-committee advice); minor (considered by PBAC without full independent evaluation); and secretariat submissions (not requiring consideration by PBAC). While these categories assist in ensuring that the assessment and decision making process prioritises its resources based on complexity of submissions, it should be possible to further prioritise HTA reviews. For example, different options of tiering HTA reviews might be (1) tiering by relative clinical and pricing claims mediated by the type of supporting evidence (e.g. indirect versus direct comparisons) (2) triaging during enhanced pre-submission consultation based on the nature of the supportive data (3) tiering on a continuum of complexity, and (4) spending more time on assessing those products which will have a significant budget impact.
Improving Efficiency by Enhanced Communication
As discussed later under Terms of Reference 3, uncertainty in clinical and economic data is a major reason for reimbursement application rejection, which in turn results in re-submissions and places further demands and analysis on the HTA agency and the technology sponsor. Allowing enhanced formal and informal communication between the sponsor and the HTA agency (and other stakeholders) throughout the assessment, appraisal and decision making processes should result in a more efficient system, with less application rejections due to better pre-submission understanding of issues. For example, the opportunity should exist for more detailed and extensive pre-submission meetings between the sponsor and HTA agency. In these meetings key areas of uncertainty would be more clearly identified and discussions held relating to how these may be addressed either prior to or during the assessment period. Additional formal and informal meetings should be had as appropriate throughout the assessment and appraisal process. For example, as part of the PBAC appraisal process, industry is allowed to do a face-to-face presentation to this committee.

Applying International HTA Decisions to Australian Context
As more countries use HTA to inform decisions on the reimbursement of health technologies, harmonisation or standardisation of evidence requirements between different countries and within countries has been proposed, mainly on the grounds of improved efficiency. It is argued that harmonisation has the potential to avoid duplication of effort for both industry and the HTA agencies involved in preparing and reviewing HTA submissions for new and existing technologies. A recent review on this issue by Hutton et al (2008) concluded that “it also carries risks of loss of local control over decisions, the application of general data standards which are not universally accepted and slowing the rate of development of innovation in the analytical disciplines supporting HTA”. 3

HTA assessment and appraisal should be tailored for local decision making requirements. While most clinical trials to support HTA are from multi-national trials with or without Australia participation, trial data can be adjusted to reflect local populations. Due to the high costs of Phase 3 trials and logistics of recruiting sufficient patients it is unrealistic to expect that Australian specific clinical trial data be generated for regulatory and initial reimbursement purposes. Economic analyses on the other hand, are less transferable from international settings and will be highly sensitive to local variables including clinical practice, choice of comparator and health system costs. Also, the overarching perspective, health system funding and financial incentives to health professional may significantly differ between countries.

The International Group for HTA Advancement (2008), members whom are international experts in HTA, conclude that “generalisability and transferability across patients, populations, countries and systems become more problematic the broader the range of stakeholder and decision-maker perspectives and preferences”. 1 Thus while HTA agencies in Australia need to be mindful of international decisions, local HTA
assessments will need to be undertaken taking into account local perspectives and stakeholder inputs.

Evidence Impediments
The over-reliance of HTA bodies on the head-to-head double blind RCT as primary evidence to reimburse a new technology is a significant reimbursement hurdle in Australia both for pharmaceuticals and devices. It should be recognised that in some cases head-to-head RCTs may not be available against the appropriate comparator from multi-national trials at the time of product launch. In these cases additional data sources such as indirect comparisons of RCTs and other forms of studies including observational data should be considered appropriate evidence for HTA. This is particularly the case for medical devices where the double blind RCT may not be possible to undertake, may be inappropriate or not considered ethical.

Term of Reference 2
Improving role clarity and addressing duplication between processes, where it exists, including consideration of consolidating functions with the Australian HTA system

Key Questions
1. What HTA roles and functions require clarification?
2. Does duplication and/or overlap of HTA processes occur? If so, where? How could this be resolved?

Separation of the Role of Assessment, Appraisal and Decision Making
Principles of good governance should be applied to any HTA system. To avoid conflicts of interest, there should be a clear separation of the roles and functions of the assessment, evaluation, appraisal and decision making processes.

Assessment refers to the assembly of evidence base considered by the HTA (often prepared and submitted by industry in the PBS system or in the case of a complex technology for MSAC undertaken by an academic organisation). It involves the systematic identification and synthesis of evidence on comparative clinical effectiveness, safety and cost-effectiveness.

Evaluation refers to a critique of the evidence (as for example performed by the academic centres and the Economic Sub-committee as part of the PBS).

Appraisal refers to the process of using the evidence base to derive recommendations about use of the technology. This involves value judgements (that must be made explicit) about the applicability of the evidence, cost-effectiveness thresholds for it to be
accepted by payers and the wider social considerations. The PBAC and MSAC play this role within the pharmaceutical and medical devices sector.

**Decision making process** takes into account the recommendations from the appraisal process to make the final decision to reimburse the product (in the PBS and MBS processes the ultimate decision maker is the Minister for Health and Aging). Generally there are two models internationally. In the first model, responsibility of undertaking HTA lies within the Ministry of Health or insurance funds. The second approach is an “arms length” model where payers (or Government) make decisions based on independent assessment and appraisals of HTA evidence conducted by separate agencies – that is, the payers are not responsible for undertaking the HTA.

The distinction between assessment, evaluation and appraisal (and the fact that they are two different procedures) should be accompanied by a separation of the tasks between different bodies. With the PBS, the sponsor does the assessment (application based on synthesis of clinical and economic data) while an academic body (university) does the evaluation. The PBAC (and its sub-committee) does the appraisal and provides recommendations to the Minister.

Under the first model where, in the Australian context, the Department of Health and Ageing continues to manage the evaluation process, one option to reduce duplication and improve coordination is to have a coordination mechanism across the different HTA areas. This would involve some sort of committee or review structure such that the different HTA processes in the Australian Government, such as PBAC and MSAC, can be coordinate to facilitate speedier listing of new medical technologies. Such a process would not require a separate agency but may generate significant administrative efficiencies that do not unduly delay the reimbursement of new medical technologies due to the administration of different HTA processes. Such a committee process may also help ensure that the different parts of the Department of Health and Ageing also coordinate the evaluation of submissions through different evaluation committees.

The possibility exists, however, that such a committee would potentially be a further drain on scarce administrative time and resources and could actually result in further administrative delays, unless delivering clear benefits in terms of better coordination and administration.

It could be argued that the evaluation process is not truly independent of Government as the policy division within the Department of Health and Ageing responsible for pharmaceutical benefits oversees, and administers and advises the evaluation process. In addition, while the PBAC provides recommendation to reimburse or not to the Minister who is the final decision maker, it could be argued that the PBAC is the decision maker. Thus is due to the fact that very few PBAC positive recommendations have been overturned by the Minister and the Minister cannot decide to reimburse a product unless the PBAC provide a positive recommendation. Thus the appraisal and decision making process is blurred.
The lack of an arm’s length relationship between the evaluators, the decision makers and the policy makers in Australia’s PBS process gives rise to a number of characteristics and adverse outcomes. The fact that the policy arm of government responsible for developing HTA policy (DoHA) is, essentially, the same body that administers the day-to-day operation of the HTA system has the potential to compromise DoHA’s ability to review and monitor the HTA system. For example, DoHA, the agency that manages, influences and funds the PBAC evaluation process, also manages the control of PBS expenditure. While PBAC evaluations of company submissions are conducted by external universities for the PBAC, DoHA can play an influential role in reviewing these submissions and their external evaluations. The potential exists that the HTA evaluation could be influenced by broader policy and budgetary issues in addition to straight HTA issues.

Such a situation is in contrast to trends in other areas of public administration in the Australian Government which are structured using the purchaser-provider model. Essentially, this structure requires the two parts of program development – the policy function and the administration function – to be conducted at arms length from each other to help preserve administrative efficiency and policy intent. Under this model, the policy function (the purchaser) develops the specifications for an administered program or service that is provided by the provider. In various settings the purchaser is the policy arm of government and the provider can be another part of the same portfolio, another different part of government, or even a private sector provider. Examples where this model operates in other portfolios of the Australian Government include the use of AusIndustry to administer innovation grant programs for the Department of Innovation, Industry, Science and Research, and the Job Network system for providing employment services to unemployed people for the Department of Employment and Workplace Relations.

Independent reviews of technology evidence bring greater transparency, avoid conflicts of interest (e.g. negative assessment of technology to achieve budgetary goals), widen the expertise to undertake the HTA review, and bring broader perspectives to the assessment process. A single separate HTA agency could potentially assist in coordinating HTA across different technology areas like pharmaceuticals, devices and procedures. A separate agency, however, would need to be sufficiently resourced and professionally structured to ensure administrative integrity and impartiality. If reviews are undertaken by an independent agency, there should be processes in place to ensure effective coordination and communication between those conducting the assessment, the appraisal body and the ultimate decision maker.

The risks of establishing a separate HTA agency are that it becomes more, not less, bureaucratic and imposes further regulatory burdens on industry. This would be particularly important in the event that PBS cost recovery is finally introduced. There is also the question of how such an agency would be structured and staffed, given the HTA skill shortages already present in Australia.
Wider Stakeholder Input

MA believes that broad stakeholder input is needed at two levels:

1. **At the level of an HTA assessment of a particular product or technology:** There should be an iterative process to ensure that stakeholder input and involvement is proactively sought throughout the assessment, appraisal and decision making process. Key stakeholders include patients and patient groups, carers, doctors and other health professionals, and industry. While this may be resource intensive, as Drummond et al. (2008) states, “it may lead to better assessments, reduce the number of Appeals and result in better implementation of HTA decisions”.

Decisions on reimbursement based on HTA recommendations should involve key stakeholder input, particularly from clinicians, consumers and consumer organisations as well as carers. The majority of PBAC members are practicing clinicians from a number of medical specialties, but they may not represent the consensus views of the clinical community. The PBAC and the Pharmaceutical Benefits Pricing Authority (PBPA) currently each have a single consumer representative.

It may not be possible for consumer members on these committees to represent all the views and interests of particular consumers potentially impacted by the reimbursement or otherwise of a technology. Thus it may be beneficial to allow a more structured consumer input via a consumer impact statement written by the relevant health consumer organisation or even a Consumer sub-committee (see below) to provide more comprehensive input to the assessment and decision making process. The PBAC is currently trailing Consumer Impact Statements which allow patients to present, in their own words, details about how a condition affects their daily life and the impact on carers. The PBAC also invites comments from consumers when it publishes its agenda.

It is recommended that increased opportunities for consumer and carer involvement in the HTA of medical devices should be explored. The NICE approach provides a good model to adapt. Consumers can participate in the NICE technology assessment processes in several ways, including as members of various NICE committees, patient or carer groups, or as part of an organisation through the Patient and Public Involvement Programme (PPIP) and/or the Citizens Council. The PPIP, a unit of NICE, provides advice on patient and carer involvement and identifies patient and carer organisations interested in contributing to NICE appraisal. The Citizens Council, an organisation with 30 members drawn from all sections of the population, assists NICE in understanding the views of the public to inform the NICE HTA guidance. The concept of a Citizen’s Council concept for Australia was one proposal discussed during the 2008 DOHA/MA Joint Medicines Policy Conference.

Given the importance of stakeholder input there are various potential models to include wider stakeholder input to the appraisal and decision making process. The key goal is to
provide relevant stakeholder input in reviewing a particular HTA analysis within a wider stakeholder context. MA recommends that consideration be given to an HTA process that includes three broad forms of consumer input:

- Standard mechanism during the HTA evaluation of individual submissions, as an input to the HTA recommendation and decision
- Continue in depth consumer impact statements for selected products
- Establish a Citizen’s Council akin to that in the UK to advise on higher level policy issues

2. **At the policy level**: In addition to stakeholder input at the individual assessment level, MA believes that a policy-based Citizens Council should be established. Such a Council would consider policy issues related to the HTA framework and process, such as: what societal values should be considered in the HTA framework; what value should be placed on end-of-life medicines, etc. Such a body would provide a forum for consumer groups to discuss the system and trends in HTA decisions and provide advice to Government on value sets in HTA decision making.

**Duplication of HTA**

Duplication of HTA can currently occur for hybrid and co-dependent therapies where both MSAC and the PBAC will do independent assessments. For example if a diagnostic test is available to identify those patients most likely to benefit from a medicine, MSAC might do an evaluation of the diagnostic, and the PBAC will evaluate the medicine. From an HTA perspective it is important to undertake a cost-effectiveness analysis of both the diagnostic and medicine in the one analysis. This will be addressed in more detail under Term of Reference 5.

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**Term of Reference 3**

**Enhancing post marketing surveillance mechanisms to ensure the on-going safety and efficacy of medical devices**

**Key Questions**

1. **What changes, if any, are needed to current HTA arrangements for post marketing surveillance of health technologies?**
2. **How could the arrangements for post marketing surveillance of medical devices for ongoing safety and clinical effectiveness be improved?**
3. **What additional arrangements for post market surveillance could be considered or implemented?**
   How could post marketing surveillance be managed?
The focus in this MA submission under this term of reference will be in relation to HTA post-marketing surveillance as it relates to managing the issue of uncertainty of clinical, economic and financial data at the time of reimbursement application. The focus is also on the importance of allowing interim reimbursement conditional on collection of post-marketing data. Significant theoretical work and debate has already been undertaken in this area both in Australia and internationally. The work being undertaken by the AMWG will be informative to the HTA Review. HTA for medical devices and pharmaceuticals in Australia and internationally is mostly undertaken once the regulatory or marketing approval has been granted (ex-ante approach relying on RCTs and modelling cost-effectiveness). There must be the recognition by the HTA agency that not all information about the costs and benefits of a technology will be available at this time. This is particularly the case with medical devices where the RCT may not be possible or appropriate or when the effectiveness of the technology is difficult to separate from the proficiency of the user of the product.

A major reason for not recommending a technology for reimbursement is due to either lack of or uncertainty with respect to clinical or economic data. This often delays patient access to much needed healthcare. This in turn can lead to an increase in the rate of resubmissions, which places a further demand on the resources and analysis required to evaluate the medicine. This in turn can further increase resource demand on industry and the assessment and appraisal bodies and Government. This can delay the listing of new technologies.

Decision making processes must be flexible enough to handle such uncertainty and decisions to reimburse technologies should be driven by good judgment. Where there is an important clinical need for the product but data is not available at time of launch, rather than deny patient access to the intervention, reimbursement should be granted and an agreement or commitment established between the government and the sponsor which may involve post-launch collection of clinical, economic and financial data. Under certain circumstances this is currently allowed under MSAC procedures. In addition, companies (and other relevant stakeholders) should be able to submit new effectiveness and cost-effectiveness information to the relevant HTA body through the product’s life-cycle – real-world data may in many instances be more reliable in assessing the value of a technology. This ex-post approach may rely on additional data sources such as observational studies and/or pragmatic trials as the RCT is less applicable to the real world setting.

There are a number of different tools that could be used to manage uncertainty which may warrant further investigation in the Australian context for use in assessing medical devices. These include:

1. **Agreements based on expected clinical outcomes.** This method has been used in the UK (NICE) and Canada. Reimbursement is agreed on the basis that additional data is forthcoming from studies that will further clarify or strengthen the claim in regard to clinical outcomes. Studies must be of appropriate quality
and size to address the area of uncertainty and the technology involved. For devices, such studies could be a randomised (non blinded study), an observational study, registry or in certain situations case series analyses.

2. **Coverage with evidence development (CED)**. This has been undertaken predominantly in the US. CED is a term used mainly in the US which applies to Medicare coverage (reimbursement) with the condition that additional data (evidence) be developed. This evidence development may be via various methods, again with consideration of size and quality of the research relevant to the technology involved. The reimbursement during this period of further development of evidence may occur via limited and formal trial participation, or on a wider basis with separate evidence development on an ongoing basis.

3. **Price Volume/dosage arrangements**. Where the uncertainty is related to the daily cost of the medication or the potential for market leakage beyond the approved indication, reimbursement decisions may be made on the assumption of a certain cost and volume. The risk sharing arrangement may require some change to the price or coverage decision if the overall cost and sales varies from that estimated at the time of initial reimbursement.

It is recommended that the current MSAC process explore expanding the use of mechanisms such as those outlined above as tools for managing uncertainty under pre-defined circumstances. Specifically, coverage with evidence development is applicable to the medical devices sector. Key issues to be considered include: defining circumstances where interim listing is appropriate; identifying relevant solutions to uncertainty for each situation; timelines and evaluation to ensure currency of data and subsequent decision making; funding arrangements for collection of post-marketing data; options for agreements including rewards and penalties associated with confirmation or otherwise of clinical effectiveness and cost-effectiveness. The lack of data linkage between Commonwealth and state utilisation data sets is a significant barrier to collecting valid data in the real world.

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<td><strong>Strengthening transparency and procedural fairness in the assessment, decision making and fee negotiation processes through improved communication with stakeholders about processes, methodologies, outcomes and performance against indicators</strong></td>
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<th>Key Questions</th>
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<td>1. What aspects of Australia’s HTA system are working well in relation to transparency and procedural fairness? Please provide specific examples</td>
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2. What could be improved to assist transparency and procedural fairness? Please provide specific examples.

3. What key performance indicators could be developed and reported to improve transparency for HTA processes?

Transparency of Assessment, Appraisal and Decision Making
In any HTA system processes that need to be clearly defined include: objectives of the HTA; role and timing of submissions, assessment, appraisal and decision making process; role of peer review and independent review of evidence; process and criteria for decision making; weight given to different components of evidence, and the appeals procedures. The criteria used for decision making (including how the cost-effectiveness ratio was used to inform decisions) should be clearly stated and the evidence base underpinning decisions should be made publicly available. For the PBS since 2005 publication of reasons for the PBAC recommending or rejecting a submission for reimbursement, through Public Summary Documents, have improved the transparency of decision making.

Such public summary documents need to be accessible by a range of stakeholders including industry, clinicians and patients. Thus it is recommended that a technical summary as well as a summary that is understandable by the general population is provided.

Appeals Process and Other Accountability Measures
To improve accountability of a HTA system processes should be introduced to ensure consistency and procedural fairness of the HTA and the decision making process. These measures should include an appeals process, quality audit of the HTA and key performance indicators (KPIs). With the introduction of cost recovery proposed for HTA in Australia, it is important that accountability measures be heightened to improve administrative efficiency, professionalism and impartiality of the system. The Government has already proposed cost recovery for pharmaceuticals through the PBS listing process, making accountability measures in the PBS even more important. Should cost recovery be subsequently be extended to other areas of Australian Government HTA, such as devices and procedures evaluated for reimbursement on the MBS, accountability processes will also become more important in these systems.

An appeals process should be available to resolve disputes that are not resolved through consultation between HTA agencies and stakeholders (e.g. sponsors). There should be clearly defined criteria for a decision to go to an appeal which will include disputes over interpretations of the technical (HTA) evidence and/or procedural/process issues. The appeals body should be different and independent from the initial appraisal body. Transparency should apply with regard to the Appeal process.

Currently, the PBS system has an independent review mechanism in place for applications not recommended for listing by the PBAC, an initiative coming out of the
Australia-United States Free Trade Agreement (AUSFTA). This review process, while being outsourced to a different assessment body, is not entirely independent as its recommendation goes back to the PBAC for final review and recommendation. To date only two products have been subject to an independent review in the four and half years since the AUSFTA came into effect. This is in contrast to the United Kingdom’s NICE which has an appeals mechanism where approximately 30% of NICE decisions have gone to appeal and approximately 50% of decisions have been upheld. An appeals mechanism is an important platform to ensure the integrity of the decision making process and accountability on the part of the decision maker.

A quality audit of the evaluation and appraisal process should be undertaken regularly to ensure consistency of both approaches to evaluating evidence and the recommendation made. Rottingen et al (2008) have developed a quality framework for HTA based on a number of dimensions including relevance, applicability, validity, timeliness, accessibility, efficiency and equity. In addition, KPIs which measure the performance of the HTA system in meeting its objectives should be developed and implemented. Such measures need to be jointly developed by Government and industry and involve consultation with other key stakeholders. The PBAC and DOHA in collaboration with industry have developed some initial KPIs for the PBAC process.

Key indicators that should be developed would include time to reimbursement from regulatory approval, the approval rate of reimbursement applications, and time from reimbursement approval to effective listing on the reimbursement list. In developing the KPIs, data with which they are to be populated should be publicly available and independently verifiable, such as in the form of the reporting of PBAC outcomes and public summary documents.

KPIs should also focus on the quality of the evaluation of the clinical, economic and financial evidence included in sponsor applications. A system to ensure that the evaluations that are conducted are consistent, professional, impartial and informed by the latest knowledge is important. Moreover, consideration should be given to a system whereby evaluations are themselves routinely given quality assurance checks to ensure that errors in evaluation are not systematically delaying the listing of medicines due to technical issues, out-of-date knowledge and skill sets and systematic errors in interpretation and analysis.

The PBAC process is supported by several evaluation units that evaluate HTA submissions put forward by sponsor companies. However, there is no comprehensive structure, set of guidelines, or quality assurance measures that industry is aware of to ensure that the evaluators themselves are evaluated. If there is such a system of quality assurance, then industry has not been informed about it, or involved in monitoring its effectiveness.
### Term of Reference 5

**Enhanced arrangements for the assessment of co-dependent and hybrid technologies**

### Key Questions

1. **What are the key issues for government, regulators, medical and health professionals, industry and consumers in relation to the assessment of co-dependent and hybrid technologies?**
2. **What enhancements to current arrangements for assessment of co-dependent and hybrid technologies could be introduced?**
3. **What are the implications for assessment of clinical effectiveness and cost effectiveness for hybrid and co-dependent technologies in relation to decision making about funding?**

The recent advances in co-dependent (in the main genetically targeted therapies, sometimes termed “personalised” medicines) and hybrid technologies (e.g. drug eluting stents) pose significant challenges to drug development, regulation and reimbursement processes in Australia where there are multiple approval systems.

Co-dependent therapies are those therapies that are dependent on another technology either to achieve their intended effect or to enhance their intended effect. These may include a variety of therapies but the most common emerging group of co-dependent therapies are those that are targeted to distinct patient populations and require a specific diagnostic technology in order to be delivered to the appropriate patient population. The key advantage of targeted therapies is that tailoring drug therapy by patient genotype (or other diagnostic test), will ensure maximum effectiveness and minimal side effects. Potentially such therapies can be highly efficient in consumption of healthcare resources by providing the medicine to only those people who are most likely to respond. This concept is becoming well-established in oncology treatment, in which the decision to use a therapeutic drug is based upon the identification of proteomic or genomic evidence of a genetic abnormality. For example, for Herceptin®, breast cancer patients are tested to examine whether a particular gene, human epidermal growth factor receptor 2 (HER2), is present in the cancer cells. Herceptin® is only effective when cancer cells have extra copies of the HER2 genes. Much research is being undertaken on whether pharmacogenomics may be useful in clinical decision making for a variety of therapeutic areas including mental disorders, hypertension, and diabetes.

A key issue for both co-dependent and hybrid technologies in Australia is that separate committees, MSAC and PBAC, undertake separate HTA for the device and pharmaceuticals and the products are funded under separate budgets, the MBS and PBS. This has resulted in less than optimal coordination between the committees with subsequent unnecessary delays in patient access to treatment. A relevant example was
the bisphosphonates for osteoporosis where one of the barriers to achieve PBS listing was the restricted subsidy for bone mineral density (BMD) testing on the MBS leading to delays of several years to access. This case study highlights that without clear accountability for approval of both parts of a co-dependent therapy it is likely that therapies may be delayed simply because agencies are unable to agree among themselves on who should approve which part of the co-dependent therapy first.

Better coordination between MSAC and PBAC will be most important to reduce unnecessary duplication of efforts and resource use and will allow more timely decision making. To achieve this there are multiple structural models: the structures need to be able to manage medical devices and pharmaceuticals individually as well as when the technologies are combined as either hybrid or co-dependent technologies. More coordinated assessment of the technologies will result in administrative benefits, and may better foster the development of experience and expertise in HTA, in short supply in Australia.

One model to achieve better coordination is to create a ‘committee of chairs’, whereby the different evaluation committees meet regularly and interact to a greater extent to resolve the coordination problems in the administration of the different HTA committees. There could be a requirement for regular dialogue between the committees. Another model could be to have a single HTA agency that services all the committees, which would allow for coordination of the evaluation of co-dependent technologies.

It is important to note while some analytical techniques may differ when undertaking a clinical or economic evaluation of a device versus medicine (or when combined), the technical skills required to undertake the analyses are essentially the same. Thus most well trained and experienced epidemiologists, biostatisticians and health economists would be able to undertake HTA for either a device or a medicine. Thus closer coordination or greater use of shared resources is easily achievable. The principle danger is that while techniques are common, standards or benchmarks can and will differ between technologies for a number of reasons such as the availability of evidence.

Implications for Assessment of Clinical Effectiveness and Cost-Effectiveness
A further complication to the HTA of co-dependent technologies in particular is that the development of the products may not co-exist in time; this may be driven by different timeframes for development of the pharmaceutical or the device or different evaluation timelines. In many instances the development of diagnostic tests (including genetic tests) and a medicine (for co-dependent technologies) are undertaken separately by different companies. This can have a significant impact on the quality and type of trial evidence available for both products in combination available at the time of product launch. In addition, some devices and tests have been developed by small scale researchers without the resources to do long term studies to estimate the long-term costs and outcomes associated with the test.
Diagnostic technologies for example, do not in themselves directly impact on long-term patient outcomes. Instead, the results of diagnostic tests can influence the care recommended to patients, and in that way, they may affect long-term costs and outcomes.

The benefits associated with the use of a specific diagnostic technology may also depend on the performance characteristics (e.g. sensitivity and specificity) of the test and on other factors such as the prevalence of disease and the effectiveness of available treatments options for the disease in question.7,8 Thus most clinical trials for these tests will be based on short-term endpoints such as diagnostic accuracy defined by using sensitivity and specificity, positive and negative predictive values. If cost-effectiveness analysis is used for funding the test under the MSAC process it may require modelling diagnostic efficacy to final patient outcomes such as survival and QALYs. This will be very much dependent on what therapeutic regimens are available at the time of the analysis and may differ depending on which therapy is included in the modelling, which will become highly complex by having to take into account the impact of false positives and false negatives on patient outcomes, quality of life and healthcare costs. Thus the cost-effectiveness of a diagnostic test may also change over time dependent upon the current range of treatment alternatives available.

Importantly, diagnostic tests that are integral to targeted therapies may either not meet acceptance criteria or may not meet evidentiary requirements when viewed in isolation. As much as the co-dependent technologies are dependent on each other, so are the assessments interlinked and co-dependent.

Similarly, if a medicine applies for funding under the PBS for a restricted population based on a diagnostic test (say certain level of BMD) there are a wide range of scenarios the PBAC may be interested in. This may include a comparison of the new drug with the comparator drug both under the scenarios of targeted population (as identified by test or marker) and the wider patient (non-targeted) population. This will require extensive evidence, much of which may not be available at the time of the launch of the new product.

Decision analytic or disease models will need to be used to model many of the scenarios and assumptions. Such analyses will require detailed data with regards the test characteristics of the diagnostic and the clinical trial evidence and other evidence on the longer terms costs and benefits of for the medicine. Given the complexity of this task it may make sense that the HTA has to be undertaken in a coordinated way between the MSAC and PBS agencies, or as discussed by a single agency.
References


