RESPONSE TO THE

Health Technology Assessment Policy and Methods Review

Consultation Options Paper

23 February 2024

Company Snapshot

CSL Limited is an Australian multinational biotechnology company and a global leader in protein science and plasma-derived therapies.

CSL is headquartered in Melbourne with substantial plasma fractionation and vaccine manufacturing facilities in Australia, the United States, Germany, Switzerland, and the UK.

CSL owns three subsidiary businesses, CSL, CSL Seqirus, and CSL Vifor all of which are underpinned by a significant research and development effort.

Comment

CSL is pleased to provide a response to the HTA Policy and Methods Review – Consultation Options Paper.

We have provided issue specific commentary and recommendations below aligned to the chapters and options as structured in the Options Paper. However, as an overarching commentary we are concerned that there is an under-emphasis in this document on how the PBAC, if it becomes the single entry HTA gateway, will manage appraisal of non-standard therapies – nominally vaccines and blood products.

If the appraisal and funding/funding pathways for blood products were only even raised to the existing level of HTA appraisal, transparency, communication etc. it would be a huge leap forward in reaching the Review's stated objective of 'delivering Australians equitable, timely, safe and affordable access to a high quality and reliable supply of medicines for all Australians'.

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1.0 Transparency, Communication & Stakeholder Involvement

1.2 Consumer, clinician and other stakeholder engagement and consideration in HTA

Develop an engagement framework

CSL welcomes the intention to increase stakeholder engagement with the HTA process by developing a framework to include consumers, clinicians and other stakeholders more consistently throughout the HTA processes (1.2.1).

However, we are concerned that the framework outlined in the proposal does not specifically address the inclusion of submission sponsors.

It is also unclear how ongoing dialogue between the sponsor, submission evaluators (clinical and economic) and advisory committees (e.g. ATAGI) will be incorporated in the framework.

International jurisdictions generally integrate meaningful ongoing consultation between sponsors and the agency during the HTA process (e.g., in UK: JCVI via the protocol for manufacturer engagement and NICE via "Checkpoints" during the evaluation and sponsor participation in the appraisal committee meeting), which benefits both parties as potential misconceptions are able to be resolved during the appraisal process.

As the proposed reforms under the Vaccine pathway (2.1.1c) also entail a *"single comprehensive assessment report"* being produced jointly by the ATAGI and PBAC evaluators, consultation with the sponsor will be essential to resolve any questions raised, or differences of opinion between, the evaluators.

CSL is also concerned that the involvement of "patients as stakeholders" may depend on the existence of a patient advocacy organisation with which the agency can engage.

For those disease areas where a patient organisation does not exist (which is the case for many vaccine-preventable diseases) the engagement process may rely on individual consumers to provide comments during the evaluation.

This may introduce inequity in the extent to which the patient voice is taken into account for those submissions, compared with the inclusion of feedback from organised, systematic and well-funded patient groups during submissions for highly prevalent chronic conditions (e.g., cancer, heart disease, asthma).

Recommendations:

- ATAGI and PBAC must allow sponsors the opportunity to formally engage with them during the assessment process.

- The proposed engagement framework should include processes for ensuring that consumer feedback is obtained equally for submissions in disease areas with no readily identifiable patient organisation or peak body of clinicians, as well as those where a recognised patient organisation exists.

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Strengthen consumer evidence

CSL welcomes the proposals to formalise the recognition and acceptance of real-world evidence (RWE) and statistical methodologies for presenting real-world data (RWD) in the PBAC guidelines.

However, any new guidance regarding the inclusion of RWE and preferred methodologies should be developed in close consultation with industry, to ensure that the proposed requirements are feasible and realistic.

Further, HTA agencies need to acknowledge that it may not be possible for sponsors to implement new guidance regarding RWE immediately. In line with the later proposal in the methodology section (3.2.3b) that the use of non-randomised studies should be *"prospectively designed in collaboration with HTA or regulatory scientific advice"*, the collection of RWE, design of observational studies and inclusion of additional patient-reported outcomes (PROs), health state measures or utility instruments in clinical development programs will need to be planned as part of sponsors' global evidence generation.

As these programs are usually designed at the time of the decision to commit to Phase 3 development and are difficult to implement retrospectively into existing trials, they will take time (years) to implement. Furthermore, additional evidence requirements for Australian HTA should be applicable to different jurisdictions rather than Australia-specific, to permit their inclusion in global evidence generation plans.

Recommendations:

- Any new guidance regarding the inclusion of RWE and preferred methodologies must be developed in close consultation with industry, to ensure that the proposed requirements are feasible and realistic.
- A transition period is required for the adoption of any new guidance regarding the inclusion of RWE in HTA submissions.
- Additional evidence requirements for RWE should be aligned with those of other jurisdictions.

1.4 State and territory government collaboration in HTA

Development of central standardised data sharing system for utilisation and outcome data

CSL supports state and territory government collaboration with federal HTA agencies to centralise and facilitate the sharing of utilisation and outcome data, and believes that this will benefit the Commonwealth, patients, clinicians and sponsors.

An immediate option for reform could be the linkage of the Australian Immunisation Register (AIR) to hospital admission data, which would allow monitoring of vaccine effectiveness in real time.

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Recommendation:

- Proposed initiatives to centralise sharing of utilisation and outcome data must be developed in consultation with industry, to ensure that the data collected are useful, informative and fit for purpose.

Health Technologies that are jointly funded by the Commonwealth and state and territory governments (such as high cost HST's delivered to inpatients in public hospitals)

The proposed reform option currently only specifies high-cost Highly Specialised Therapy (HST's) delivered to inpatients in public hospitals.

However, each of the points for reform could also be applied to HSTs that will be delivered to outpatients and are jointly funded by the Commonwealth and state and territory governments.

CSL strongly supports an expansion of this option to explicitly include all high-cost HSTs, delivered in all clinical settings, such as near-market gene therapies to be funded through the National Blood Authority (NBA). This would help to ensure equitable, timely and a cohesive, national approach to HTA for all high-cost HSTs.

Recommendation:

- Reform option should explicitly include all high-cost HSTs, delivered in all clinical settings, such as near-market gene therapies to be funded through the National Blood Authority (NBA).

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2.0 Health Technology Funding and Assessment Pathways

2.1 Streamlining and aligning HTA pathways and advisory committees

Vaccine pathway

CSL supports the overarching goal of a *"simplified single entry HTA gateway"* (i.e., a single submission to PBAC for NIP listing, with ATAGI and PBAC evaluators collaborating to develop a single assessment report) but believes that the option to seek pre-submission advice from ATAGI must also be retained.

Notwithstanding our support for alignment of the evaluation processes for vaccines and pharmaceuticals through the single entry HTA gateway proposal, we maintain that there are some important considerations unique to the evaluation of vaccines that must be accommodated within a new amalgamated process.

It is unclear how and when during the process the PBAC and ATAGI evaluators will interact, and whether this is via individual collaboration or committee discussion to gain consensus. It is important that the opinions of the PBAC and ATAGI evaluators are able to be presented independently and given equal consideration in the evaluation process.

In line with our recommendation in Section 1.2, CSL also strongly believes that ATAGI and PBAC must allow sponsors the opportunity to formally engage with them during the evaluation process. This should include the opportunity for face-to-face meetings to discuss and resolve key issues during the HTA process, similar to the UK's NICE (National Institute for Health and Care Excellence) process which allows sponsors to participate in the appraisal committee meeting to respond to questions regarding the evaluation.

Additionally, the options for reform (point 2.1.1.c) state that under the new process, the Economic Sub-Committee of the PBAC (ESC) will be supplemented by the appropriate ATAGI representatives. CSL believes that it is essential to ensure that modelling experts from ATAGI, who have expertise in the dynamic modelling required for infectious diseases, are included in the ESC discussion, in addition to clinical experts. It is of the utmost importance that any external evaluation groups contracted by either ATAGI or PBAC are selected on the basis of their expertise relevant to the specific product and disease area.

Recommendations:

- The nature and timing of interactions between the PBAC and ATAGI evaluators, and the evaluators and sponsors, must be clearly defined within the new amalgamated PBAC/ATAGI process.

- Planned interactions must allow for more frequent opportunities for discussion and resolution of questions between the evaluators and sponsors.

- Experts and evaluation groups selected to evaluate vaccine submissions and provide advice to ATAGI, PBAC and ESC must have relevant expertise in the specific disease area and be highly skilled in dynamic modelling required for infectious diseases.

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Expanding the Role of the PBAC (medium term)

1. *"Further expanding the advisory role of the PBAC to enable it to make the HTA recommendation to the Minister for Health for a broader range of health technologies including codependent health technologies (short term)*
2. *The HTA advice does not presume all subsequent funding decisions would take effect through the PBS."*

This option needs significantly more clarity and detail to fully understand the implications. In this section, issues related to a broad range of situations including advanced therapies (including cell and gene therapies), co-dependent technologies, medicines for ultra-rare conditions and vaccines are discussed. For example, it is unclear how the expansion of the PBAC HTA advice would affect therapies traditionally funded through the NBA such as blood and blood-related products, and gene therapies funded through the NHRA or NBA.

Unified HTA pathway for all health technologies with Commonwealth funding (medium to long-term)

CSL is concerned that in this section there is no mention that in comparison to the pathway for PBAC funded products, the funding pathway for new blood and blood-related products is complex, uncertain, and repetitive. Blood products (and the patients who rely on them or are waiting for them) are significantly disadvantaged relative to products evaluated by the PBAC and the wait, on average, to access them is around 3 years and 7 months LONGER than the average time for non-blood orphan products.

Clear, no cost options which would improve the access and appraisal pathway for new blood and blood-related products were recommended by the [Zimmerman] *Inquiry into approval processes for new drugs and novel medical technologies in Australia* in November 2021 and accepted by the Government in their November 2023 response (page 7).

Essentially the proposals for reform include:

- Provide specific guidance and documentation to explicitly allow a parallel registration-reimbursement assessment process.
- Develop a clearly documented process including consolidation of existing process guidelines and templates.
- Development of new guideline documents having regard to both how and when referrals are made to the MSAC and how NBA, JBC and MSAC processes will be harmonised to ensure efficiency.
- Development of fit-for-purpose processes, for the National Blood Authority, to ensure expedited access to new blood and blood-related products.
- Develop and publish an appraisal calendar with meeting dates, deadlines, opportunities for input (from sponsor, healthcare professionals and consumers) and notification of outcomes.

Recommendation:

Reform of the HTA pathways for appraisal and funding of blood products should be included in the recommendations of this Review and patients who need blood products should have comparable transparent and timely access to therapies inline with patients of non-blood products.

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For all health technologies, HTA pathways, unified or not, should be transparent, equitable, with established timelines and published decisions.

2.2 Proportionate Appraisal Pathways: Development of pathways to calibrate the level of appraisal required for HTA submissions to the level of risk (levels of uncertainty and potential fiscal impact)

Triaging submissions

CSL supports in principle the triaging of vaccine submissions and their evaluation being proportionate to the level of risk identified, provided that addition of a triaging step does not itself add time and complexity to the HTA process.

Expedited evaluation of new vaccines that represent a low fiscal risk to the Commonwealth would be beneficial to patients by allowing them faster access to new vaccine technologies.

Recommendation:

- Before triaging of submissions is implemented consultation with sponsors is required to agree how far ahead of the submission triaging would be required to take place, and what information sponsors would need to provide to inform the process.

Development of a disease specific common model (reference case) for disease area with high active product development

CSL supports in principle the development of a consistent model structure in disease areas where there are many potential candidates, with the understanding that any such common model must be developed in close consultation with sponsors of the relevant technologies.

As an example, modelling for vaccines should involve experts in the dynamic modelling of infectious diseases (with expertise in development of SEIR models).

Consideration must also be given to the scenario where many candidates are in development, but not all will be prepared for simultaneous HTA evaluation. It will be important to ensure that any technologies undergoing later evaluation are not disadvantaged by having to use the reference case model developed earlier.

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3.0 Methods for HTA for Australian government subsidy (technical methods)

3.4 Economic evaluation

Selection of the comparator

CSL believes that it is essential that there is further discussion between sponsors and the PBAC to agree suitable methodology for the selection of the appropriate comparator for use in submissions.

As highlighted in section 1.1.3.1 of the research paper *"Australian HTA Review HTA methods: Economic evaluation"*, a disconnect currently exists between identification of the most appropriate comparator based on clinical criteria (i.e. the alternative that is most likely to be replaced by the new intervention) and the lowest cost alternative comparator for pricing purposes as stipulated by Section 101(3B) of the NH Act (which is often not the therapy most likely to be replaced). This is particularly problematic for submissions claiming non-inferiority.

Recommendation:

- Additional discussion between sponsors and the PBAC is required to agree suitable methodology for the selection of the appropriate comparator for use in submissions when there are multiple potential comparators, particularly those claiming non-inferiority. The criteria for comparator selection must balance clinical relevance (i.e. the current extent of use and market share) with the requirements of Section 101(3B) of the NH Act.

Valuing of long-term benefits

CSL agrees that the standard base-case discount rate for economic evaluations should be reduced in line with the rates used in other jurisdictions.

While the rates cited in Table 8 of the research paper *"Australian HTA Review HTA methods: Economic evaluation"* vary, those employed by the jurisdictions with the most similar health systems to Australia and comparable approach to the use of economic evaluation in healthcare decision making (i.e. England and Wales, Scotland, Canada and New Zealand) range from 1.5% - 3.5%. Furthermore, although the annual discount rate used by NICE is 3.5% for the base case, the agency's manual for health technology evaluations also identifies specific circumstances where the use of a 1.5% discount rate may be appropriate.

CSL strongly agrees with the statement in the Options consultation paper (p32) that *"there are circumstances where it may be reasonable to have an alternative (lower) discount rate for some therapies and in some circumstances"*, particularly for technologies offering benefits that accrue over a long period of time such as vaccines and gene therapies.

Recommendations:

- The base case discount rate for economic evaluations for healthcare in Australia should be no higher than 3.5% per year.

- Circumstances where a lower discount rate of 1.5% may be applicable in economic evaluation (e.g. vaccines and gene therapies) should be explored.

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Valuing overall

The PBAC has on several instances argued that the Incremental Cost Effectiveness Ratio (ICER) should be lower for preventative interventions. The following statement was in the Minutes for the submission for Gardasil, CSL's Human Papillomavirus vaccine:

> *"Thus, overall, the PBAC rejected the application for this population-based intervention (for both the primary cohort and both catch-up cohorts) based on unacceptable and uncertain cost-effectiveness at the price requested. In this context, the PBAC noted that the cost effectiveness of the vaccine should be compared to other population preventative interventions such as lipid-lowering and anti-hypertensive drugs rather than with treatment of patients with severe symptomatic disease such as late stage cancer."*
>
> (5.1.71 of the Minutes; Section 12 of the Public Summary Document Nov 2006)

The PBAC reiterated this statement in the decision for Zostavax (zoster virus vaccine) in March 2008 and November 2014.

The routinely lower ICERs for preventative medicines and vaccines especially disadvantages vaccines and we are concerned that this has not been addressed in the proposed options for reform.

The valuation of vaccines for disease prevention compared to traditional pharmaceutical products for the treatment of established disease is an inherent part of HTA methodology and within the defined scope of the review. This valuation issue must be addressed urgently, particularly in the context of developing pandemic vaccines.

Recommendation:

- The precedent for routinely requiring lower ICERs for preventative medicines and vaccines especially disadvantages vaccines and should be considered and addressed by this HTA Review.

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4.0 Health Technology Funding and Purchasing Approaches

4.1 Approaches to funding or purchasing new health technologies

Recognising competition between new health technologies that deliver similar outcomes

CSL supports a streamlined submission pathway and faster process for the evaluation of cost-minimisation submissions consistent with the approach taken by NICE and the SMC. However, we are opposed to the proposal that new technologies being submitted with a claim of non-inferiority to the current standard of care may be required to list at a lower price.

This may jeopardise the commercial viability of listing new technologies that may offer significant benefits to patients (e.g. a different, but non-inferior side effect profile versus current therapy) in the absence of a net gain in health outcomes at population level.

The consequent reduction in choice of available treatments will be detrimental to patients. Furthermore, this proposal runs contrary to recognised principles of health economic theory, which support equivalent value being attributed to equivalent health benefits.

Recommendation:

- The Review Committee should not pursue any proposal that requires health technologies that offer non-inferior health outcomes to agree to a lower price than the standard of care to gain listing. Any such initiative will seriously limit patients' choice of available treatments.

Post-listing re-assessment of health technologies

CSL is concerned that this proposed re-assessment of listed health technologies is focused solely on consideration of opportunities for disinvestment.

Another important issue is the static pricing of vaccines, for which the cost of goods may often increase due to increasing manufacturing costs over time, which may jeopardise the viability of maintaining supply of these essential medicines.

In line with other PBS items, and to reduce discrimination of vaccines, an annual review of the reimbursed price of vaccines without a full PBAC submission should be allowed to permit an assessment of the potential risk to supply posed by inflation in the cost of goods.

Recommendation:

- A mechanism for the review of the pricing, similar to that available for PBS medications (i.e., not requiring a new PBAC submission), should be developed and available for vaccines listed on the NIP.

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Investigate further options to address budget impact implications of high-cost/high impact health technologies

CSL supports this option to identify appropriate alternate contract funding/financing tools and instruments (e.g., annuity payments, patient-level product warranties) in consultation with stakeholders. This process should include consultation with industry and with state and territory representatives of the JBC in relation to next generation therapies funding through the NBA such as gene therapies.

Recommendation:

- New next-generation therapies offering long-term benefits should be supported by consideration of new funding/financing tools and instruments. This consideration should include ALL funding pathways including nominally "blood" (cell and gene) products which are required to be funded through NBA / JBC.

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5. Futureproofing Australia's systems and processes

5.1 Proactively addressing areas of unmet clinical need

Development of priority list

CSL supports the surveillance of vaccine preventable diseases to inform prioritisation of areas of high unmet clinical need (HUCN).

We believe that in considering HUCN, it is important to identify areas of clinical need where there is currently sub-optimal therapy, rather than an absence of available treatment.

For example, for existing vaccines with sub-optimal absolute vaccine efficacy (VE), incremental improvements in relative vaccine efficacy (rVE) compared with the current standard of care may produce significant health gain and prevent a large number of deaths when magnified over the population at risk.

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