CMA Submission: Reforms to the regulatory framework for complementary medicines - Assessment pathways

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Introduction

Complementary Medicines Australia (CMA) welcomes the opportunity to provide feedback on the Department of Health's Therapeutic Goods Administration (TGA) reforms to the regulatory framework for complementary medicines consultation paper, dated February 2017.

On 8 April 2015, CMA made a comprehensive submission to the Expert Panel Review of Medicines and Medical Devices Regulation, announced by the then Minister for Health, the Hon Peter Dutton MP and the Assistant Minister for Health, Senator the Hon Fiona Nash and chaired by Emeritus Professor Lloyd Sansom AO. On the 15 September 2016, following consultation with industry, consumers and healthcare professionals, the Government provided its response, which largely supported the package of recommendations of the review to the Medicines and Medical Devices Regulation (MMDR).

Many of the recent criticisms with the current regulatory system appear to arise because complementary medicines do not fit seamlessly within a regulatory model designed primarily to accommodate over-the-counter and prescription medicines. However, industry is of the firm belief that the current regulatory burden can be reduced while continuing to maintain the highest standards in safety and quality of complementary medicines available to Australian consumers. It is therefore, pleasing to see that many of the principle reforms proposed by industry to the Panel, including the option of a new assessment pathway for listing complementary medicines on the ARTG and incentives for innovation, have been agreed to by government and their appropriate implementation addressed in this consultation.

CMA supports the main themes of the Review; that is to identify ways to improve access to therapeutic goods for consumers and ensure that the regulatory settings are appropriately aligned to risk and to remove unnecessary regulatory and administrative burden for industry, whilst maintaining the safety of therapeutic goods in Australia. Removal of over-regulation will

help the Australian complementary medicines industry gain its position as an innovative and competitive market that is able to meet growing consumer demands.

Assessment Pathways for complementary medicines

The development of a three-tiered risk-based framework for the assessment of complementary medicines will introduce an option for sponsors to elect to have their otherwise lower risk listed medicine pre-market assessed for efficacy to support higher level indication(s). To support this process sponsors will have the option to label the product as having been independently assessed for evidence, as well as on other promotional material.

CMA strongly supports the implementation of the new assessment pathway as an opt-in option for sponsors who have invested into the generation of specific evidence to support certain higher-level indications than those currently permitted for use in listed medicines. An enabler to this pathway includes the supporting incentives for innovation, including data protection and market exclusivity for products and new ingredients.

The new pathway will offer consumers additional confidence in the available and growing body of evidence, in addition to established safety and quality principles, to support informed choice when self-selecting complementary medicines. However, the new pathway must not be used to mandate certain product(s) or product categories enter into the assessment pathway or be utilised by the TGA to require products with indications that are currently permitted in listed medicines to be "up-graded' into the new pathway or otherwise have the indications removed. That is, the implementation of this recommendation must stay within the remit of the principles guiding the reforms; that the Government's focus be on reducing unnecessary red tape to enable Australian businesses to be competitive on the global stage, while maintaining public health and safety.

The new pathway should be implemented with the following principle criteria:

1. The sponsor elects to enter the product on the ARTG utilising the new assessment pathway via self-certification, supplemented with pre-market assessment of efficacy for product indications.
2. The medicine contains only permitted ingredient(s) and meets the requirements associated with their use in listed medicines[1].
3. The medicine is produced under GMP principles[2].
4. The medicine makes indication(s) that are higher than those available for selection in the permitted indications list (list yet to be consulted and finalised).
5. Pre-market assessment is conducted on the efficacy of the evidence in support of the proposed higher-level indications and a risk appropriate review of any general level indications.
6. The sponsor elects to include the positive claimer on the product label and promotional material. For example "The efficacy of the medicine has been independently assessed for the approved indication(s)" or words to that effect (RX 45 refers).
7. Should the sponsor opt-in for full assessment of all evidence claims at the point of pre-market, then this product would <u>not</u> be subject to further cost-recovered post-market review under normal circumstances.
8. Would not require an individual assessment of the quality and safety aspects of the medicine as this would have been considered as part of the ingredient(s) already being permitted as safe for use under relevant GMP principles.

[1] The ingredients that are permitted for use in the listed medicines and requirements associated with their use are specified in the Therapeutic Goods (Permissible Ingredients) Determination.
[2] Medicinal products supplied in Australia are required to meet PIC/S guide to Good Manufacturing Practice (GMP) and relevant Orders and technical guidance applied to the domestic complementary medicines framework in Australia.

To elaborate further on point 7, it would not be an efficient use of cost-recovered resources to mandate that a medicine having gone through successful assessment under the new pathway should continue to be subjected to post-market review of the evidence to support indications and claims. The proposed increase to the number of post market reviews should focus on, as it was originally established for, those products that are not subject to pre-market assessment scrutiny due to their inherent lower risk profile i.e. current AUSTL products.

Current listing pathway

CMA broadly supports the implementation of recommendation 49; to increase post-market compliance (random/target) monitoring of current AUSTL products. However, as stated above cost-recovered compliance monitoring for pre-market assessed products (new pathway) should only occur in circumstances where additional intelligence is available in relation to safety or quality matters of the good.

Classification of a medicine

One of the factors listed in the consultation document that is taken into consideration when classifying a medicine is:

The risk associated with the intended use(s) (indications) of the product (e.g. whether incorrect use could lead to the consumer delaying necessary medical treatment.

While the risk of a consumer misusing a medicine or consequently seeking appropriate medical treatment is relevant across all medicine categories, it is important to note that for listed medicines mandatory label disclaimers are required to off-set risk by stipulating that "if symptoms persist or worsen, see a health professional" or words to similar effect.

In addition, the medicines Labelling Order (The Therapeutic Goods Order No. 69 - General requirements for labels for medicines /TGO 92 Standard for labels of non-prescription medicines) requires the labels of some over-the-counter and complementary medicines to contain particular warning statements ('advisory statements') about specific risks related to use of the medicines. While regulators cannot regulate for 'no risk', complementary medicines represent a lower risk profile in general.

Please refer to Attachment 1: Table 1: CMA comment on eligibility criteria and the regulatory requirements for the three assessment pathways (industry input)

Establishing a risk-based hierarchy for therapeutic indications

Low level indications

CMA agrees in principle with the proposed hierarchy for lowest level indications, given this is representative of the current AUST L framework and would include both specific and non-specific indications based on a tradition of use and scientific evidence[3].
CMA only agrees in principle as the revised list of permitted indications are yet to be consulted on with industry and may require further refining prior to finalisation.

Criteria for low level indications to be included in a permitted list should include indications that are:

- Self diagnosable
- Self-manageable
- Self limiting

[3] The indications proposed by the sponsor of the listed medicine must not be for the treatment of a disease, condition, ailment or defect specified in Part 1 or 2 of Appendix 6 to the Therapeutic Goods Advertising Code: see Therapeutic Goods Regulations 1990, Schedule 4, Item 3(d).

And refer to:

- General health maintenance
- Health enhancement
- Prevention of dietary deficiency
- Benefit to a non-serious form of a disease, ailment, defect or injury

Or are otherwise labeled for 'practitioner dispensing only' in compliance with the Labelling Order.

The above criteria will ensure that the indications selected are suitable for products that are only assessed at the point of post-market or otherwise come under the supervision of a health professional/complementary healthcare practitioner[4] (Labelling Order refers). This would also include listed complementary medicines prefixed with the term "medically diagnosed" such as "For the symptomatic relief of medically diagnosed Irritable Bowel Syndrome". This is because the use of these products occurs after diagnosis with a healthcare/medical practitioner.

The above criteria must also support those lower level indications currently being utilised by sponsors of listed medicines that have been subject to a recent[5] TGA post-market review without the indication(s) being challenged.

Intermediate indications

The principles for establishing intermediate indications appears logical; however industry is of the firm belief that this assessment pathway be utilised as in opt-in option for medicine sponsors that have invested in the generation of product or ingredient specific research to

[4] TGO 69 definition: Persons registered under a law of a State or Territory as herbalists, homeopathic practitioners, chiropractors, naturopaths, nutritionists, practitioners of TCM, podiatrists or osteopaths.
[5] Post-market review conducted and closed out on that AUST L number within the last 3 years.

support new, specific indications. It should therefore remain undefined and flexible in its application for the first phase of its pilot roll out.

Biomarker & Restricted Representations Indications

The consultation paper makes reference to certain indications that are currently being used in listed medicines that may not meet the revised criteria for lower level indications (e.g biomarker[6] and restricted representation indications[7]), as this may result in the consumer delaying appropriate medical treatment. An example indication is given, such as 'may assist in the effective management of reducing cholesterol levels'.

CMA submits that indications currently being utilised in listed medicines including; biomarker indications that have undergone successful post market compliance monitoring and restricted representation[8] indications that have been reviewed for evidence, should continue to be permitted as the evidence held supporting their use has recently been reviewed. The new pathway must not be utilised as a mandatory class for this category of goods. Specifically, the types of indications this refers to are qualified with statements around the modulation of normal healthy levels of (biomarkers such as cholesterol) within healthy individuals. This qualified indication and words to similar effect, along with any required label advisory statements, provides a clear message to the consumer that the product is not intended to treat hypercholesterolaemia or cure said condition.

With regards to restricted representations, the Secretary can approve (under Section DF of the *Therapeutic Goods Act 1989*) or permit (under Section 42DK(1)) the use of a restricted representation. Approval can be obtained from the TGA, which is required to consider any

[6] Biomarker is a measurable biological parameter that is predictive of the risk of a serious disease when present at an abnormal level in the human body. E.g blood glucose and cholesterol.
[7] A restricted representation is any reference to a serious disease, condition, aliment or defect specified in Table 1 of Part 2 of Appendix 6 of the Therapeutic Goods Advertising Code 2015.
[8] Refers to restricted representations that have written notices of approval or permission for the use of restricted representations in advertising therapeutic goods to consumers.

recommendation from the Therapeutic Goods Advertising Code Council (TGACC) or appropriate expert committee or committees.

Approval for the use of a restricted representation can be granted only for therapeutic goods entered or therapeutic goods exempt from inclusion on the Australian Register of Therapeutic Goods (ARTG). Any proposed restricted representation must be consistent with:

- the product's accepted indications or intended purpose, as per its ARTG entry; and/or
- any mandatory warning or cautionary statements which are required to be included in the product packaging/labelling in order to satisfy other regulatory requirements[9]

In some instances approval has been granted for certain listed medicines to use restricted representations in advertising to consumers and these have been subject to the public interest criteria. Further a number of these approvals are category wide approvals for all listed medicines with a specified ingredient for example. Therefore these approvals must remain valid.

Public interest criteria applied by TGACC

In making a recommendation to the Secretary, the TGACC must take in to account:

1. Consumers, or certain groups of consumers, vulnerability when faced with the disease, condition, ailment or defect;

2. Whether the reference would be likely to result in consumers not seeking timely professional advice where appropriate (such as where timely professional advice is important to prevent negative health consequences or irrevocable deterioration or progression of disease);

[9] Which therapeutic goods can seek approval to use a restricted representation? https://www.tga.gov.au/form/application-approval-use-restricted-representation-advertising

3. Whether the reference would be likely (alone or through repetition or together with other references) to have a negative impact on public health (or to have an effect on persons other than those to whom the advertisement is directed); and

4. Such other aspects of the public interest as may appear to be appropriate.

5. The World Health Organization notes that responsible self-medication can:

    - Help prevent and treat symptoms and ailments that do not require medical consultation;

    - Reduce the increasing pressure on medical services for the relief of minor ailments, especially when financial and human resources are limited;

    - Increase the availability of health care to populations living in rural or remote areas where access to medical advice may be difficult; and

    - Enable patients to control their own chronic conditions.

Therefore, it is CMA's position that the criteria for intermediate indications is not embedded in legislation prior to the consultation and finalisation of the permitted indications project. Specifically, indications qualified for use within the remits of "medically diagnosed indications", biomarkers (appropriately qualified for use in healthy individuals, within a healthy range) and restricted representations that have been granted approval, be transitioned over into the new pathway fee-free, acknowledging the review of the evidence that has already occurred.

Guidance on the assessment of potential restricted representations

To assist in determining the types of indications that may be utilised in the advertising of listed medicines, the Complementary Medicines Branch and the Office of Product Review jointly

developed an internal draft guidance document titled '*Guidance on the Assessment of Potentially Restricted Representations Included in Advertising Claims Based on Indications for Listed Medicine*' (reference R14/684839). This document, while never finalised or published, provided general guidance on the types of indications used by listed medicines that are eligible for listing as per the requirements in Schedule 4 of the Regulations[10]. The document was drafted to assist with the assessment of advertising claims by differentiating between non-serious and serious forms of the diseases, conditions, ailments or defects listed in Appendix 6 of the Advertising Code, including any "relevant considerations" that may further assist in the determination of whether a reference to a disease, condition, ailments or defect is potentially a reference to a serious form.

It is therefore equitable to expect that there be an alignment between what has been considered to meet the criteria of a non-restricted representation as per the above guidance document and that of recent advice the Complementary Medicines Branch has provided to industry regarding suitable indications for use in listed medicines (permitted indications project).

While CMA acknowledges that regulatory decision are not stagnant, some level of regulatory consistency is required to promote business processes and performance in industry.

Higher level indications

CMA agrees that higher level indications remain consistent with current requirements for registered complementary medicines. Specifically, higher level indications are those that refer to the treatment, cure or prevention of a serious form of a disease, disorder or condition, for

[10] A determination as to whether a statement is a restricted representation in the context of a particular advertisement, needs to be undertaken on a case by case basis for compliance with section 5(2) of the Advertising Code

example: 'For the treatment of iron deficiency anaemia'. In addition, higher level indications must not refer to a prohibited representation[11].

Proposal one: A risk based approach for therapeutic indications

Proposal two: Products excluded from the new pathway

The TGA propose that the following products will <u>not</u> be accepted for evaluation through the new pathway:

Products that only have 'standard' permitted indications.

Products that have indications based **solely** on evidence of traditional use, unless they also provide adequate scientific evidence supporting the indications.

The new pathway is also proposed to not be a provisional approval pathway pending the outcome of clinical trials (i.e. the evidence of efficacy is required at the time of application to the TGA).

CMA agrees with the proposed approach to products excluded from the new pathway.

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

<u>Low level indications</u>

CMA agrees in principle with the proposed hierarchy for lowest level indications, given this is representative of the current AUST L framework and would include both specific and non-specific indications based on a tradition of use and scientific evidence.

<u>Intermediate indications</u>

The new assessment pathway should be utilised as an opt-in option for medicine sponsors that have invested in the generation of product or ingredient specific research to support new,

[11] Appendix 6 Therapeutic Goods Advertising Code

specific indications. CMA submits it should therefore remain undefined and flexible in its application for the first phase of its pilot roll out.

Higher level indications

CMA agrees that the criteria for higher level indications remains consistent with current requirements for registered complementary medicines.

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

The proposed criteria to include restricted representations with existing approvals into the mandatory transition to the new pathway is **not** supported by industry.

As stated above, CMA submits that biomarker and restricted representation indications that are currently being utilised in listed medicines and/or have past recent post-market compliance monitoring unchallenged should continue to be permitted for use under the current AUST L framework.

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

A valid consideration in implementing the new pathway would be the development of appropriate target timeframes for regulatory decisions to be made in relation to new ingredients approved for use in listed medicines (Rx 41(c) refers to legislated timeframes).

Careful consideration of how existing traditional complementary medicine products will be portrayed in the market is required and needs to form part of any education campaign.

Approaches to establishing efficacy

CMA supports that the efficacy evidence for products assessed via the new pathway be based on a) finished product evidence or b) justification of the evidence to substantiate each substance used in the formulation. In circumstance where finished product evidence is used, the sponsor would be able to communicate this as "clinically proven' or words to that effect to the consumer. CMA supports that products evaluated through the new pathway require an *intermediate* evidence package. The sponsor will self-assess the products safety and quality as per the current listing system (listed medicines may only use pre-approved ingredients with suitable safety and quality characteristics) and will require a high quality *intermediate* efficacy package to be submitted for pre-market assessment. Comparable to establishing the efficacy of a registered complementary medicine, the new pathway proposes efficacy be established based on:

a) clinical data on the finished product; or
b) a dossier showing the proposed product delivers *appropriate* bioavailability of all active ingredients that have been established to be efficacious. The data package would require evidence in relation to bioequivalence: dissolution or in some instances comparative dissolution and bioavailability with appropriate scientific justification where required.

The new pathway method 2, should not be restricted to complementary medicine products containing vitamins, minerals or amino acids only and should be extended to probiotics and other designated active ingredients.

Existing restricted representation approvals

CMA does not agree that indications referring to restricted representations that have already received prior approval should be required to transition to the new pathway. As stated, the intent of the new pathway, from an industry perspective was to encourage and provide incentives for the generation of a wider evidence base for complementary medicines and that this pathway be accessible as an opt-in arrangement. Consumers will be able to distinguish this category of goods from other listed medicines by the presence of an optional label claimer and similar on promotion material.

It is therefore reasonable to suspect that medicine sponsors having sought the appropriate approvals for use of restricted representations in advertising will seek to move their product into the new pathway in order to communicate to consumers that pre-market assessment of the product efficacy has occurred. It should not, however be a mandatory requirement that these products undergo additional assessment within the transition period, on top of having satisfied the public interest test criteria. Mandating such an approach is not an efficient use of TGA cost-recovered resources.

Proposal three: approaches to establishing efficacy

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

CMA supports the principle criteria for establishing the efficacy of products entering the new assessment pathway. However, it is agreed that the medicines evaluated through this pathway require an 'intermediate' evidence package and therefore scientific justifications should be permitted were unique requirements are presented.

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

There may be some circumstances where approval can be given to a listed medicine for the use of a restricted representation, this is in circumstances where:

a) the proposed representation refers to risk factors associated with a serious form of a disease, condition, ailment and/or defect; and

b) a clear public health benefit of such advertising can be demonstrated (in line with the Public Interest Criteria).

In some instances approval has been granted to use certain restricted representations in advertising to consumers where evidence has been provided to show the use of the restricted representation meets the public interest criteria included in Appendix 6 of the Therapeutic Goods Advertising Code. Therefore the decisions made by the Secretary to the Department of Health (or delegate) in relation to these approvals must remain valid.

For new applications via the new assessment pathway that contain a restricted representation, the approval must also provide for approval of that representation in advertising i.e. this should be streamlined and the sponsors should not be required to undertake a separate approval process as is current practice.

Proposal four: Evidence requirements

The principles of the existing evidence requirements for listed and registered complementary medicines will be retained to establish efficacy for low and high level indications respectively.

CMA supports a comprehensive review of the evidence guidelines, in consultation, to establish a intelligible set of criteria across the three pathways.

CMA proposes that sponsors seeking to include a complementary medicines on the ARTG via

the new pathway meet the principle criteria for evidence requirements as outlined in tables 2 and 3 of the consultation paper.

Note: Table 3: Proposed minimum literature requirements should be amended to refer to 'traditional' and 'scientific' not 'low level scientific' with regards to listed medicines.

Evidence requirements

3.6 Are the evidence requirements appropriate for the new pathway?

As stated above, evidence packages to support applications for the new pathway should be of an *intermediate* level and allow scientific justifications were unique requirements are presented. The pre-market assessment of products via the new pathway should involve the assessment of the medicine presentation, including a copy of the product label.

As applications submitted via the new pathway will be assessed for efficacy at a *similar* standard to registered CMs, it should be sufficient that the individuals used in the trials be accepted as 'non-healthy', that is, have a condition and be on medication(s).

Table 4: Method 2: Dissolution data and bioequivalence data should refer to requirements and guidance contained in the Australian Regulatory Guidelines for Complementary Medicines (ARGCM) rather than the currently referred document: Guidance 15: Biopharmaceutic studies, which relates to prescription medicine requirements.

This document should be used only as a general guide for lower risk listed medicines entering the new pathway establishing dissolution/comparative dissolution and bioequivalence on the product.

All evidence will be subject to the minimum requirements as outlined in the Evidence Guidelines for listed medicines (July 2014) for relevance, quality and consistency.

Industry requests efficacy assessments using method 2 allow bioequivalence to be established for existing products in overseas markets.

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

The proposed levels of evidence assessment are aligned with higher risk registered medicines. Products entering the new pathway are for all other purposes lower risk listed medicines entering into a more robust pathway due to the evidence held to substantiate more specific therapeutic indications. It is therefore appropriate that a greater, intermediate level of assessment be conducted on these products to expand the evidence base for complementary medicines.

Consideration will however be required when assessing products through the new pathway that include a mix of higher level indications and traditional use indications, as to the degree of evidence used support each paradigm.

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

As mentioned above, this assessment pathway should be allocated for medicine sponsors to opt-in for assessment on the evidence generated (product or ingredient) to support specific indications. It should therefore remain undefined and flexible in its application for the first phase of its roll out and reassessed at 12 and 24 months for continued improvements and related guidance material to stakeholders.

Implementing the list of permitted indications

The Government has accepted recommendation 38; that the TGA establish a list of permitted indications from which sponsors must exclusively draw from in order to include a listed medicine on the ARTG. To give effect to this recommendation it is proposed that access to the free text field will be removed so that sponsors will be required to select indications from the permitted indications list only. It is noted that the TGA will draw extensively from the work previously undertaken on the permitted indications project and that implementation will require legislative change, all of which will be subject to further consultation with consumers, sponsors and health professionals.

Criteria for permitted indications

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

CMA supports that *low* level indications which meet the proposed amended criteria below be included into the list of permitted indications.

- The indication must meet the definition of a therapeutic indication (i.e. must describe a therapeutic use for the goods)[12] and be classified as a specific or non-specific indication.
- "The indication must be a low level indication". CMA supports this criteria be amended to: include permitted indications that are consistent with what is appropriate/suitable for use in listed medicines, as detailed in the ARGCM[13].

  The ARGCM should then be expanded to provide additional clarity to sponsors as part of this reform process. The reason for removing reference to 'low level indication' keeps

[12] All other statements and claims relating to a medicine (for example,'25% more' or 'new and improved formula') are not indications and will not be able to be included in the permitted indications list.
[13] Indications permitted for use in listed complementary medicines, ARGM October 2016, p44-

alignment with the principle of selecting an indication from the permitted indications list does not absolve a sponsor from any obligations under the Act or related Regulations.

- The indication must be capable of complying with the Therapeutic goods Advertising Code when included on product label and promotional materials.
- The indication must be consistent with the relevant paradigm (scientific and or traditional use).
- The indications should be sufficiently flexible to enable sponsors to have market differentiation[14].

By implementing the above criteria will ensure that indications considered appropriate for listed medicines will be accepted for inclusion on the permitted indications list.

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

CMA supports that the criteria for indications will not reduce the ability of sponsors to use indications which are currently appropriate for listed medicines.

Another consideration relates to the proposed control on restricted representation indications. The Electronic Listing Facility (ELF) currently provides a list of 'coded indications', which under these reforms will be updated to represent the conclusions of the permitted indications project. Sponsors may then choose from the list of permitted indications when self-listing their medicine on the Australian Register of Therapeutic Goods (ARTG). The fact that an advertisement for a medicine includes a therapeutic claim based on a permitted indication listed in the ARTG does not automatically mean that the advertising claim is acceptable. The

[14] The Expert panel noted that permitted indications should be sufficiently flexible to enable sponsors to have market differentiation.

sponsors must also certify that in relation to the medicine, they will comply with every requirement relating to advertising applicable under Part 5-1 of the *Therapeutic Goods Act 1989* (the Act) and under the *Therapeutic Goods Regulations 1990* (the Regulations) including the Advertising Code. In particular, advertisements for therapeutic goods must not refer, expressly or by implication to a "prohibited representation" under any circumstances or a "restricted representation" unless prior TGA approval has been obtained under sections 42DF or DK of the Act (see also section 5(2) of the Advertising Code). It is also the responsibility of the advertiser to ensure that restricted representations are not used without the necessary approval under 42DF or 42DK of the Act and that the advertisement complies with any condition that may apply for that approval. There will be a number of examples in which prior approval has been obtained and applies to complementary medicines and that need to be catered for in the permitted indications list and functionality.

Indications suitable for inclusion in the permitted indications list

A low level indication, and therefore a permitted indication, may refer to:

- health enhancement
- health maintenance
- prevention of dietary deficiency
- a disease, ailment, defect or injury other than a serious form of those diseases.

Indication qualifiers

A permitted indication must not refer to or imply prevention, alleviation or cure of any form of disease, aliment, defect or injury other than a serious form of those diseases.

Table 1 in Part 2 of Appendix 6 to the Advertising Code contains a list of broad categories of diseases, conditions, ailments or defects. Within each category will be many different individual forms of the disease, condition, ailment or defect, these will include forms that are considered "non-serious" due to certain qualifiers; and others considered to be "serious" which are considered to be restricted representations and require "approval".

It is therefore important to note that the way in which claims are qualified is extremely important and must be done within the context of the likely take-out by a reasonable consumer. The use of indication qualifiers and it reflection of the evidence held by the sponsor needs to be taken into account in implementing the permitted indications list. This will also provide sponsors with the ability to differentiate their listed products in the market.

The *Evidence Guidelines for Listed Medicines* (July 2014) states the mandatory components that an indication is made up of includes: the traditional context (if applicable), action and target components. These mandatory components can be qualified with optional qualifying terms such as action qualifiers, target qualifiers and indications qualifiers to further specify the therapeutic use of the goods.

CMA supports in principle that the existing indication structure will be maintained and will provide specific comment in line with the follow up consultation on the list of permitted indications.

As this set of recommendations was consulted on in the absence of the detail surrounding the permitted indications project, CMA reserves the right to provide additional responses on aspects of this consultation in due course.

Indications not suitable for inclusion in the permitted indications list

Please see the section above for CMA's position on the inclusion of biomarker indications into the permitted indications list.

A low level indication, and therefore a permitted indication, must not:

- Refer to, or imply, the prevention, alleviation, or cure of any form of disease, aliment, defect or injury;
- Contain a prohibited representation ;
- Contain a restricted representation, unless prior approval has been granted; or
- Have been specified in a non-permitted indications list (to be consulted on).

CMA suggests that to distinguish those indications that have been granted prior approval for use in advertising to consumers, while still meeting the requirements of a correct ARTG entry, the indications list could include those restricted representations but not make them 'selectable' for new AUST L products entered into the ARTG, unless additional approval is granted.

Mechanisms to allow market differentiation of products

CMA agrees with the principle of sponsors being able to vary the wording of the permitted indication(s) on the product label and other advertising, providing the meaning and intent are not changed. This and the use of indication qualifiers to reflect the evidence held by the sponsor will provide sponsors with the ability to differentiate their listed products in the market.

Structure of permitted indication

CMA does not agree with the broad statement that the use of indication qualifiers requires sponsors to hold commensurately more specific evidence (page25), if that specific evidence is referring to clinically trialled evidence only. As demonstrated above, there are instances where the use of qualifying statements actually justifies the use of the medicines within the listed paradigm e.g. May help, healthy, mild, occasional and for the temporary relief of, etc.

This criteria should only relate to specific target indications. This would also appear to be in line with the wording of the current evidence guidelines with reference to specific and non-specific core indications (Evidence Guideline 2014, p13).

Implementation of the permitted indications lists

Options for implementation of the permitted indications list

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.

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

CMA is generally supportive of option 2: core permitted indications which can be modified with pre-approved qualifiers. Under this option the core permitted indications would be specified in a legislative instrument. Applicants could modify the core indications to align with supporting evidence by selecting pre-approved qualifiers from a drop-down list. This would allow for specific indication qualifiers to be approved through administrative measures rather than being legislative in nature, reducing the overall number of inductions required. Under this option that TGA, will

develop a comprehensive list of traditional and scientific core indications and qualifying terms in consultation with stakeholders.

Additional requirements for the use of permitted indications

As outlined throughout this submission, CMA supports appropriate risk mitigating strategies which offset that listed medicines are not subject to full pre-market approval prior to market. The examples provided in this section of the consultation paper appear consistent with the current regulatory framework.

Claiming evidence of efficacy

To support the use of the new pathway, sponsors will be able to elect to use a label claimer to communicate that the products efficacy has been independently assessed. This will also allow products that have been assessed under the new pathway to differentiate themselves in the market.

CMA supports that the use of label claimers be supported by a TGA education campaign to translate the benefits to stakeholders more broadly.

Criteria for use of 'claimers'

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

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

CMA agrees with the majority of the criteria proposed in the consultation paper for the use of positive claimers and that legislative change will be required to implement this recommendation. We are supportive of a claimer being approved for complementary medicines evaluated by the TGA via the new pathway and registered complementary medicines that have undergone pre-market assessment. However, as stated earlier in this submission, it is incumbent on the regulator to make efficient use of cost-recovered resources, including post-market listing compliance of complementary medicines. Therefore, CMA's position is that the proposed increase to the number of post market reviews should focus on, as it was originally established for, those products that are not subject to pre-market assessment scrutiny.

Presentation of claimer statements

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

CMA suggests that to address any unintended consequences the introduction of this type of label claimer may present, an education and awareness campaign should accompany the changes, similar to that recently conducted for changes to medicines labeling names.

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

CMA outlines that label space will become an issue for some sponsors and that a choice of statement or visual symbol be offered. Given the inclusion of the claimer will be optional, should the sponsor elect to include the claimer then the visual identify may be another optional addition in conjunction with the statement and noting the comment provided in 5.3.

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

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

The proposed presentation of the label claimer should be subject to consumer user testing to determine what is the most appropriate form of communication, especially given the font size of the claimer should be in line with that of other indications and advisory statements for medicines.

Incentives for Innovation

CMA strongly supports the recommendation for mechanisms to improve the competitiveness of the Australian complementary medicines industry by providing incentives for innovation. While this aligns with increasing the evidence base for CMs and being able to communicate this to consumers more readily, through a combination of market exclusivity and data protection options, it will also allow sponsors to update or redevelop premium products for future growth as well as the incentive to launch new offerings to the market. CMA considers this to be a particularly important reform recommendation given recent government reviews have made recommendations to remove the Innovation Patent that applies to this sector.

In determining the criteria for innovation incentives, concepts are explored such as not permitting incentives where marginal innovations are made. CMA submits that such criteria will need to be supported by additional guidance material and come under further consultation for appropriate implementation.

Protection of new ingredients

CMA strongly supports that a 3 year period of market exclusivity be provided to successful applicants of complementary medicine ingredient(s). The proposed approach would allow a 'first to market advantage' while also encouraging further research into new ingredients. Under this proposal the use of the protected ingredient would be limited to the applicant or persons nominated by the applicant. CMA agrees that the compositional guideline[15] relating to the applicants new ingredient not be made public until the ingredient reverts to a general approval (after two years).

[15] A TGA compositional guideline is a summary of descriptions, tests and appropriate acceptance criteria (which are numerical limits, ranges or other criteria) that define the characteristics and specify the composition of an ingredient permitted for use in listed medicines.

6.1 Is the proposed process and mechanism to provide market protection for new ingredients applications appropriate?

CMA agrees with the proposed mechanism to provide market protection to applicants of new complementary medicine ingredients.

6.2 Is the proposed 2 year period of exclusivity an appropriate period to reward innovation and allow for a return on the investment made?

CMA agrees with a **three year** period of market exclusivity as this will, for the majority of applicants, provide the desired return on investment. This is especially true given the culmination of MMDR reform recommendations relating to greater use of overseas NRA decisions.

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?

CMA agrees that this recommendation will still provide a 'first to market advantage' for the original applicant provided subsequent applicants are not afforded an abridge assessment off the back of the existence of the original applicants (protected) work.

Protection of efficacy data from clinical studies

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?

CMA proposes a 5 year data protection or market exclusivity period for new formulation / indication combinations. Criteria for data protection to acknowledge that the efficacy assessment will be conducted to a registerable level and therefore equitable timeframes should apply.

6.7 Should protection be available for new users of existing substances and/or be available for information that is not in he public domain?

6.8 what other considerations should be taken into account in implementing the propose incentives for innovation?

CMA supports that in line with the implementation of the new assessment pathway, higher level indications may be subject to exclusive use.

CMA agrees that a period of data protection be provided to applicants of medicines approved through the new pathway that provide direct clinical data on the finished product formulation. It is appropriate in this circumstance that the protection be commensurate with that provided to registered medicines under section 25A of the Act (5 year period of protection), given the investment of resources to prepare clinical data on the finished product.

In addition, CMA supports that modified forms of data protection be further explored that would allow for protection for instances where published clinical studies refer to a specific brand named product or specific formulation.

Implementation

Transitional arrangements

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

7.2 what other factors should be considered?

CMA welcomes the opportunity to continue to work with the regulator in developing the associated business processes and guidance documents to support the implementation of the reforms.

CMA proposes a four year transition arrangement to bring existing listed products in line with the revised permitted indications list and that this would allow for an overlap with the transition period for the Therapeutic Goods Order TGO 92 – *Standard for labels of non-prescription medicines*. The transition period for the new assessment pathways should commence from the time the pathway becomes available. See CMA's earlier comments on considerations for listed products with biomarker indications and restricted representation approvals.

Administration

Fees, charges and timeframes

CMA agrees in principle with the proposed creation of application and evaluation fees to accommodate the new pathway and implementation of the indications project and that the fees will align with the principles of the *Australian Government Cost Recovery Guidelines*.

CMA supports that the timeframes for applications via the new pathway be significantly reduced compared to registered complementary medicines due to only the efficacy of the product requiring pre-market assessment.

With regards to efficacy assessments, legislated timeframes for which TGA decisions must be made should be established once pilot assessments have been conducted and benchmarks established.

Conclusion

With these reforms and a combination of self/ co-regulatory mechanisms outlined in the package of MMDR reforms, the TGA will continue to operate effectively and efficiently in respect of regulatory imposts such as timeframes and costs to industry, while also maintaining appropriate public health and safety protections.

About Complementary Medicines Australia

Complementary Medicines Australia (CMA) is the peak industry body for the complementary medicines industry, representing members throughout the value chain: manufacturers, raw material suppliers, distributors, retailers, practitioners and consultants. CMA promotes industry viability and growth, and a marketplace where consumers can enjoy the positive health benefits of high quality complementary medicines. We are the principal reference point for members, the government, the media and consumers to communicate about issues relating to the complementary medicines industry.

Complementary medicines include vitamins, mineral and nutritional supplements, homoeopathic, aromatherapy products and herbal medicines (unless specifically exempt). The term 'complementary medicines' also comprises traditional medicines, including traditional Chinese medicines, Ayurvedic, Australian Indigenous and Western herbal medicines. Traditional and long-term use is taken into account in establishing safety as a medicine.

Over the last few decades, the complementary medicine sector has evolved into a major industry which requires complex supply chains, clinical trials, global marketing and export acumen. The majority of complementary medicines are indicated for the relief of symptoms of minor, self-limiting conditions, maintaining health and wellbeing, or the promotion or enhancement of health[16]. Increasingly, complementary medicines are being found to contribute to improved health outcomes, through increased effectiveness, safety and cost-effectiveness, and integration with conventional medical care.[17]

[16] Source TGA, http://www.tga.gov.au/industry/cm-basics-regulation-overview.htm
[17] National Institute of Complementary Medicine, (2013), Research Priorities for complementary medicine in Australia. Retrieved from: http://www.nicm.edu.au/__data/assets/pdf_file/0009/537840/Research_Priorities_for_CM.pdf

Attachments

Attachment 1: Table 1 CMA comment on eligibility criteria and the regulatory requirements for the three assessment pathways

References

TGA Round table document references

Therapeutic Goods Administration (2014), Guidelines on the evidence required to support indications for listed complementary medicines, Version 2.1, July 2014, Commonwealth of Australia, p. 7. Downloaded from: https://www.tga.gov.au/book/guidelines-evidence-required-support-indications-listed-complementary-medicines.

Attachment 1: Table 1: CMA comment on the eligibility criteria and the regulatory requirements for the three assessment pathways

	Listed Medicines	New Pathway	Registered Medicines	CMA comment
Risk Level	Lowest level of risk based on their ingredients, indications, the way they are presented and administered, and the potential harm associated with their use.	Low level risk based on their ingredients, the way they are presented and administered, and the potential harm associated with their use. Make intermediate level indications. Risk consideration of products in the new pathway can be mitigated when prescribed by a (complementary) healthcare practitioner and when labelled "for practitioner dispensing only"	Higher level risk based on their ingredients and the level of indications.	
Ingredients	Must draw exclusively from the permitted ingredients list. Ingredients must not be included (or meet the criteria for inclusion) in a schedule to the Poisons Standard.	Must draw exclusively from the permitted ingredients list. Ingredients must not be included (or meet the criteria for inclusion) in a schedule to the Poisons Standard.	Includes those ingredients included (or meet the criteria for inclusion) in a schedule to the Poisons Standard, other than Schedule, 4, 8 or 9.	

	Listed Medicines	New Pathway	Registered Medicines	CMA comment
Indications	Low level indications drawn exclusively from the **permitted indications** list.	Intermediate level indications that exceed the permitted indications list but are not high level indications.	High level indications, ineligible for listing or the new pathway.	Eligibility criteria for the new pathway to include transitioning over products with indications referring to (appropriately qualified) biomarkers, indications qualified as "medically diagnosed" and restricted representations that have been granted advertising approval.
Product quality	Must comply with applicable standards. Non-sterile medicines only.	Must comply with applicable standards. Non-sterile medicines only.	Must comply with applicable standards. May include sterile medicines.	
Manufacturing quality	Must meet the PIC/S Guide to GMP.	Must meet the PIC/S Guide to GMP.	Must meet the PIC/S Guide to GMP.	
Application procedure	Self-certification.	Self-certification supplemented with premarket assessment of efficacy.	Full premarket assessment.	
Level of pre-market assessment	Approval initiated by electronic application lodgement facility based on information provided by the applicant. No evaluation of the quality, safety or efficacy of the finished product prior to the approval.	Approval by delegate of the Secretary. **Assessment of the efficacy of the finished product** and label prior to the approval. No evaluation of the quality or, safety prior to the approval.	Approval by delegate of the Secretary. Assessment of the quality, safety, efficacy of the finished product and label prior to the approval.	

	Listed Medicines	New Pathway	Registered Medicines	CMA comment
Evidence requirements	Evidence held by the sponsor to support indications and claims.	Evidence **submitted** by sponsor to support associated indications and claims.	Evidence **submitted** by sponsor to support associated indications, claims and safety and quality of the finished product.	Criteria for the new pathway to include "*intermediate*" evidence package to support associated indications and claims
Presentation	Presentation cannot state or imply that the medicine has effectiveness or has been assessed by the TGA.	Sponsor able to use a '**claimer**' on the label and other promotional material to indicate that product has been independently assessed to support associated indications and claims.	Sponsor able to use a '**claimer**' on the label and other promotional material to indicate that product has been independently assessed.	Consumer educational campaign to support the delivery of the positive attributes to the label claimer, while not taking away from lower risk listed medicines.
Incentives for innovation	3 years **market exclusivity** for new ingredients.	3 years **market exclusivity** for new ingredients; and / or 5 years data protection or market exclusivity for new formulation / indication combinations.	5 years data protection for new active ingredients.	Criteria for market exclusivity of new ingredients to acknowledge that 3 years is reflective of commercial realities. Criteria for data protection to acknowledge that the efficacy assessment will be conducted to a registerable level and therefore equitable timeframes should apply.

	Listed Medicines	New Pathway	Registered Medicines	CMA comment
Conditions of approval	Consistent with current conditions of listing. Additional conditions relating to the use of permitted indications to be considered.	Consistent with current conditions of listing. Additional conditions relating to efficacy evidence and use of label claimer to be considered.	Consistent with current conditions of registration. Additional conditions relating to use of label claimer to be considered.	Additional conditions relating to the use of permitted indications to be consulted.
Post-market compliance	Product may be selected for random or targeted review to confirm applicant certifications correct. Compliance review to include evidence review.	Product may be selected for random or targeted review to confirm applicant certifications correct. Efficacy evidence would not be routinely re-assessed post-market.	Product may be selected for post-market review; for example if there are safety concerns.	Should the sponsor opt-in for full assessment of all evidence indications/claims at the point of pre-market, then this product would not be subject to further cost-recovered post-market review under normal circumstances.