

# Consultation: Reforms to the regulatory framework for complementary medicines

## Assessment pathways

### Approaches to establishing efficacy

3.1 Do you agree with the proposed indication hierarchy and the criteria proposed to distinguish the three medicine pathways?

In principle yes, but see comments below.

3.2 Do you envisage any difficulties with criteria used to include or exclude products from the new pathway?

Yes.

How many indications will actually fall into the category of 'intermediate indications' that exceed the permitted indications list but are not high level indications. You have classified intermediate indications as referring to:

- a **serious disease** (i.e. restricted representations); OR
- the prevention or alleviation of a disease, ailment, defect or injury **other than a serious form of those diseases.**

versus a high level indication which may refer to:

- the prevention, alleviation, cure or management of a **serious form of a disease**, ailment, defect or injury (i.e. restricted representations).

In reference to both intermediate and high level indication as being able to prevent or alleviate a disease, the only defining factor is whether the ailment is classified as a serious or non-serious form of a disease.

Greater clarity needs to be given to differentiate intermediate and high level forms of disease.

3.3 What other considerations may need to be taken into account in implementing the new pathway?

It is a possibility that clinical studies subsequently conducted are contrary to the outcome of the evidence presented in the pre-market assessment. As a requirement to evaluate the balance of total evidence available, it would be advisable that evidence of efficacy is reviewed in every post-market assessment.

3.4 Do you agree with the proposed methods to establish efficacy for products included via the new pathway?

Yes, but will there be issues with conflict of interest over who funds research (see part below)

3.5 Is the proposed approach to establish efficacy for current listed products that have a restricted representation exemption appropriate?

We assume that this means that the approvals granted through the CMA 42DK application for all folic acid (prevention of neural tube defects/spina bifida) and calcium (may assist in the prevention of osteoporosis when dietary intake is inadequate/ a diet deficient in calcium can lead to osteoporosis later in life) listed supplements, provided they meet eligibility criteria, will have to go through the new approval pathway. Some of these products have been on the market for several years, and consumers may be repeat purchasers (especially in the calcium supplement category, for the prevention of osteoporosis, amongst older users). The removal of an indication relating to reducing the risk of osteoporosis from a product that has been marketed for a long time, may cause confusion to consumers. Also, considering FSANZ permits “reduces risk of osteoporosis’ for a food that contains no less than 290mg of calcium per serve, we propose that current folic acid and calcium supplements are grandfathered in being able to continue to use the restricted representations outlined.

All other restricted representations on current listed products will go through the new pathway.

3.6 Are the evidence requirements appropriate for the new pathway?

No

The new pathway for intermediate level indications, for the primary indication, requires a minimum of:

A) One Category D evidence (double blind randomised controlled trials [including crossover trials, or cross-over trials]/systematic review)

OR

B) A minimum of 2 types of evidence from Category B (non-systematic, generalised reviews - including databases/Publicised international Regulatory Authority Articles/Evidence based reference text – scientific/Scientific Monographs/Pharmacopoeias) and at least one from Category C (Observational studies e.g. cohort and case control studies /Comparative studies [non-control])

Part A) above is actually the current requirement is for a specific low risk indication for a low-risk listed medicines

Part B) above is actually on par with the current requirement for a non-specific indication for a low-risk listed medicine, and is currently not accepted for a specific indication for listed medicines, ie. it is below the current requirement for specific indication on a product classified as lower risk.

Please see below

3.7 Do the proposed levels of assessment align with the proposed risk-based hierarchy?

No.

The whole consultation paper with regards to the requirement for evidence to substantiate indications for listed Complementary Medicines is completely inconsistent with the current 2014 Evidence Guidelines , even though the paper states on page page 17-19

*“Tables 2 and 3 provide the **current** as well as the proposed minimum number and types of studies required for the three proposed assessment pathways for complementary medicines.”*

*“Note that all secondary low level indications drawn from the permitted indications list should also be supported by evidence appropriate for listed medicines outlined in Tables 2 and 3 (i.e. supplementary evidence).”*

*“All evidence will be subject to minimum requirements for relevance, quality and consistency. **These requirements are currently specified in the Evidence Guidelines for listed medicines, which will be updated accordingly.**”*

Evidence guidelines outlined in Tables 2 and 3 is inconsistent with current evidence guidelines for permitted indications.

Currently Listed medicines that make low risk indication, which are considered specific, include all indications referring to:

Health enhancement

A disease, ailment, defect or injury other than a serious form including:

- Reduction in risk, frequency, duration
- Management or relief

Table 5 on page 22 of the Consultation provides examples of indications appropriate for inclusion in the permitted indication list (i.e. for low risk complementary medicines), and includes reference to non-specific and specific indication types. Tables 2 and 3 (page 17-18), provide requirements for evidence to support ‘Listed Medicines – Low Level Scientific’. The requirement stated here is

- A minimum of 2 types of evidence from Category B (Non-systematic, generalised reviews - including databases/Publicised international Regulatory Authority Articles/Evidence based reference text – scientific/Scientific Monographs/Pharmacopoeias) AND
- At least one from Category C, **where required** (Observational studies e.g. cohort and case control studies/Comparative studies [non-control]) AND

- Additionally for specific indications, a minimum of one from Category B as supplementary evidence.

NB. What is the requirement for 'where required'?

Compare the above to current evidence guidelines. Page 38 of current 2014 Evidence Guidelines for Specific indications state:

You must hold scientific evidence to support the specific indication. Such as:

- Evidence obtained from well-designed controlled trials with randomisation; OR
- Evidence obtained from well-designed analytical studies preferably from more than one centre or research group, including epidemiological cohort and case-control studies; OR
- Evidence obtained from multiple time series with or without intervention, including within country and between country population studies.

### 3.8 What other considerations may need to be taken into account in implementing the new pathway?

Current post market reviews of products within our range for specific indications have currently not been able to satisfy the post-market review office. Assessment of clinical evidence has not been able to satisfy TGA level of criteria to be acceptable.

As the new pathway must have evidence requirements that are at the very minimum the same as current evidence requirements for specific indications for listed medicines, in reality, it may be more difficult to find evidence to satisfy TGA requirements for the new pathway, given the difficulty with satisfying TGA even with low-risk medicine indications.

Criteria for permitted indications.

### 4.1 Are the proposed criteria for inclusion of an indication on the permitted indications list appropriate?

Table 5 states that an indication appropriate for inclusion in the permitted indications list includes the reference to the word 'management'.

Under the coded indications project that has been worked on already, all indications that contained the word management have been re-written eg.

'EAR5 May assist in the management of itchy ears', is now 'SCI-BDEAIT-RE May relieve symptoms of itchy ears'

### 4.2 What other considerations should be taken into account in implementing the permitted indications list?

To avoid industry confusion, TGA needs to define more clearly for industry the distinction between non-specific and specific indications. Perhaps when compiling the permitted indication list, as part of this project, each indication can be classified as non-specific or specific. Industry is currently confused about this.

4.3 Is Option 2 for selecting indications for inclusion on the ARTG and on product labels and promotional material suitable to address the objectives for permitted indications?

I believe option 3 is the best option. If all components of a structured indication are able to be selected from a drop down list, the probability of the indication accurately reflecting the evidence is more likely to be accurate, as all components can be selected from a drop down list.

Option 2 may not permit such accurate representation of the evidence. For example, the evidence may show that Viburnum may assist in the prevention of muscle aches and pains, rather than relieves muscle aches and pains.

Option 1 is not suitable as sponsors who may wish to get a product to the market with a certain indication may take a risk based approach to the likelihood of a post-market review, and launch a product on the market before TGA updates the indication list.

4.4 What other considerations should be taken into account in implementing the permitted indications list?

Page 42 of current 2014 Evidence Guidelines:

*“Relevance of the study population*

*The health status of the study population should be representative of the target population for your medicine. Many listed medicines are used by healthy individuals.”*

Instead of having a qualifier ‘in healthy individuals’, for selection, for certain indications, as it appears low risk products are only suitable for ‘healthy individuals’, and to avoid confusion as to when this qualifier needs using, why not have a disclaimer on every label that states ‘this medicine is suitable for use in healthy individuals’. Alternatively, TGA could flag the permitted indications that have the potential to indicate use for a disease, if this qualifier is not used.

Actually, we don’t think the consumer understands the qualifier ‘in healthy individuals’. Has any consumer group been consulted on their perception of this qualifier?

### **Criteria for the use of a claimer**

5.1 Do the proposed criteria for the use of a claimer address the objectives for the recommendation?

Yes.

5.2 What other considerations should be taken into account in implementing this recommendation?

It is a possibility that clinical studies subsequently conducted are contrary to the outcome of the evidence presented in the pre-market assessment. This would result in the product indication and efficacy evaluation claim not being applicable any more.

5.3 Will the use of a claimer on complementary medicines have any unintended consequences?

For those Listed medicines that could potentially have **exactly the same** ingredients, and haven't gone through the pre-market assessment, the use of a claimer on one product, but not on another identical product may confuse consumers. For example, one sponsor with 500mcg of folic acid has an indication for reducing the risk of neural tube defects, and a claim to say that the product has been evaluated for efficacy, whilst another sponsor has exactly the same product without this indication or efficacy claim.

### **Presentation of claimers.**

5.4 Should the claimer be presented as a visual identifier as well as a statement?

Yes, as it is doubtful that consumers read all the information presented on a CM label, and a statement could easily be missed.

5.5 Do you have any views on the possible wording or design of the label claimer?

Something that the consumers understand

I doubt the average consumer, without context, understands evidence guidelines, what/who a sponsor or TGA is, or even the word 'efficacy' or 'indication', so references to these words are not appropriate (this has been verified by us, by asking people outside the industry)

Wording such as the following may be more appropriate:

'Statements referring to health benefits have been independently assessed'.

5.6 What other considerations should be taken into account in implementing the claimer?

Positioning on the label, as mentioned I doubt a consumer reads all information on the label anyway. For this new listing pathway to be meaningful, positioning needs to be prominent.

### **Protection for new ingredients**

6.1 Is the proposed process and mechanism to provide market protection for new ingredient applicants appropriate?

- 6.2 Is the proposed 2 year period of exclusivity an appropriate period to reward the innovation and allow for a return on the investment made?
- 6.3 Should multiple applicants be able to apply for exclusive use of the same new ingredients using their own data during the exclusivity period?
- 6.4 What other considerations should be taken into account in implementing the proposed incentive for innovation?

This recommendation benefits large companies only, and SME are at a disadvantage as they would not have the funds to pay for approval of a new ingredient with TGA.

Therefore, innovation in the industry puts the big players ahead.

Is there any way that TGA can support SME over this proposal eg reduced fees depending on total annual turnover of the enterprise?

### **Protection for efficacy data**

- 6.5 Is the proposed process and mechanism to provide data protection for efficacy data appropriate?
- 6.6 Is the proposed 3 year data protection period for efficacy data appropriate to reward innovation and allow for a return on the investment made? Is it excessive?
- 6.7 Should protection be available for new uses of existing substances and /or be available for information that is not in the public domain?
- 6.8 What other considerations should be taken into account in implementing the proposed incentives for innovation?

Clinical data generated by sponsors on their own products with data protection again benefits the biggest players, who have the resources to undertake costly clinical trials. It is hard to see how such a proposal could be utilised by SME, especially as data would need to be generated on the Australian population (costly to run clinical trials here). Additionally, the detractors of complementary medicines will constantly be in the media discrediting clinical trials due to conflict of interest over the sponsor funding the trials. This may offset any benefit derived from spending the money on data.

### **Transition arrangements**

- 7.1 Do you agree with the proposed principles to support transition arrangements?

Yes

- 7.2 What other factors should we consider?

TGO 92 must be in place across all products by September 2020. If a 3 year transition period is given, which includes a fee-free period for the first 18 months, then the Permitted Indications need to be ready and finalised by September 2018. This allows for the 18 month fee-free period, plus a 6 month time period to get labels printed and product packed, without incurring financial burden to industry.

We do not support adding new indications to the permitted indications list at the cost of the sponsor. The list may not be compiled comprehensively at publications and may need to be updated constantly following sponsors recommendation and TGA review. Even though we anticipate a consultation period for permitted indications, it is not until we come to update the products, that we anticipate we will find omissions from the permitted indication list.

Thank you for your consideration. We request the publish of our submission as anonymous.