PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types

General/overall comments

Please note, comments that are beyond the scope of PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types will not be considered

The challenges facing public healthcare systems in the era of precision medicine are well known. Here we focus on a solution. The perfect solution needs to preserve high quality drug evaluation in the public interest, based on randomised clinical trials evidence and health economic analysis, while addressing the accelerating rate of emergence of clearly effective therapies for patients with high unmet need.

The immediate challenge is a transition phase between an era of anatomic and histologic classifications, and the era of universally accessible molecular pathology to guide optimal use of treatment.

An interim solution is required that enables patient access to treatments with a minimal threshold of activity, but which fail to meet a mandatory evidentiary standard required for drug listing. Such a solution will enable PBAC (and where relevant MSAC) to acquire the information required for decision making while simultaneously providing expedited, controlled access to potentially life-saving drugs. At the end of this document we propose such a mechanism that is already funded and that can be implemented immediately.

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It is critical that the advent of science-led therapies based on molecular biomarkers is rendered compatible with the best of the drug evaluation system in the PBAC and MSAC. It is also important to adapt the principles behind randomised clinical trials-based evidence to the new realities of drug development.

In an era of increasingly targeted therapies, maximising the cost-benefit for drug development will depend on the capacity to identify molecular targets. These targets may be shared by multiple cancer types, and although not invariably linked to response across all histologies, this is more often the case than not.

The histologic classification of cancer historically used for drug development and reimbursement has given way recently to pan-cancer approvals, exemplified by the FDA approval of Pembrolizumab for any advanced cancer with mismatch repair deficiency (dMMR).

To retain our global reputation as a leader in health care, Australia needs to consider how it will adapt its regulatory drug evaluation processes to accommodate the irreversible trend to biomarker-defined subgroups of patients who benefit from therapy.

The benefits of this adaptation will be greatest for the many Australians with rare and less common cancers, for whom the sample sizes preclude classic randomised data collection. These folk amount to almost half of all cancer deaths.

It is also the easiest way of preserving the role of randomised trial evidence in drug evaluation, because aggregation of histologic subtypes sharing a common molecular biomarker overcomes the problems of insufficient numbers.

There are two specific addressable challenges:

1. the creation of an accessible, equitable national platform for molecular classification of patients with advanced cancer, irrespective of histotype. This is a substantive issue that will inevitably be addressed by accumulating benefits from biomarker-driven drug development, and decreasing costs of molecular testing.
2. the bias that accepts variation in response on the basis of undefined molecular heterogeneity within a homogeneous histologic subgroup, but rejects the same magnitude of variation due to undefined histologic heterogeneity within homogeneous molecular subgroups. Uncertainty has, and will continue to be, an inevitable feature of drug evaluation. The key is to apply the same standards for tolerance of uncertainty evenly and fairly.

Notably, the solutions proposed above are not incompatible with histologic classifications and defined evaluations. It may be that these solutions will be applied exclusively for rare and less common cancers, for two reasons. First, on the basis of equity of taxpayer investment for a large group who will not otherwise equally

benefit from medical advances. Second, on the basis that histotype-by-histotype regulatory evaluations are impractical in any reasonable timeframe for the enormous number of these conditions. A mechanism for efficiently evaluating carefully defined disadvantaged and diverse cancer types in one application presents efficiencies to the system in the face of an increasing number of drugs.

Finally, we anticipate that molecular pathology will ultimately evolve over the next decade to allow universal access to genomic (or other) tests that will stratify therapy, starting with advanced disease. The immediate challenge is to prepare for this era by creating a national framework that addresses unmet need and clinical opportunity at the population scale, and building capacity in molecular pathology with national standards. Such a framework will not only allow greater and earlier access to novel therapies through enhanced trials, but enable the generation of real-world evidence to substantiate drug approvals while preserving the proper roles of PBAC and MSAC.

We describe such a mechanism—the Australian Genomic Cancer Medicine Program—in Q13.

Specific responses

Please insert your comments against the consultation questions below.

Question 1

What do you/your organisation see as the potential advantages of the PBAC considering the PD-1 and PD-L1 checkpoint inhibitors for multi-tumour listings?

The major advantages are:

1. There is good evidence that for patients with diverse metastatic cancers sharing a common biomarker, that the magnitude of the benefit for those people is at least as great as is the case for current conventional monohistotype. The example is the magnitude of benefit from immunotherapies for MMR-deficient (dMMR) non-colorectal cancers, compared to melanoma and non-small-cell lung cancer (NSCLC). This logic is particularly important for rare and less common cancers. This is primarily a question of equity and social justice, and science.

2. Efficiency. Assuming that for rare and less common cancer types, there are at least 108 histologic entities, the prospect for PBAC of individually assessing each of those serially is both impractical and adds cost into the system. It also delays access to those therapies for patients who clearly would already benefit from them.

Accordingly, pan-cancer listings distribute the benefits to the community to those who will clearly benefit, at a level which we have already judged to be reasonable in respect of histologic classification, and to do so in the most cost-efficient and expedited fashion.

Question 2

What do you/your organisation see as the potential disadvantages of the PBAC considering the PD-1 and PD-L1 checkpoint inhibitors for multi-tumour listings?

There are three major disadvantages:

1. In order to identify a common property that links together multiple disparate histological entities, one needs in place a universally accessible platform for identifying that common property. For a dMMR biomarker, this means the establishment of an accessible program for molecular testing for all patients with advanced or incurable cancers. Such molecular profiling is not yet available to all patients without discrimination. It is currently available for all patients with colorectal cancer.

This can be broken down into two subparts:
a. Choice of platform. Immunohistochemistry (IHC), or genomic panels. We believe the latter are the logical choice, for the following reasons. First, some MMR proteins are not currently tested by IHC: eg, POLE mutations that predict for mismatch repair deficiency. Second, genomic tests can measure evidence for mismatch repair deficiency directly, or by mutations of known causal genes, while at the same time testing for other candidates for biomarker-driven therapies. Third, costs will drop progressively for genomic tests and the value proposition rise with further drug development. Finally, other biomarkers that will be increasingly relevant to immunotherapy can be assayed, like

increased tumour mutational burden (TMB). There is some work is being done to demonstrate at least equivalence for genomic and IHC tests, although it would not be difficult to generate such data.

b. The implementation of this technology as a standard across the country in all states and territories in such a way as to enable equitable access for all Australians to this testing. There is marked variation across the country in the standards for molecular testing, particularly using genomic panels. There is also considerable variation in, and low levels of experience with, immunohistochemical staining, outside of colorectal cancer, as an assay for mismatch repair deficiency. Accordingly, in addition to the decision regarding which platforms should comprise eligible criteria for mismatch repair deficiency, the implementation of those platforms across the country constitutes, in itself, a practical challenge going forward. However, not only are these challenges surmountable, but they must be surmounted in the near future if Australia is to remain at the forefront of healthcare systems globally.

2. A second potential disadvantage is that there may be histological subgroups that, for reasons we do not yet understand, may not respond to immunotherapies, which would be lumped in in any pan-tumour approval, regardless of whether they share the property of mismatch repair deficiency. However, the same magnitude of uncertainty is the case currently with histologic approvals, such as melanoma and NSCLC.

3. The third challenge is the rapid evolution of molecular testing in this space. Clearly, the current pan-tumour indication is limited to mismatch repair deficiency, specifically in respect of the immunotherapies. However, it is clear that over the next 5-10 years there will be multiple drugs that will have this property of having activity across multiple cancer types based on a shared molecular indication. For example, the drug Larotrectinib, the results of which were released at the 2017 American Society of Clinical Oncologists (ASCO) meeting, is highly active and provides significant benefit for patients who share the property of NTRK fusion mutations, regardless of histotype. This is one reason the choice of the platform to be implemented for screening becomes critical. It is likely over the next five years that additional examples of this kind will be developed, and therefore it is our view that the future of molecular screening for cancers in order to determine their eligibility for access to drugs is likely to focus increasingly upon genomic panel tests. This platform will have a durable utility over the foreseeable future, anticipating that there will inevitably be additional opportunities to approve drugs on the basis of a shared molecular profile.

Question 3

What is urgent unmet clinical need? How should it be established? For which patient groups?

Clearly any patient with an advanced cancer who has run out of conventional treatment options, for whom novel therapies, including immunotherapies, are likely to prove effective would benefit from a pan-tumour recommendation. The largest group that is currently disenfranchised from the drug evaluation process are those with rare and less common cancers, where low numbers have systematically precluded empiric trials-based drug development. This is because taken by histological subtype individually, the evaluation process is cumbersome and inefficient and statistically challenging. There are consequently far fewer drugs available and far less research being conducted based around a drug evaluation process that focuses upon individual histotypes. Collectively, the group of patients with rare and less common cancers accounts for some 52,000 diagnoses and 25,000 deaths a year in Australia. A pan-tumour indication would bring a significant fraction of these patients into the fold and provide evidence-based access for these individuals on a more equal footing to patients with melanoma and NSCLC.

Question 4

What is the minimum level of evidence of effectiveness that you/your organisation think should be required before a PD-1 and PD-L1 checkpoint inhibitors is considered for subsidy for a particular kind of cancer? Why?

There are multiple considerations:

The absence of alternatives – clearly the evidence of benefit needs to be significantly greater, than currently available options. In some cases, single arm data may be sufficient. The US Food and Drugs Administration (FDA) recently issued a position statement in the *New England Journal of Medicine* indicating the conditions under which single-arm trial data would be considered acceptable for drug evaluation. They particularly noted rarity, unmet need, poor outcomes and magnitude of benefit. Under these circumstances, single-arm data could be buttressed by real-world data generation under managed-entry schemes.

Critically, randomised clinical trials actually become possible in pan-tumour indications, where aggregation of numbers sharing a common biomarker allows sufficient numbers to be enrolled in a feasible time frame. The critical issue remains histologic diversity, which may necessitate an increase in sample size in those arms. This is, in our view, more than offset by the advantages of conducting a randomised evaluation. In order to proceed with a randomised pan-tumour clinical trial designed with registration in mind, there has to be prior agreement between the pharmaceutical company and the regulatory authority. Such an agreement might take the following form: that, subject to the emergence of evidence for favourable cost–benefit, the authority would recommend listing of the drug for that indication across multiple cancer types. It is critical that drug development in a pan-tumour era continues to use the trusted tool of a randomised clinical trial design.

We assume the existence of a population-level molecular screening program to enable the identification of such cases with reasonable efficiency and cost effectiveness for the pharmaceutical companies. For example, while a randomised study of 300 patients (150 on each arm) might well be sufficiently powered to identify evidence of significant benefit for the intervention in question, if the molecular target is present in the screened population of 3% frequency, in order to identify the 300 trial patients, 10,000 would have to be screened. A specific task will be to establish a national framework for population-level access to molecular screening, meeting consistent national standards, supporting both clinical trials and conventional drug access.

Question 5

Do you/your organisation think it is possible for the PBAC to be able extrapolate, or apply, the evidence of effectiveness of a checkpoint inhibitor in one kind of cancer to another kind of cancer, or from late stage cancer to early stage cancer? Why? How?

Yes, with caveats. It is possible for the PBAC to extrapolate the evidence of effectiveness of a checkpoint inhibitor in one kind of cancer to another kind of cancer. There are some common properties to the response patterns for immunotherapies, including the notable durable nature of the benefit to trial patients responding to such agents. There have been sufficient trials across multiple individual histological subtypes confirming these patterns, and surrogate markers such as progression-free survival at six months, to enable the more efficient conduct of clinical trials of newer agents. These efficiencies are essential to expediting and reducing the costs of drug development, ultimately borne by the taxpayer. This is particularly important for rare and less common cancers.

This is not the case for moving from late stage cancers to early cancers. Fundamentally, in our view, any trial of adjuvant immunotherapy will require a randomised design to demonstrate improved relapse-free and overall survival for the intervention. Many drugs that are effective in the context of advanced cancer do not have benefit in respect of early stage cancer (for example small-cell lung cancer (SCLC) or the use of chemotherapy for the common types of adult-onset sarcoma). Fewer trials of immunotherapy have been conducted in early-stage disease.

In this situation a pan-tumour approach based on a shared molecular profile may well be the only mechanism that makes such randomised trials feasible.

Question 6

Do you/your organisation think it is possible for PBAC to satisfy itself that treatment with a PD-1 or PD-L1 checkpoint inhibitor is cost-effective without an economic model that is specific to that kind of cancer? How?

- Is it possible to group different cancer types together based on particular characteristics that are similar, and construct a single model for the group?
- Are other approaches to establishing cost-effectiveness across cancer types possible? What are those approaches and how would they operate?

Uncertainty is unavoidable in drug evaluation. The sources of uncertainty may arise within a single histological entity due to the existence of unrecognised molecular diversity, or within a single molecular subgroup due to histologic diversity. The key issue is the magnitude of that uncertainty, and our tolerance of it. The magnitude of uncertainty that is tolerable and still consistent with drug listing has been established by precedent (see NSCLC, melanoma). It is arguable that a greater tolerance of uncertainty is justified in situations of high unmet need.

For example, the overall survival for patients with non-colorectal dMMR cancers exposed to immunotherapy was >60% at two years, with the characteristic plateau effect observed in single-histotype clinical trials. The probability

that this magnitude of benefit would not satisfy a health economic argument across these cancer types appears remote, where standard-of-care options are few or absent. For cancer types with high unmet need, that are historically disadvantaged, it is arguable that a greater degree of uncertainty should be tolerated. The evidentiary standard could be buttressed both by adapting conventional randomised clinical trials design to enable health economic evaluations in a classical sense, and by real-world data collection under managed-entry schemes.

Data may need to be obtained in a real-world environment relevant to the PBAC within an Australian context. Should such data be required in order for PBAC to come to a final conclusion and recommendation to the Minister, it is important to have an infrastructure that enables the conduct of such studies in a way that does not unduly delay a drug access where there is evidence of clinical benefit.

The creation or generation of real-world outcome data for populations with rare and less common cancers is clearly critical as an aid to PBAC in determining the natural history of disease and should be a part of any investment strategy going forward. Registries of such outcomes will provide real-world information on which to base comparators.

Question 7

What do you/your organisation think is a reasonable subsidy price for Government to pay for a PD-1 or PD-L1 medicines for cancer types where the benefit is potentially very modest?

The question is, can one scale a price according to the magnitude of benefit, with perhaps the greatest investment for the greatest benefit, and the least investment where that benefit is least? This is a complicated area and would require close discussion with the pharmaceutical industry as to a mechanism that would make this possible.

An interesting idea that could be applied to rare cancers is to fund after evidence of response, where the first doses are provided free by the pharmaceutical company. Here the evidence for individual benefit is clear. For example, if an individual who pays for access to an immunotherapy has complete resolution of their cancer, should the government fund the drug after four cycles? This approach has much to recommend it in a shared-risk model, but is difficult to render susceptible to conventional health economic evaluation, and also to disinvestment.

This might well be appropriate for patients who have rare or less common cancers who would otherwise not participate in trials that would generate evidence for conventional models of funding.

Question 8

Do you/your organisation think PD-1 and PD-L1 medicines should be made available to all patients whose cancers display a particular biomarker? Why? Which biomarker?

Yes, where the magnitude of the benefit reaches an agreed standard. This is the case for trial patients who share the property of mismatch repair deficiency across multiple cancer types, where the benefit is at least as large at the magnitude of benefit for patients with melanoma exposed to the same therapies. It appears neither equitable nor rational to conclude otherwise.

Other biomarkers (aside from mismatch repair deficiency) include tumour mutational burden, which is likely to be even more important as a predictor of response.

A related issue is the integration of such biomarkers with histologic categories (a mixed model). Eg, high tumour mutational burden cancers with a population frequency less than 6:100,000.

This is a problem whose time is coming. There are multiple other examples of such biomarkers. NTRK is another biomarker with similar properties. It has a 3% frequency across multiple cancer types, with huge benefit. One can't generalise, but the overwhelming evidence is accumulating that biomarker-driven approaches are providing benefit. There are emerging multiple institutional case series that all confirm the benefit in late-stage populations for biomarker-driven therapies in general, even though there may be individual circumstances where those rules do not apply. As a generalisation biomarker-driven trials are much more effective than non-biomarker-driven therapies.

Question 9

Do you/your organisation think it is appropriate for the PBAC to extrapolate the evidence from one PD-1 or PD-L1 checkpoint inhibitor to other medicines in the same class(es). This could provide patients with more choice and give Government the

opportunity to negotiate better subsidy prices by utilising the competition between sponsors of medicines.

Yes, as a general rule, as the equivalent of a Bayesian prior. Provided that there is some existing data about a magnitude of benefit with a similar compound in same class, it is reasonable then to approve those compounds using, as part of the decision-making process, information derived from other drugs within same class. However, different drugs have different properties and different side-effect profiles and they shouldn't be assumed to be all equivalent, and there must be at least some clinical data about the benefits for those immunotherapies. Practically, the disadvantages in increased uncertainty attached to such assumptions may be offset by the market benefits in the avoidance of monopolies.

In summary, provided that there is some basis for comparability with other drugs with known efficacy within a class, it is reasonable to include that information in the evaluation of any new drug, thereby decreasing the evidentiary burden. Although this will introduce some uncertainty, this is acceptable given the benefits from the market perspective and avoiding monopolies.

Question 10

Do you/your organisation think that different evidentiary requirements are appropriate for rare cancers? How do you think cost-effectiveness should be established in this case?

Yes, there is a social justice issue to be addressed. Patients with rare and less common cancers, who comprise a very large fraction of the cancer population, pay the same taxes as patients with common cancers. However, patients with common cancers have access to the benefits of medical advances and therapies thanks to participation in the research enterprise. Patients with rare cancers have been systematically excluded from participation in research that would qualify them for access to new therapies. Thus, they pay taxes for research and drug access for others, but do not benefit to the same extent themselves. This is manifestly unjust.

It is important that we:

1. collect information on the natural history of rare and less common cancers to act as a useful comparator for drug evaluation of single-arm data;
2. facilitate pan-tumour randomised trial data generation where possible;
3. buttress weak evidence while expediting drug access where there is unmet need and some evidence of clinical benefit, by managed-access schemes which generate the data required for unconditional listing.

Question 11

Do you/your organisation think PBAC should set aside one of its meetings each year to consider only PD-1 or PD-L1 inhibitors for cancer? (This would mean no other submissions for other medicines, including other cancer medicines, or other diseases would be considered at that meeting.)

If the volume of work is sufficiently large, and if the nature of that work is sufficiently distinct and homogeneous that it might benefit from a single sitting to consider it, that is entirely a matter for PBAC. We don't see in principle any reason for immunotherapies, other than by virtue of their volume, to be treated as a distinct subgroup in respect of any assessment process. It may well be that the volume of work is increasing such that PBAC needs to reconsider its schedule, but that's a different matter.

Question 12

If limited evidence is available at the time of subsidy of a PD-1 or PD-L1 inhibitor for a type of cancer, what do you/your organisation think should happen afterwards?

- Should sponsors be required to collect more evidence?
- What should happen if the new evidence shows the medicine is less effective or has greater safety risks than expected?
- Should the medicine continue to be subsidised but at a price commensurate with its benefit? Should the sponsor be compelled to continue to make the medicine available even if it thinks the price is too low?

Where existing evidentiary standards don't satisfy PBAC for listing, and where the nature of the missing data can be

identified and is attainable by common agreement with the pharmaceutical or other sponsor, then it follows that by negotiation with a sponsor, real-world studies should be set up within the Australian environment that achieve two things – expedited access where there is at least some threshold for evidence of benefit and the generation of the residual data required for unconditional listing. The properties of such real-world studies are that there should be prior agreement between PBAC and the sponsor that achieving a certain threshold of evidence of benefit, that PBAC will recommend listing, otherwise you disincentivise the sponsor.

In the event that that evidentiary threshold is not achieved, there will not be a listing and the drug will be withdrawn from the evaluation process and therefore also for conditional access to the population in question. Practically, the implications are that such real-world studies would need to be conducted in such a way that there is, to the extent reasonable, access to all Australians to the drug and in a contained clinical trial environment where the discontinuation of drug access through this mechanism falls within the conceptual framework conventionally accepted for clinical trials.

Finally, it should be agreed the conduct of such studies within an Australian environment constitutes a specific requirement of PBAC and there should be a shared-investment model agreed by PBAC and the pharmaceutical industry. That shared investment model will be negotiated on a case-by-case basis, but founded on the principles that there is residual data to be generated prior to an unconditional listing, but that there is also an intent to provide expedited access where there is some prior evidence for clinical benefit in a population with high levels of unmet need. Therefore, on that basis one might expect to have some degree of support from the Federal Government in the conduct of the trial, perhaps paying for the data generation, whilst the provision of the drug should be made universally available, along with some funding for the collection of the data from the pharmaceutical partner. This constitutes a shared risk-and-benefit model for expediting drug access, subject to suitable data generation.

Questions about the scaling of price to benefit and whether a sponsor should be compelled to provide a drug have no easy answers. It depends on the drug and the magnitude of benefit, and so forth. These decisions are properly the province of expert review in each case, as occurs for PBAC. It is not possible to make any general statements about the relationship between the magnitude of benefit and the reimbursement, other than to say that it has some appealing features, but would depend upon how you went about measuring that benefit and the reimbursement models. It is likely that the only way to be confident about the magnitude of benefit within any individual patient at some final resolution, would be post hoc. While it would be worthwhile exploring mechanisms that would enable that evaluation, or benefit-linked reimbursement, that would require a different model for reimbursement.

As to compelling a company to continue to provide a drug, that sounds challenging.

Question 13

(For industry/clinical groups) Clinical study information: (Please use the template provided for this information.)

- In what indications has your organisation completed clinical trials with a PD-1 and PDL1 inhibitor? Please include both positive and negative studies.
- In what indications is your organisation currently conducting or planning to conduct clinical trials with PD-1 or PD-L1 inhibitors? If usual PBAC processes were to be followed, when would you expect to make an application for subsidy for these indications?
- How does your organisation decide which indications to study and which to prioritise for registration or subsidy?

Through Garvan's Genomic Cancer Medicine Program, we have conducted a dozen or more clinical trials for rare and less common cancers, as well as histotype specific and early-phase indications. We prioritise indications on the basis of unmet need and opportunity to maximise the clinical benefit.

In only 18 months, the demand for these clinical trials has resulted in close to 1000 patients travelling to the Garvan in Sydney from all over the country (*See summary of Molecular Screening and Therapeutics clinical trials attached)*. This overwhelming demonstration of unmet need has compelled the creation of a national network of Australia's eight major cancer centres and three leading research institutes to deliver genomic cancer medicine clinical trials to thousands of Australians with rare, less common and early-onset cancers, who currently have no other options. This **Australian Genomic Cancer Medicine Program** allows patients to participate in trials in their home state or territory and builds the infrastructure needed to develop precision medicine nationally.

In their August 2017 report, *Rare Solutions: A Time to Act*, Rare Cancers Australia called for trial designs that provide evidence to allow drug registration submissions to the TGA and PBAC. We are keen to ensure that Australian

Genomic Cancer Medicine Program trials, particularly in the national context, are fit-for-purpose in terms of assisting them with data for drug listing for rare and less common cancers.

The Australian Genomic Cancer Medicine Program also has the capacity to support PBAC by enabling the generation of fit-for-purpose, real-world economic and effectiveness data in an era of increasingly high-cost molecular therapies, while expediting early drug access for underserved populations.

As a national network, the Australian Genomic Cancer Medicine Program offers PBAC a mechanism for providing immediate but conditional access to novel drugs in rare cancers. These 'post-market' trials, conducted in all states and territories at participating Australian Genomic Cancer Medicine Program centres, can capture real-world outcome and resource utilisation data where it is lacking. This mechanism allows early patient access to drugs, while data on agreed endpoints (evidence of benefit, health resource utilisation, etc), is collected over an agreed timeframe.

With this information, PBAC is enabled to make a firm decision as to whether to list unconditionally, or not to list. These trials would be a shared risk-benefit partnership between pharma, government, researchers and patients, to address unresolved issues and enhance access to novel therapies for patients with rare and less common cancers.

The issues around registration of PD1/PD-L1 checkpoint inhibitor immunotherapies for pan-tumour indications present an opportunity to develop and pilot a fit-for-purpose 'post-market' trial using the Australian Genomic Cancer Medicine Program network. This model can then be leveraged for managing future multi-indication treatments, including for other cancers and other diseases, such as autoimmune and other chronic conditions.

Question 14

Are there effective international models for multi-tumour subsidy that could be applied in Australia within the current regulatory framework?

Obviously, there is the FDA's approval of Keytruda, but that is not the same thing as Australian reimbursement approval. The FDA's decision to consider pan-tumour indications is the only the first of other examples to follow. For equity of access issues, PBAC needs also to consider molecular pathology access, something not considered by the FDA.

Question 15

(For Industry) What information can you provide regarding established international agreements for multi-tumour subsidy and how could these apply in the Australian regulatory context?

N/A

Question 16

Is there anything else you/your organisation would like to add?