Consultation submission cover sheet

This form accompanies a submission on:

The document 'Evidence required to support indications for listed medicines (excluding sunscreens and disinfectants)'	
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I would like the comments I have provided to be kept confidential: *(Please give reasons and identify specific sections of response if applicable)*	☐ Yes ☒ No
I would like my name to be removed from all documents prior to publication and not be included within the list of submissions on the TGA website.	☐ Yes ☒ No

It would help in the analysis of stakeholder comments if you provide the information requested below.

I am, or I represent, a: *(tick all that apply)*

Business in the therapeutics industry *(please tick sector):*

☐ Prescription medicines ☒ Complementary medicines ☒ OTC medicines

☐ Medical devices ☐ Blood, tissues, biological ☐ Other

☐ Sole trader ☒ Business with 360 employees

☐ Importer ☒ Manufacturer ☐ Supplier ☐ Industry organisation

☐ Government ☐ Researcher ☐ Professional body

☐ Consumer organisation ☐ Institution (e.g. university, hospital)

☐ Regulatory affairs consultant ☐ Laboratory professional

☐ Health professional – *please indicate type of practice*:

☐ Other - *please specify*:

The World Health Assembly (WHA) resolution 62.13, passed in May 2009 by the World Health Organisation (WHO) Member States urges national governments to respect, preserve and widely communicate traditional medicine knowledge while formulating national policies and regulations to promote appropriate, safe, and effective use; to further develop traditional medicine based on research and innovation, and to consider the inclusion of traditional medicine into their national health systems. WHA 62.13 also urges Member States to cooperate with each other and to share knowledge while working to strengthen communication between conventional and traditional practitioners (WHO 2011).

It is our opinion that the draft document in question does not work to further develop traditional medicine research and innovation and does not consider the inclusion of traditional medicine into the national health system. On the contrary, it seems to try to place complementary medicine into the specific conforms of allopathic medicine which, as would be expected, utilises very specific approaches that are not in line with the complementary medicine, patient centred, model of care. We are very concerned that the end consumer will not benefit from this reform as the information generated from the evidence reports may not be an accurate or a true reflection of the potential benefit to the consumer's general health and wellbeing, which is the intended use of complementary medicines.

It is recognised within the existing Australian regulatory framework that listed complementary medicines are of low risk. It is this definition that has been the basis of the development of the complementary medicines industry within Australia which offers the consumer access to low risk medicines for indications for which they have been shown to be efficacious (through history of use or scientific studies), a choice of modalities to manage their own health outcomes, and information about medicines which are designed to support their general health and well-being. We are concerned that the proposed regulations will restrict the sale and marketing of various complementary medicines which will ultimately result in choice being taken away from the Australian consumer.

With a potentially reduced availability of choice from Australian brands and the easy accessibility of complementary medicines from overseas manufacturers through internet purchases Australian consumers are more likely to purchase complementary medicines through these channels. This could increase risk to consumers in that those products may be manufactured in facilities that do not adhere to the high standards with which TGA licensed facilities must, in terms of both material selection and qualification and manufacturing processes. Such medicines may also be found to be making claims on efficacy that are beyond the scope of the medicine and which are not in line with the current TGA regulations, notwithstanding the proposed changes. This also negatively impacts on industry at all levels including, but not limited to, retail, manufacturing, distribution and marketing companies, due to reduction of purchase of products manufactured, marketed and sold in Australia.

It is this same risk based approach that allows for some over the counter and registered drugs that are provided exemptions within the SUSDP to be of a lower schedule, and some instances unscheduled, than would normally be the case. Ibuprofen present at a dosage rate of 200mg per tablet in packs smaller than 25 units are an example of this. These exemptions provide the consumer increased access to these medicines and provides the opportunity to self-diagnose potentially serious illnesses and select potentially dangerous registered products despite their inherent higher risk profile and opportunity for misuse.

We strongly believe the regulations proposed are going well beyond the scope required for low risk listed medicines. We believe the consumer should have the right to be informed of the indications that these medicines have been studied for, whether it be in self-diagnosable conditions or not, as long as the information being given is accurate, it should be allowed to be conveyed to the consumer. The consumer should then have the right as an educated consumer to choose from either the listed or registered medicine (or potentially both) by making an informed choice, and of course discussing this with their health care professional(s). It seems the regulations put forward are taking the choice away from the consumer by limiting the scope of claims for listed medicines and introducing confusing and long winded requirements - we believe educated and empowered Australians deserve better.

It would help in the analysis of stakeholder comments if you provide the information requested below.

Comments

An assessment of how the proposed change will impact on you. That is, what do you see as the likely benefits or costs to you (these may be financial or non-financial). If possible, please attempt to quantify these costs and benefits.
As a large manufacturer of complementary medicines in Australia our core business includes the purchasing, testing and storing of raw materials right through to the manufacturing of various finished goods to release for sale which includes the testing required to do so. As such our business is structured to comply with the TGA regulations and to provide our customers with various ingredients and products suited to their needs while adhering to these guidelines. Any changes to the current regulations would directly impact on the day to day running of our business as core procedures and competences would need to change to accommodate for any new regulations. The impacts on sponsors selling listed medicines would also impact directly on our company, who manufactures the products. The benefits of the regulations put forward include: * The opportunity that the document brings to clarify certain 'grey areas' of the current legislation so that sponsors can produce and market products with accurate claims for Australian consumers. * The establishment of 'Sources of Established Evidence' - this will allow an easily accessible list of accepted resources which can be used to substantiate claims. * The establishment of guidelines regarding the compilation of an evidence report. Although there are aspects of the process we do not agree with, in principle we support a set standard for reviewing literature and reporting outcomes. In fact assessing the balance of evidence has always been a part of the regulations and so adding more detail to the scope of how to conduct a report is a positive aspect for the industry provided that it is relevant to the scope of claims intended. * Unpublished studies can be used as evidence for claims – we welcome this as it is important to note that there are numerous high quality studies which are unpublished and this evidence should be allowed to be used as evidence to substantiate therapeutic indications. The concerns our company has regarding the regulations put forward include: * Listed medicines are considered low risk and are not intended for use in serious diseases, as such the current system has an excellent track record for safety and we therefore see no reason for an increase in the level, scope and type of resources required to make a claim for therapeutic benefit. There is inadequate justification then to increase the rigor, requirements and resources needed to assess evidence to make basic structure and function or health maintenance claims. We believe that there is no reason to warrant a major overhaul of the current regulations which will increase the strain on resources on our company and industry as a whole for no real benefit to consumers as the quality of the product and claims on listed medicines will be no different to what is currently available.

* The proposed regulations surrounding evidence are very strict in terms of the acceptance criteria for individual pieces of evidence to support traditional indications. Evidence to support traditional claims is often drawn from multiple texts which all include different aspects of the traditional use such as dose and preparation. Few texts contain all of the criteria, thus adherence to the proposed regulations would rule out numerous pieces of well recognised traditional evidence as acceptable.

* The proposed regulations state that traditional claims are not to imply efficacy. Clarification and examples are required from the TGA of traditional claims that are acceptable as it is our view that there is inherent implication of efficacy in referencing the tradition of use in the wording of an indication.

* It is well established and accepted that there is natural variation in herbal extracts depending on growing and harvest times, geographical origin of starting material, seasonal and weather patterns, etc. This level of variation in the chemical profile is acceptable in that extracts of the same species may be used in the same indications to elicit a therapeutic benefit. For this reason different means of preparation of extracts may be utilised to garner herbal extracts with a comparable chemical profile. The proposed regulations are not clear as to what level of substantiation will be required to demonstrate that extracts are comparable with those used to generate the body of evidence. For example where evidence is based on a water extraction and the preparation of an extract for use in tableting is based on a hydro-ethanolic extract, how does one adequately justify the difference in extraction methods? Will justifications such as those currently applied be acceptable or will more detail investigation into phyto-equivalence be required?

This type of detailed investigation will add cost and result in a strain on resources. Demonstrating phyto-equivalence between materials that have been used in clinical trials or traditionally used and prepared raw materials and the extracts intended for use in manufacturing of finished goods will be very costly and at times not possible for logistical reasons. We would need to source a sample of the clinically trialled material/traditional raw material or chromatography of this and compare with chromatography of our own extract. Suppliers and manufacturers are the only organisations in the supply chain who realistically have the capability of managing this in terms of testing and sourcing, putting significant strain on these businesses.

Depending on the types and varieties of evidence supporting different herbal species we may require multiple extracts of species in order to satisfy variability in evidence. This will result in increased cost of materials (lower usage), increased testing, increase evaluation costs, increased time to market for new products, more warehousing requirements, more inventory holding and slower inventory turn-over which will impact our business.

* The restrictions placed on health status and biomarkers of study populations in clinical trials in the proposed regulations pose a particular challenge which we believe cannot practically be applied and will ultimately result in a large body of quality evidence being deemed as unacceptable. The claims that can be made relating to biomarkers have been specified by the TGA and relate to maintaining healthy levels in healthy individuals. In reality there are very few studies that include these parameters (15-20% above normal) as there is minimal benefit for companies to conduct studies with such limited commercial application. If studies in which safe low risk medicines have been used for management of a condition are deemed acceptable such medicines will cease to be marketed to the consumer for this application. This restricts a consumer's right to choice and/or information about the medicines they are taking. Furthermore, looking at biomarkers in isolation does not necessarily mean the person in question is unhealthy or has a serious disease; biomarkers in isolation may not reflect the general health of the person and their risk of disease.

* The proposed guidelines will require that indications be worded in such a way so as to very accurately convey to the consumer the specific parameters as determined by the supporting evidence. There is a disparity between application of the proposed guidelines and the TGA's coded indications project in that those specificities from the evidence to support an indication will require free text to ensure it is conveyed correctly. As such we strongly support retaining free text to accommodate for the proposed guidelines.

* Indications for listed medicines, in general, must only refer to ailments that are self-diagnosable – this is extremely difficult to define and is a grey area of the current system. It is also very limiting to consumer choice that safe and efficacious listed medicines are not able to claim what the product has been clinical trialled to do for example lower cholesterol levels. It is unreasonable that food products like spreads and margarine's can make claims that listed medicines cannot. In addition to this, many Aust R products are available over the counter without the constraints that are being proposed for the CM industry whilst acknowledging that these pharmaceutical active ingredients are far more potent and a higher safety risk than listed medicines. From a risk and safety point of view the choice for the consumer to use a listed medicine for various disease states should be allowed.

Whether or not you support the revised Evidence Requirements. If not supported, please provide reasons why.

The intended TGA reforms are essentially founded on the ANAO report and subsequent blueprint for the future as published by the TGA. From this report it was revealed that 90% of post market reviews conducted by the TGA were found to be non-compliant with the regulatory requirements. Although we have concerns with the small number (31) of cases reviewed, the actual non-compliance and related concerns can in fact mostly relate to simple re-wording, claim qualifiers and simple issues such as size of font. This then could potentially be rectified with updating and clarification of some points of the current regulations where areas of non-compliance were more prevalent, rather than the introduction of a new set of guidelines that as has been discussed above presents issues for industry, consumers and the regulator.

We fully support that regulations are constantly updated and improved as ultimately the benefits are passed on the consumers who use the products. In saying this we cannot see how the current changes proposed will benefit the end consumer. The claims will be identical on pack, the evidence used to make claims will be essentially the same as what is currently expected and the quality and safety aspects of the medicines will be the same. The only aspect which has changed is that the industry is expected to increase the amount of rigor in compiling evidence and use complicated and unfounded methods of analysis to judge on the balance of evidence available. This seems disproportionate to the claims being made, for example health maintenance claims, and the level of risk the product poses to the consumer.

Any additional information on issues not asked in the above questions.

If your comments relate to specific parts of the document please provide the page number and reference.

Page 6

TGA "Part A sets out what is required for an assessment of evidence supporting indications, this may be achieved in one of two ways; through the use of Sources of Established Evidence (SEE) recognised by the TGA, or through a comprehensive and objective review of the available evidence that is relevant to the proposed indication (Evidence Report)"

Our view:

Sources of Established Evidence – this is welcomed however will this list be updated? The amount of work required to complete a report will be exhaustive and not warranted for the level of risk and so the more resources on the SEE list the better.

Page 11

TGA -"traditional claims must not imply efficacy"

Our view:

e.g. traditionally used for fever - implies that it reduces fever. Examples required demonstrating how the TGA anticipate traditional claims can be used. This is also in direct conflict with the coded indications project as free text will be required to qualify these statements. We completely support retaining free text to accommodate for the proposed guidelines.

Page 12

TGA – "where traditional terminology is unclear the information should be communicated using appropriate conventional terminology"

Our view:

This will require free text which is not in line with current stance of the TGA on free text. We completely support retaining free text to accommodate for the proposed guidelines.

Page 15

TGA "studies in other languages should be considered and need to be translated"

Our view:

On every evidence report a qualified translator will need to be engaged - this will add significant cost and is going too far for a listed product.

Strain on resources will occur as having to download every study on the subject that might not be relevant and adds cost. Can a judgement be made from the abstract on relevance? Some studies will need to be bought as they are not free or included in subscription services which adds considerable cost.

Page 16

TGA - "Population in clinical studies are identical to target population for clinical studies"

Our view:

The document should clearly state that studies from other countries are relevant and that different race of study population does not mean it is not representative of the Australian population. The current statement is ambiguous and unrealistic – and not in line with current international standards.

page 18

TGA - "For each study, the meaningfulness of the observed effect/s to consumers at an individual and/or population level (clinical significance) must be assessed."

Our view:

Clinical significance should not be included as a must as clinical significance is not often measured in studies as it is often difficult or impossible to ascertain e.g. calcium supplements do not result in any obvious perceived clinical outcomes for patients.

The TGA themselves deem clinical significance difficult to assess so asking for all clinical studies to include this is going too far for listed medicines.

Page 18 - TGA "For indications relating to weight loss in overweight individuals (BMI 25-30 kg/m2. A mean overall loss of at least five per cent initial body weight in the treatment group, which is at least three per cent greater (for RCT) OR five per cent greater (for non-RCT) than that of the placebo/control group. In both cases the difference must be statistically significant ($p<0.05$);), clinical significance is only achieved if supporting evidence demonstrates:

AND

at least 50 per cent of participants in the treatment group must have achieved a loss of at least five per cent of initial body weight."

Our view:

The addition of the requirement for weight loss for at least 50 per cent of people to achieve a loss of at least 5% cannot be worked out as it is too difficult to obtain the data (as this will only be held by the researcher in their raw data) - it is Intellectual Property and will often not be shared. In addition EFSA have done a lot of word on weight loss guidelines – we should adopt a worldwide accepted model rather than create our own. We would then be in line with international standards.

Page 20-21

TGA - "must have ALL relevance criteria to include a traditional evidence."

Our view:

We see no reason to rule out a traditional piece of evidence because it is missing one of the 'necessary' parameters (as this may be included on a different traditional history and so the body of evidence is complete). Not all traditional references are set up to this standard and so its traditional use should not be lost due to the evidence not conforming to the TGA's definition of evidence.

Page 22 - under listable indications - the TGA document uses words that are not allowed in listed medicines, i.e. prevent, treat. Are these words/claims now allowed? If not these need to be removed them and the document updated to use relevant terms for listed medicines as this is adding confusion to the regulations.

Page 23

TGA "must only refer to ailments or health states that are self-diagnosable"

Our view:

Defining self-diagnosable conditions is very difficult – we believe the consumer should have the right to choose to use listed medicines for various indications. Especially once diagnosed by a Health Care Professional. Consumers should be able to take control of their health and self-select to improve symptoms of their condition e.g. arthritis diagnosed by a doctor – they should then be able to purchase fish oil as the label states it may assist with arthritis. This is not at all misleading and so should be allowed. In addition the listed medicines are low risk where as many registered medicines available over the counter are high risk – so the consumer should have the choice of what they would like to use.

Page 35

TGA - "unfortunately many trials of otherwise high quality inadequately describe or characterise the composition of the herbal intervention"

Our view:

Does this mean we have to rule out studies which inadequately describe the herbal intervention? We believe by deducing the information available to a reasonable explanation and conversion that the study should be allowed so that quality studies are not lost due to this requirement.

Page 36

TGA - "Establishing relevant study populations for listable indications that claim favourable modulation of measurable validated biomarkers of disease (such as BMI, blood pressure, blood glucose and cholesterol) in the healthy Australian population poses a particular challenge. Although a small change in a given biomarker may be associated with negligible biological dysfunction and minimal increase in risk of serious forms of disease, larger changes are more likely to be associated with pathophysiological processes and increased risk of overt illness that require health practitioner involvement. For these reasons, it is unlikely that study populations with baseline biomarker levels greater than 15-20 per cent above the accepted upper limit of 'normal' would be considered relevant to support indications relating to favourable modulation of measurable biomarkers of disease in the healthy Australian population."

Our view:

Reference to study population in relation to biomarkers should not be taken into account given there is limited evidence on people with biomarkers in the healthy range - there is no viable reason to conduct studies on healthy populations.

High cholesterol is a risk factor, not a serious illness. It could be argued that people with elevated cholesterol are healthy, depending on their other risk factors for heart disease. Likewise people with a high BMI may not be necessarily unhealthy. Placing restrictions on levels of biomarkers in studies will rule out many studies of high quality and the incentive for sponsors to conduct studies on these populations is small.

Page 40

TGA - Evidence that describes an effect on a biological process generally does not contribute to the evidence base for an indication that refers to a clinical outcome. Such data may, however, be useful in demonstrating biological plausibility of a clinical outcome.

Example:

An indication relating to weight loss refers to a specific biological outcome. Changes in enhanced fat metabolism, thermogenesis, or metabolic rate do not necessarily translate into weight loss and evidence supporting these indications does not substantiate indications for weight loss.

Our view:

We should be able to claim on whatever was measured in a study for the purpose it was measured. There are many claims ruled out because they are said to imply weight loss however these claims might be applied to products to enhance sports performance, toning specific body areas, fat metabolising for exercise benefits etc.

EFSA has done a lot of work on weight loss claims we should follow their lead and not reinvent the wheel so that we are in line with international standards.

Page 43

TGA "For each included study, add together all four relevance rating scores to produce the study relevance score.

RS = RM + RP + RB + R

Where RS=study relevance score, RM=relevance to medicine, RP=relevance to target population, RB=relevance to health benefit, and RC=relevance to context."

Our view:

The mathematical equations are over the top for the scope of looking at evidence and assessing the balance. This will add considerable time and confusion to a straight forward process of assessing the balance of evidence and as such do not believe it is warranted.

General recommendations:

As an organisation we encourage an update of the current levels of evidence documentation. However we propose that the current documentation should be retained and used as a base to build upon. We propose changes be implemented to make the current guidelines clear, more transparent and easier to follow.

In addition to this we encourage the allocation of extra resources to the TGA so that the TGA can be more transparent and swifter in responding to industry concerns.

We strongly believe that creation of a new draft document and system for complementary medicines, as is proposed, will cause more confusion and will unnecessarily and negatively affect the industry and consumers.

Further to building and improving from the current regulations we strongly believe that there should be more encouragement for innovation and research from the TGA to the industry. This may be enhanced by providing more incentives to the industry for listing new ingredients and conducting research – such as granting exclusivity periods and considering data protection. These models are currently being used successfully in other countries such as China and we strongly encourage the TGA to seriously consider these actions.