13 November 2019

Medsafe
Ministry of Health

Re: Prescriber Update
September 2019-11-13
Attention: s 9(2)(g)(ii) [redacted]
cc. Hon Winston Peters
cc Hon Andrew Little

Re: *Artemisia annua* Schedule

It has come to my attention that the Ministry of Health's proposal to schedule *Artemisia annua* as a prescription medicine was discussed at the 63rd meeting of the Medicines Classification Meeting on 10 October 2019.

International Alcohol Industry
I do hope that the Alcohol Industry Board was included in that meeting, as the herb *Artemisia* is often used in the production of Gin and Vermouth. These are alcohol drinks manufactured by international companies. I'm not sure that would adhere to adding a proposed prescription medicine

I realise this is but one small area of your major safety investigations, but it has serious implications for the food and alcohol industry, based on a dosage issue, not the specific herb itself.

Chinese Government Research
Also, did you know that the Chinese Government are implicated in this issue as the international researcher of the benefits of this herb was from China Academy of Chinese Medical Sciences, Professor YouYou, who received the World Laurette Nobel Peace Prize in 2015, on her research on *Artemisa* (wormwood) namely for malaria, that has since saved millions of lives internationally and was a serious contributor to Chinese global health.
ref The discovery of *artemisinin* and Nobel Prize in Physiology or Medicine
https://www.ncbi.nlm.nih.gov › pmc › articles › PMC4966551

As the Director of Herbal Education Resources Centre, herbal educational school, registered in 1985, I have found, over the decades issues such as this often lack the consultation process with related herbal industry expertise, or the educational standards from the 1989 Education Act acted upon. For instance the international educational standard qualification for herbal consultation is Master Herbology Degree. Consequently, Medsafe discussions on herbs are often acted upon without understanding appropriate dietary guidance, dosage and historic use. In this case dosage warnings would be recommended, not the status of the herb itself. Whilst the safety of the public lies in your hands, certainly a huge task, may I suggest a little more

appropriate investigation may save Medsafe from extra challenges, if not a legal issue, in this case from the Alcohol Industry or from a visit from a Chinese Government representative.

I look forward to assisting Medsafe in any appropriate way.

For instance, did your realise that the Artemisia herb under question is part of eleven botanical varieties used.

Such as: Types of Artemisia

- Southernwood *(Artemisia abrotanum)* ...
- Wormwood (*Artemisia absinthium)* ...
- Western Mugwort *(Artemisia ludoviciana)* ...
- White Mugwort (*Artemisia lactiflora)* ...
- Roman Wormwood (*Artemisia pontica)* ...
- Silver Mound *(Artemisia schmidtiana)* ...
- Beach Wormwood (*Artemisia stellerana)* ...
- Artemisia *chamaemelifolia*
- Artemisia *annua* sweet wormwood.

The one under proposed regulation is:
Artemisia annua (also known as Qing hao, Sweet Annie or Sweet Wormwood) dried herb or extract are constituents in several natural health products available in New Zealand.
Artemisinin is a constituent in all *Artemisia* and its derivatives form the basis of the *artemisinin*-based combination therapies (ACTs) now recommended by WHO for treating certain types of malaria·

Yours sincerely

s 9(2)(a)
[redacted]
Herbal Education Resources Centre
Herbal Ltd
P O Box 6041
Tauranga 3146
++s 9(2)(a)
e: s 9(2)(a) [redacted]

p.s. enclosed letter has also been posted.

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

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New Zealand
T +64 4 496 2000

5 February 2020

s 9(2)(a)
Herbal Education Resources Centre
Herbal Ltd
Email: s 9(2)(a)

Dear s 9(2)(a)

Reclassification of Artemisia annua – objection to the recommendation made by the Medicines Classification Committee at the 63rd meeting on 10 October 2019

Thank you for your email, dated 9 December 2019, following a recommendation by the Medicines Classification Committee (the Committee) that Artemisia annua should be classified as a prescription medicine. The Committee is a ministerial advisory committee established under section 8 of the Medicines Act 1981 to advise the Minister of Health on the classification of medicines as prescription, restricted or pharmacy only medicines.

Following the publication of the Committee's recommendations, there is an opportunity to object to the recommendations. The criteria for valid objections are described in the guidance document (www.medsafe.govt.nz/downloads/How_to_change_medicine_classification.pdf).

The information you have provided on the evidence of safety concerns and benefits is not substantially different to that presented to the Committee. Information about the substance, including those that were received from the public and stakeholders during consultation, were taken into consideration by the Committee.

The process that was undertaken is standard for classifying new medicines.
The Committee was presented with a substance that Medsafe regards as a substance intended for a therapeutic purpose and therefore a medicine. The Committee was asked to determine the classification of this substance, to which the Committee recommended that it should only be supplied under the care of an authorised prescriber as a prescription medicine. The Committee was not asked to consider whether the substance was a medicine or not.

To clarify, the decision relates to Artemisia annua extract and this is intended to be clear in the Gazette notice. This will exclude dried, crushed, ground and fresh plant material.

I have reviewed the information that you have provided, and I am satisfied that the grounds on which the objection was raised do not meet the criteria for a valid objection.

The Committee's recommendation will not be referred to the next meeting for further consideration.

Yours sincerely

Chris James
Group Manager
Medsafe

Barristers.Comm
PO Box 5577 • m • Level 7 • Legal House • 101 Lambton Quay
• Wellington 6145 • New Zealand • T s 9(2)(a) • F s 9(2)(a)
M s 9(2)(a) • E s 9(2)(a) • W www.bcomm.nz

Document 3

s 9(2)(a)
BA(Hons)LLB(Hons)
BARRISTER

17 December 2019

To: Medicines Classification Committee

Subject: **SUBMISSION FROM NEW ZEALAND HEALTH TRUST OPPOSING THE RECOMMENDATION TO CLASSIFY *ARTEMISIA ANNUA* AS A PRESCRIPTION MEDICINE**

Introduction

1. This submission is filed on behalf of the New Zealand Health Trust (NZHT).

2. NZHT is an independent charitable trust. Its objective is to educate New Zealanders to make informed decisions about their health and wellbeing.

3. In the last 20 years NZHT has spent considerable time and effort advocating for balanced and appropriately permissive regulation of natural health products. It opposed the now withdrawn Natural Health Products Bill and has been vocal in lobbying for pragmatic regulation of natural health products that reflects the overall low risk of these products and provides for and protects informed consumer choice.

4. NZHT has become aware of the MCC's recommendation to classify *artemisia annua* as a prescription medicine in all doses. It has reviewed the relevant material relied on by the MCC. From what it can glean from these documents, Medsafe has applied to classify a hitherto safe herbal ingredient *artemisia annua* (incorrectly described by the MCC in its Minutes dated 10 October 2019 as a "new chemical entity") due to (apparently unsubstantiated and exaggerated) safety concerns about one particular product containing this ingredient, namely Arthrem. From NZHT's vantage point as an outside observer, this is an extraordinary example of regulatory overreach and overreaction. The motivation behind these steps is questioned.

Submission

5. NZHT opposes MCC's recommendation to classify *artemisia annua* as a prescription medicine in all doses.

6. Its primary submission is that the MCC has no power to recommend the Minister classify *artemisia annua* as a prescription medicine. MCC is authorised under the Medicines Act 1981 to make recommendations in relation to "any medicines" (s 9). *Artemesia annua* is not a medicine, it is a herb and therefore a food. To the extent it is used in products such as Arthrem, these are sold and regulated as dietary supplements under the Dietary Supplements Regulations 1985. Even Medsafe in its submission dated June 2019 stated that *artemisia annua* "is not classified as a medicine currently" and that it "is sold in products as a natural health supplement".

7. If the Minister were to accept the MCC's recommendation he would be acting unlawfully.

8. Second, even if there was jurisdiction to make such a recommendation (denied) there has been a failure to adequately consult. As a minimum MCC ought to have consulted widely with the natural health products community including those specifically marketing products containing *artemisia annua*. It has not done this. There is no evidence that the MCC has meaningfully engaged with and considered the feedback it has received as it fails to address any points raised. A requirement of consultation is that the consulter listens with an open mind. There is nothing in the MCC report to indicate this has occurred. The consultation process has fallen well below the standard required.

9. Third, there is no evidence of liver safety issues arising with *artemisia annua* per se. Neither Medsafe nor the MCC has identified any peer-reviewed scientific papers identifying harmful effects on the liver as a result of ingesting *artemisia annua*. To the best of NZHT's knowledge *artemisia annua* products have a long history of safe use with no safety concerns being raised.

10. Fourth, the evidence of potential harm arising from Arthrem is of dubious quality and reliability. Medsafe appears to rely on CARM reports as prima facie indicating a causal link between Arthrem and liver harm without undertaking any real further investigation of the individual circumstances of each report.

11. CARM reports are not sufficient to establish a causal link between Arthrem and the harm alleged. NZHT is aware that Medsafe would rarely if ever regard such reports as causal in cases involving pharmaceutical drugs[1], including vaccines. It is hypocritical for Medsafe to apply a different approach to this dietary supplement.

12. Fifth, the recommendation has chilling precedent effects for the dietary supplement and natural health product community. On the spurious pretext of alleged safety risks, a dietary supplement/ingredient can overnight be transmogrified into a prescription medicine and effectively becomes a prohibited product. This is because as Medsafe and the MCC know, the practical ability for companies to obtain approval for such products containing *artemesia annua* as prescription medicines under the Medicines Act is approximately zero. Apart from causing serious financial harm to the company selling Arthrem, the intention of this exercise is to lock up *artemisia annua* in the Medicines Regulations Schedule and prevent access to it. This outcome is antithetical to consumer choice and designed to only benefit and protect the pharmaceutical industry.

13. Further, as pointed out in submissions to the MCC (which appear to have been ignored), classifying *artemisia annua* as a prescription medicine removes a herb with thousands years of safe use from the ambit of qualified herbalists and places it under the ostensible control

[1] For example, just last month following reports of several deaths relating to Logem, Medsafe's response was, "Sadly CARM has also received three cases reporting death as an outcome. All three cases are under Coronial investigation because the cause of death in each case is unknown….Please note adverse reactions are reported to CARM based on a suspicion that the medicine could have caused the reaction. A causal link between brand changes of lamotrigine and the adverse reactions described here has not been established." (Medsafe "Suspected Adverse Reaction reports to lamotrigine changing brands" published 12 November 2019)

https://www.medsafe.govt.nz/safety/Alerts/Lamotrigine.asp

of practitioners with no training or qualifications in relation to such products. That is the antithesis of good regulatory practice.

Yours sincerely s 9(2)(a)

s 9(2)(a)

Sent by: s 9(2)(a)

07/02/2020 05:09 pm

To: "committees@health.govt.nz" <committees@health.govt.nz>
cc: s 9(2)(a)
bcc:

Subject: RE: Response to objection about recommendations made by the Medicines Classification Committee at the 63rd meeting

Hi s 9(2)(a)

Can you please pass this on to Mr James

Dear Mr James

Thanks for your letter.

1. I don't accept that it is not a valid objection. NZHT has raised important matters consistent with the criteria that justify the MCC revisiting their recommendation and in particular their jurisdiction to make such a recommendation.

2. The recommendation in any event appears to have been substantially modified by Medsafe. You say the "decision relates to Artemisia annua extract and this is intended to be clear in the Gazette notice. This will exclude dried, crushed, ground and fresh plant material".

3. The MCC's recommendation was not limited to the extract but referred artemisia annua per se. The recommendation was "that Artemesia annua should be classified as a prescription medicine".

4. The MCC did not differentiate between the extract and raw forms of the herb. So what is the basis for this altered recommendation? Where and what is the evidence justifying it? What is the evidence you rely on to say the extract is unsafe the raw form is safe? And where is the process indicating that the MCC agrees with this recommendation.

5. I am concerned by the reference to the word "decision". The MCC's role is to make a recommendation to the Minister who will separately make a decision and issue a Gazette notice. You present the matter as a fait accompli and that it has been predetermined.

6. It is particularly concerning that the Committee appears to be ignorant of the basis of its jurisdiction. You say the Committee was not asked to consider whether the substance was a medicine or not. But the Committee's powers only extend to medicines. If it isn't a medicine there is no jurisdiction to make a recommendation. Whether it is a medicine is the first question the Committee should be asking. And it's the first question the Minister should be asking too.

7. Please advise urgently what the next steps in the process are. When is this matter to be considered by the Minister?

8. You are on notice that if a decision is made to classify artemisia annua as a prescription medicine a judicial review proceeding may be filed as a matter of urgency and interim orders sought preventing the notice being gazetted pending determination of the judicial review. The primary grounds of review would be that the MCC and the Minister are acting unlawfully. Their powers to respectively recommend and classify a medicine a prescription medicine require the substance to be a medicine in the first place. Artemesia annua is not a medicine. It is a food. Additional grounds of review would address the numerous process faults and flaws.

9. I seek an urgent undertaking from you by **5 pm on Wednesday 12 February 2020** that if a decision is made to classify artemisia annua a prescription medicine no steps will be taken to gazette the notice for seven days to give NZHT sufficient time to prepare and file the relevant proceedings and to seek the appropriate interim orders. A further undertaking is sought that you would immediately advise me of any decision by the Minister and immediately provide all further relevant documents. This will ensure that any litigation could be progressed in an efficient and cost effective way.

10. If a decision has already been made please immediately advise and provide the undertakings sought.

Yours sincerely
s 9(2)(a)

From: s 9(2)(g)(ii) **On Behalf Of** committees@health.govt.nz
Sent: Wednesday, 5 February 2020 9:47 AM
To: s 9(2)(a)
Subject: Response to objection about recommendations made by the Medicines Classification Committee at the 63rd meeting

Tēnā koe s 9(2)(a)

Please see attached letter.

Ngā mihi

s 9(2)(g)(ii)
s 9(2)(g)(ii) | Advisor Science (Secretary for the MAAC and the MCC) | Medsafe | Ministry of Health |

MEDSAFE
New Zealand Medicines and Medical Devices Safety Authority

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MEDSAFE
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5 February 2020

s 9(2)(a)
Barristers.Comm
Email: s 9(2)(a)

Dear s 9(2)(a)

Reclassification of Artemisia annua – objection to the recommendation made by the Medicines Classification Committee at the 63rd meeting on 10 October 2019

Thank you for your email, dated 17 December 2019, following a recommendation by the Medicines Classification Committee (the Committee) that Artemisia annua should be classified as a prescription medicine. The Committee is a ministerial advisory committee established under section 8 of the Medicines Act 1981 to advise the Minister of Health on the classification of medicines as prescription, restricted or pharmacy only medicines.

Following the publication of the Committee's recommendations, there is an opportunity to object to the recommendations. The criteria for valid objections are described in the guidance document (www.medsafe.govt.nz/downloads/How_to_change_medicine_classification.pdf).

The information you have provided on the evidence of safety concerns and benefits is not substantially different to that presented to the Committee. Information about the substance, including those that were received from the public and stakeholders during consultation, were taken into consideration by the Committee.

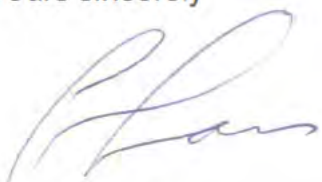
The process that was undertaken is standard for classifying new medicines.
The Committee was presented with a substance that Medsafe regards as a substance intended for a therapeutic purpose and therefore a medicine. The Committee was asked to determine the classification of this substance, to which the Committee recommended that it should only be supplied under the care of an authorised prescriber as a prescription medicine. The Committee was not asked to consider whether the substance was a medicine or not.

Medsafe operates a process where there are consultation opportunities both before and after a meeting of the Committee. As you will be aware, the agenda and items for consideration are made available on the Medsafe website prior to a meeting and Medsafe may also inform parties whom it is aware may have an interest. This is done as a courtesy, however, the expectation is that those interested will proactively engage with the process. I note that you have availed yourself of this process.

To clarify, the decision relates to Artemisia annua extract and this is intended to be clear in the Gazette notice. This will exclude dried, crushed, ground and fresh plant material.

I have reviewed the information that you have provided, and I am satisfied that the grounds on which the objection was raised do not meet the criteria for a valid objection. The Committee's recommendation will not be referred to the next meeting for further consideration.

Yours sincerely



Chris James
Group Manager
Medsafe

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12 February 2020

s 9(2)(a)
Barristers.Comm
Email: s 9(2)(a)

Dear s 9(2)(a)

Thank you for your email of 10 February 2020 responding to the letter from Medsafe advising that your objection to the Medicines Classification Committee (the Committee) recommendation to reclassify *Artemisia annua* is considered not valid. Medsafe acknowledges that you disagree with this finding.

The Minister of Health has delegated the power to classify medicines by notice in the Gazette to the Group Manager, Medsafe (the Minister's delegate). The Minister's delegate reviewed the objections received against the criteria described in the guidance document:
https://www.medsafe.govt.nz/downloads/How_to_change_medicine_classification.pdf

The criteria for valid objections are:

- the Committee did not consider all the safety issues correctly (for example a new safety concern that may have been identified since the start of the consultation)
- the Committee did not consider all the benefits
- there was a breach of the appropriate process.

The Minister's delegate was satisfied that the grounds on which the objection was raised do not meet these criteria. As mentioned in the letter from Medsafe to you dated 5 February, this was because the information provided by you in your objection on the safety grounds and on the substance was not substantially different from that provided to, and considered by, the Committee. *Artemisia annua* was brought to the Committee as significant adverse effects, including liver failure, have been experienced by users of products containing an extract of this substance.

Your objection highlighted that the recommendation in the minutes regarding *Artemisia annua* was imprecise. Medsafe reviewed the supporting paper presented to the Committee and notes that it referred to "*Artemisia annua* extract" although this was not reflected in the minutes. Further clarification was sought from committee members post-meeting, and it was verified that the Committee's recommendation related to the extract rather than the plant.

An extract is a preparation containing the active ingredients of a plant in a concentrated form.

Medsafe notes your concern regarding the word "decision" in the letter dated 5 February and accepts that its use was incorrect when relating to the Committee's recommendation. However, its use is correct when referring to the decision by the Minister's delegate with regard to valid or invalid objections.

With regard to your suggestion that the Committee should be asking whether the substance is a medicine or not, as you noted the Committee's jurisdiction is only for medicines. There is no need for the Committee to question whether a substance is a medicine or not as only substances that are considered medicines are put forward for their consideration. It is Medsafe's opinion that *Artemisia annua* extract is not a food and has been marketed with a therapeutic purpose, therefore it is considered a medicine.

Once objections are considered, the Minister's delegate makes the final decision. The Minister's delegate has, following consideration of the minutes and objections, decided to support the classification recommendations made at the 63rd meeting of the Committee.

Following the Minister's delegate's decision, any required changes to the classification of medicines are implemented by publication of a Gazette Notice. This typically occurs four weeks after the minutes were published. However, this has been delayed to avoid the Christmas and New Year season, and also at the request of the Minister's delegate so that he may thoroughly review the points raised in the objections received before making a decision.

It is intended that a Gazette Notice to implement the recommendations made at the 63rd meeting, with the exception of codeine due to the required implementation process, will be published four weeks after the date that objectors were notified of the outcome of their objection. The notice to classify *Artemisia annua* extract is expected to be published on 4 March 2020.

I hope that you find this information helpful.

Yours sincerely

Chris James
Group Manager
Medsafe

NATURE'S SUNSHINE®

Objection to proposal to classify Artemisia annua as a prescription medicine

Nature's Sunshine Products New Zealand

Nature's Sunshine Products New Zealand
344a Rosedale Road, Albany, Auckland, 0632
PO Box 302447, North Harbour, Auckland, 0751
Tel: 09 415 7781 Facsimile: 09 415 7786 Toll Free: 05 08 707070
Website: www.naturessunshine.co.nz

Introduction

1) Nature's Sunshine became aware of Medsafe's proposal to classify the herb Artemisia Annua as a prescription-only medicine shortly before the Medicines Classification Committee's scheduled meeting.
2) We took advice as soon as practicable and prepared and submitted a submission which was rejected by Medsafe, as they deemed it to be too late.
3) Others made submissions to the MCC; these were ignored.
4) We resubmit our previous submission as part of this objection. The issues raised are relevant to our current objection.

Lack of consultation

5) Medsafe has not consulted with those potentially adversely affected by the proposal as required by law. Despite having an extensive list of emails of Natural Health Product companies as a result of consultation over the failed Natural Health Products Bill, Medsafe chose not to use the above mentioned email list to notify NHP companies of the proposal. Companies, with no interest in medicine regulatory affairs, are expected to be informed by osmosis. Such passive 'consultation' does not accord with recognized consultation methods.
6) Good consultation should include the following actions by the decision maker. That it:
    a) Identifies those likely to be affected by a decision;
    b) Notifies and gives affected parties sufficient information to enable them to make an informed comment
    c) Ensures that the decision maker has all relevant information before it, (in a fair and reasonable summary), if necessary
    d) Provides sufficient time for comment
    e) Listens to what others have to say with an open mind
    f) Undertakes the task in a genuine and not in a cosmetic manner
    g) Properly notifies the decision

    These are well known principles of consultation which Medsafe has failed to follow.

Nature Sunshine Products Artemisia products are not medicines

7) Nature's Sunshine Products Artemisia products do not meet the definition of a medicine in s3 of the Medicines Act, nor are they sold principally for a therapeutic purpose. Our products meet the definition of a dietary supplement, are manufactured and marketed as foods, under the Food Act, and therefore are exempt from the Medicines Act under s3[1][c][ii].

Medsafe is preventing qualified practitioners from prescribing a safe herb

8) Medsafe's proposed classification of Artemisia as a prescription only medicine will prohibit the only practitioners who are qualified in dispensing herbal remedies for therapeutic purposes and put them in control of practitioners with zero training in such products. This is not only anathema to good regulatory practice, it antithesis to good risk management practice.

Medsafe has not established causality

9) Medsafe has not established a causal link between the herb Artemisia Annua and spontaneous, and in many cases, solicited adverse reactions. **Safety signals have been associated with Artemisia annua** are just that, signals; Safety signals are not evidence of causality, and are not the basis of prohibiting a generic herb, and hence other products that have had no evidence of any adverse effects, when the 'signal' applied only to a single product utilizing a novel extraction method.

10) Medsafe has assumed that passive spontaneous adverse reaction reports relating to a single product using a novel extraction method are not only causal, but apply to all Artemisia Annua products, even though there is no evidence in international literature to support such a leap of faith.

Medsafe has not undertaken a substantive risk-assessment

11) Medsafe has insufficient scientific and technical evidence to support the safety concerns that the classification purports to address. The Ministry of Health is acting on inadequate information and has failed to produce a substantive and comparative risk-assessment for any product, let alone the herb itself. As a result, it is not possible for Medsafe, the Ministry of Health, or the Minister/his Delegate to be satisfied that the proposed classification is needed to protect the public given that the information relied upon was incomplete and inadequate for this purpose. Whilst there is discretion in deciding the weight to be given to different considerations there must be evidence available to support any decision.

12) Medsafe has abused its power by not undertaking any meaningful risk assessment. It is noted that even if a causal risk had been established, Medsafe has not considered any alternative risk management options. It has failed to consider evidence provided to it such as that in Phytomed's submission.

Medsafe has misinterpreted the Medicines Act

13) Medsafe has deemed Artemisia Annua to be a New Chemical Entity under the Medicines Act when it has in fact been consumed internationally for several thousands of years, and many decades in New Zealand under food law. The Medicines Act does not refer to 'New Chemical Entities.' New medicines excludes medicines that have been on the market for five years.

14) It is worth including the entire record of the Medicines Classification Meeting as an end note as provided on Medsafe's website as it highlights Medsafe's lack of understanding of non-chemical entities.[i]

15) The MCC states; "**The Committee agreed that Artemisia annua has a therapeutic purpose** and stated that **the precedent for any new chemical entities that have a therapeutic purpose is to be classified as prescription medicines**. This is **to address any potential safety concerns for new medicines**. " Highlights added.

16) Firstly, Artemisia annua is a herb. It doesn't have any purpose. Products are manufactured, marketed and consumed for a variety of purposes.

17) Secondly, Artemisia annua can be sold or consumed for a variety of reasons. In New Zealand law, Dietary Supplements are regulated as foods, regardless of what Medsafe or its expert committee might think. Individual products are marketed or consumed for different reasons. Nature's Sunshine Products legally markets its products as dietary supplements, not medicines, and its products that contain Artemisia Annua also contain a number of other ingredients. They are not single ingredient products using novel extraction processes.

18) What is the problem?

19) Medsafe's initially stated problem appears to be that several adverse reaction reports were submitted to CARM relating to a specific product.

20) Despite stating that the product was a dietary supplement (therefore a food) Medsafe issued a privileged statement under section 98 of the Medicines Act 1981.

21) Whilst Medsafe administers the Dietary Supplement Regulations (which are regulations made under the Food Act) Medsafe does not administer the Food Act so could not use section **289 of the Food Act to publish privileged statements.** S289 (1) of the Food Act gives the chief executive of the food regulator authority to publish a statement for the purpose of protecting human life or public health or informing the public. Medsafe has no such authority.

22) Medsafe publicized the reports under the pretense that causality had been established when it hadn't been.

23) Medsafe commenced legal proceedings under the Medicines Act against the company marketing Arthrem.

24) Medsafe then republicised its concerns implying that the herb itself was hazardous, when causality had been assumed but not demonstrated.

25) Medsafe continues prosecution of the company supplying Arthrem.

26) Medsafe makes an unannounced submission to the Medicines Classification Committee to classify the herb Artemisia Annua as a prescription medicine. Consultation is assumed based on a passive system requiring a degree of clairvoyancy and ongoing monitoring of all Medsafe webpages and links that might relate to regulatory matters. Only those with an interest in pharmaceutical regulation would normally monitor Medsafe activities with any degree of vigilance. Suppliers of

products manufactured and supplied under food law would have no reason to monitor Medsafe's regulatory activities.

27) So the real problem appears to be Medsafe trying to win a philosophical argument and pre-empt any court decision by banning a safe herb that has no history of harm other than anecdotal reports relating to a single product in large part following extensive public vilification of that product.

What is the science?

28) We have not been able to find any scientific evidence to support Medsafe's conclusions regarding harm related to the herb Artemisia Annua. We refer Medsafe to Phytomed's submissions in this regard.

What is the risk?

29) We have not been able to find any scientific evidence to support Medsafe's conclusions regarding harm related to the herb Artemisia Annua. Therefore it is impossible to establish any informed risk. Spontaneous adverse reaction reports, especially following adverse publicity, does not provide a scientific basis for establishing causality. We note that hundreds of severe adverse reactions have been reported to CARM relating to vaccines, for example, that have been dismissed as 'coincidental' by CARM and Medsafe. No assessment of increases in hepatic enzyme levels in people using Artemisia Annua or case controls has been undertaken, therefore it is impossible for Medsafe to have reached the conclusions it has for objective reasons.

30) No formal or objective risk assessment has been undertaken so therefore established science must take precedent. On that basis risk is de minimis, especially for products such as those marketed by Nature's Sunshine.

31) What is an appropriate risk management response?

32) Given there is no established risk related to products such as those marketed by Nature's Sunshine, there is no need for any formal risk management response.

De ja vue all over again

33) The 2001 minutes of an MCC meeting record the following related matter,[1]

> "[T]he Minister's Delegate has accepted the following advice submitted by Medsafe:
>
> Medsafe does not recommend that the proposal to adopt the MCC proposed framework for the classification of herbal medicines be adopted at this time for the following reasons:
>
> - MCC expertise is in the practice of medicine and the practice of pharmacy: members are not skilled in the field of herbal medicines
> - The consultation process was limited in its effectiveness and therefore there is no assurance that all relevant information was considered
> - Accepting the recommendations would result in unavailability of products for which there is no evidence of consumer harm in New Zealand.

34) Of particular relevance to this proposal by Medsafe is that nothing seems to have changed.

- MCC expertise is in the practice of medicine and the practice of pharmacy: members are not skilled in the field of herbal medicines
- The consultation process was limited in its effectiveness and therefore there is no assurance that all relevant information was considered
- Accepting the recommendations would result in unavailability of products for which there is no evidence of consumer harm in New Zealand.

Conclusion

35) To avoid embarrassment, risk of legal challenge, and in the interests of good regulatory practice, Medsafe would be wise to reflect on the advice it gave to the Minister's Delegate in 2001.

- MCC expertise is in the practice of medicine and the practice of pharmacy: members are not skilled in the field of herbal medicines
- The consultation process was limited in its effectiveness and therefore there is no assurance that all relevant information was considered
- Accepting the recommendations would result in unavailability of products for which there is no evidence of consumer harm in New Zealand.

36) Failure to do so will provide the Natural Health Product industry and consumers of its products with further evidence that Medsafe is not a fit and proper regulator for such products.

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[1] Minutes of the 26th meeting of the Medicines Classification Committee - 11 December 2001
https://www.medsafe.govt.nz/profs/class/Minutes/2001-2005/mccMin11Dec01.htm

End notes:

[i] Complete public record of the Medicines Classifications Committee rationale for classifying Artemisia Annua as a prescription medicine. Bold and underline highlights added.

New medicines for classification

7 *The following new chemical entities were submitted to the Committee for classification.*

7.2 New chemical entities identified by Medsafe

Artemisia annua

Medsafe had prepared an information paper on this New Chemical Entity (PDF, 514KB, 18 pages)

Comments

Four comments were received about this agenda item that were not in support of classifying Artemisia annua.

Discussion

The Committee discussed the information paper and the feedback received during consultation. **The Committee agreed that Artemisia annua has a therapeutic purpose** and stated that **the precedent for any new chemical entities that have a therapeutic purpose is to be classified as prescription medicines**. This is **to address any potential safety concerns for new medicines**. **Safety signals have been associated with Artemisia annua**, including hepatic cirrhosis which has resulted in two safety alerts by Medsafe and referral to the Medicines Adverse Reactions Committee (MARC). **The Committee also acknowledged the opposing opinions** received from stakeholders on the benefits of Artemisia annua and their concerns around manufacturing processes. The Committee was satisfied that the potential harm identified would adequately justify controlling the access by classifying it as a prescription medicine.

7.2e The Committee was also advised that Arthrem (containing Artemisia annua) has since been withdrawn from the Australian market due to adverse reaction reports. In addition, a retail level recall in Australia was undertaken to address the safety concerns with the risk of harm to the liver. It is noted that Arthrem capsules are a complementary medicine listed on the Australian Register of Therapeutic Goods and are marketed as a natural dietary supplement. Arthrem capsules contain the substance Artemisia annua extract as the only active ingredient. Further information about Arthrem capsules and actions taken in Australia are available on the TGA website (https://www.tga.gov.au/alert/arthrem-capsules).

The Committee discussed how this is a product derived from an herb and considerations would be required in the terminology used in the classification wording as "Artemisia" includes many different species.

Existing products on the market would be considered as unapproved prescription medicines. The Committee recommended that Medsafe communicate this to prescribers should patients approach their family doctor to request a prescription for these medicines.

The Committee was also concerned that classifying these substances as prescription medicines could mislead the public that these were approved prescription medicines and emphasized that it should be clearly communicated that these products are unapproved and therefore have not been assessed for their pharmaceutical quality and safety. This same concern would also apply for octodrine (agenda item 7.2c).

Recommendation

That Artemisia annua should be classified as a prescription medicine.

PHYTOmed™ medicinal herbs ltd.

19 August 2019

Secretary
Medicines Classification Committee
Ministry of Health
133 Molesworth Street
Thorndon
Wellington 6011

FEEDBACK ON PROPOSED RE-SCHEDULING OF ARTEMISIA ANNUA TO BE PRESCRIPTION ONLY

This submission is being made on behalf of Phytomed as we are aware of a submission made by Medsafe to the Medicines Classification Committee in June, to classify Artemisia annua and its extracts, as a prescription medicine.

We recommend that the Medicines Classification Committee:

1. Does not classify Artemisia annua and its extracts as a prescription medicine.

2. Recommends to Medsafe and the Minister of Health that New Zealand's regulatory regime requires all natural-health products making therapeutic claims to be manufactured in a GMP certified facility.

3. Recommends to Medsafe and the Minister of Health that New Zealand's regulatory regime moves to a complementary medicines-based model and away from a dietary supplement model.

4. Recommends to Medsafe and the Minister of Health that New Zealand's regulatory regime requires all herbs and raw materials included in complementary medicines to be subject to a rigorous testing regime.

5. Recommends to Health Workforce NZ that New Zealand regulates the professional practice of western Herbal Medicine, as applied for by the New Zealand Association of Medical Herbalists (NZAMH), under the Health Practitioners Assurance Act.

We do not believe that the root cause of the 14 New Zealand reported cases of hepatotoxicity associated with Artemisia annua, are due to the safety of the herb. The most likely cause, given international evidence, is in the quality and/or contamination of the herb and in the manufacturing processes. Classifying it a prescription only medicine does not address the root cause. Also, making it a prescription only medicine would take it out of the reach of the many natural health practitioners and others, who currently rely on it in their daily lives.

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PHYTOmed™ medicinal herbs ltd.

About Phytomed

Phytomed Medicinal Herbs Ltd (Phytomed) is a GMP licensed company that since 1998, has manufactured herbal medicines, including an Artemisia annua hydroethanolic liquid extract sold to suitably qualified practitioners in New Zealand. The company has a comprehensive Pharmacovigilance system in place and employs staff with knowledge in the area of Pharmacovigilance in relation to Herbal Medicines, as well as in the procurement and testing, and quality assurance assessment of more than 250 different types of herbal raw materials.

Phytomed's Technical Director, Phil Rasmussen, was the NZ Chair of the Interim Expert Committee on Complementary and Alternative Medicines established by the Australian and New Zealand governments between 2006 2008, and from 2016 to 2017 was Chair of the Interim Technical Expert Committee, Natural Health Products (Permitted Substances Subcommittee), appointed by the New Zealand Ministry of Health.

About Artemisia annua

Artemisia annua is currently an unscheduled substance in New Zealand, and products containing *Artemisia annua* extract are sold in the form of:

1. Dietary supplements, such as Arthrem and Go Arthi Remedy, promoted for maintaining and supporting joint health and mobility. They can be purchased from pharmacies and online.

2. Traditional Chinese Medicine (TCM) practitioner prescribed formulations, taken by patients following consultations with TCM practitioners.

3. Western Medical Herbalist practitioner prescribed formulations, taken by patients following consultations with naturopaths or medical herbalists who have generally been trained in NZ.

4. Imported mainly Traditional Chinese Medicine based proprietary products, from Asian countries and purchased OTC predominantly by Asian ethnic communities.

We are aware of two small clinical trials involving Artemisia annua for managing symptoms of osteroarthritis [1,2], although the most compelling indication for using this herb, is in the treatment of malaria[3,4]. With drug resistance to malaria being an increasingly serious problem, Artemisia annua is a valuable and cost-effective medicine, used both traditionally and by complementary medicine practitioners, to help improve outcomes in malaria patients.

Medsafe submission

Medsafe proposes to change the rules around the availability of Artemisia annua to make *it prescription only.* Excerpts from the Medsafe submission include:

Medsafe identified a potential risk of harm to the liver and a QT prolonging effect with the use of products containing Artemisia annua extract following reports to the Centre for Adverse Reactions Monitoring (CARM). It was noted from many of the CARM reports that consumers stated they were taking this product for arthritis which is a therapeutic purpose.

There is evidence the risks of products containing Artemisia annua outweigh the benefits making it unfavourable for these products to remain unregulated and available for patient self-selection. In addition, there is another artemisinin derivative, artemether, which is classified as a prescription medicine.

Phytomed disagrees with the Medsafe recommendation. We consider that there is insufficient evidence of Artemisia annua, itself, being potentially hepatotoxic or having an unacceptable risk of adverse events (AEs). We believe that the better explanation for the AEs observed will relate to the manufacturing process and/or the purity of the raw material. This will have wider implications than just Artemisia annua.

It is particularly notable, that the 25 adverse event (AE) reports made (up to 30 September 2018) pertaining to Artemisia annua-containing products sold in New Zealand, all relate to two products (Arthrem and Go Arthi-Remedy). It would appear that no consideration of raw material quality or potential contamination or manufacturing-related factors, has been applied by the author(s) of the Medsafe submission.

International evidence for Hepatotoxicity of Artemisia annua

Scientific Literature on Artemisia annua

More than 1000 scientific papers have been published on this medicinal herb and it is mostly known as the origin of a number of 'new generation' anti-malarial drugs (such as artemisinin). Of these papers, 6 relate to the potentially beneficial effects of Artemisia annua, or its phytochemical constituents such as artemisinin or derivatives on liver function[5 11]. These studies suggest that authenticated Artemisia annua leaf may in fact exhibit beneficial effects on liver conditions such as hepatic steatosis and inflammation.

No papers in relation to harmful effects on the liver, appear to have been published in the peer-reviewed scientific literature as at the time of writing.

Reports to International PV Agencies:

EMA:

While we ourselves have not reviewed the European Medicines Agency (EMA) database for AE reports on Artemisia annua, Phytomed engages a QPPV (Qualified Person in Pharmacovigilance) in the EU, who was contacted in February 2018, to look into whether there had been any AEs in relation to this herb in Europe. Her reply received was as follows:

"I have had a look in the EMA portal and also at the MHRA system and I can't find any information on any AEs associated with Artemisia annua (by that name or any of the other 3 names). There are herbal medicines included in the systems, but the fact

that there are no reports means that for the MHRA that they have not ever had a report for that active ingredient, and for the EMA there have been no reports since EudraVigilance was set up.

The only information I can find on either site for Artemisia is an EMA mongraph for Artemesia absinthium and an SmPC on the MHRA website for Artemisia vulgaris for allergy testing so there is nothing to help I'm afraid."

Given that a wide range of Artemisia annua-containing products are sold in Europe, particularly through TCM practitioners and Chinese medicine clinics, the absence of AE reports to the EMA, is of relevance. Europe has strong regulations in terms of manufacturing standards and Pharmacovigilance requirements.

TGA

A search of the TGA Database of Adverse Event Notifications from 1971 to 2019 for all medicines containing Artemisia annua, found 13 AE reports for a total of 5 different medicines containing this herb. All of these were compound formulations, rather than as an Artemisia annua only containing product.

Artemisia annua is, however, also sold and used as an individual dried herb or extract for extemporaneous compounding by both TCM practitioners as well as western Naturopaths and Medical herbalists, in that country, as is the case here in NZ.

A copy of the TGA AE report is in the appendix of this submission. Of note is that of the 13 reports received during this 48-year period, only 5 relate to a liver condition according to the MedDRA terms used. These are Ascites (1 case), Hepatitis fulminant (1 case), Hepatomegaly (1 case), Jaundice (1 case) and Hepatic function abnormal (1 case).

Australia has a population that is 5 times that of New Zealand but has similar influences from Asian cultures and traditional medicine (including Artemisia annua) usage. As such, it would be expected to have had many more than 5 cases of hepatotoxicity from products containing this herb over this 48 year period, if Artemisia annual itself was likely to be significantly hepatotoxic. The implication is that it is not Artemisia annua that has caused the AEs in New Zealand.

Summary

In Pharmacovigilance, a signal is information that arises from one or multiple sources, which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action.

The signal management process covers all steps from detecting signals to recommending action(s) as follows:

- signal detection
- signal validation

- signal analysis and prioritisation
- signal assessment
- recommendation for action
- exchange of information.

The 14 NZ Case reports of hepatotoxicity are of great concern, as drug or herbal medicine-induced liver damage can have serious outcomes. An initial appraisal of EMA and TGA pharmacovigilance data however, as well as the published scientific literature, fails to reveal a significant association between use of Artemisia annua, and liver toxicity. It would therefore seem doubtful that New Zealand's 14 cases were in fact related to the herb itself, given this herb is taken by large numbers of people on a daily basis in many different countries.

It is more likely that deficiencies in the batch of herb(s) used in the manufacture of the specific two brands of proprietary product sold in NZ only, or other manufacturing related deficits, are responsible for these AE reports.

This is therefore a signal that the specific products for which these AE reports have been received, rather than true unadulterated or uncontaminated Artemisia annua (the herb itself), is likely to be responsible. As such, the assessments and investigations required before being able to recommend an appropriate course of action, should also include a thorough appraisal and testing of the specific products and batches concerned, including their raw materials and the manufacturing processes used.

Whilst reported cases are relatively rare in the published literature, fungal-produced mycotoxins such as aflatoxins and ochratoxins can be associated with liver damage or carcinogenesis [12-13]. The risk of fungal contamination of herbal raw materials is particularly high in low labour-cost countries including many in Africa, where temperatures and humidity are high and where Good Agricultural Practice protocols are not applied during the post-harvest washing or drying, of plant materials.

In recognition of the potential seriousness of such contamination, in the EU there is a requirement for herbal materials included in all licensed herbal medicines to undergo testing to ensure the absence of aflatoxins such as ochratoxins produced by some *Aspergillus spp.* In New Zealand, however, there is no such requirement.

Many raw herbs are imported into New Zealand from low labour cost countries, and we believe that the Artemisia annua used in proprietary products sold in New Zealand during the period in which these CARM reports were received, was grown in Africa. Poor quality raw material is known to be an issue with certain African countries, and it is therefore essential that the absence of potentially hepatotoxic mycotoxins in this raw material or the products concerned, is verified by Medsafe prior to being able to make a fully informed recommendation to the Medicines Classification Committee.

The Need for Better Regulations in NZ:

As per the Medsafe submission, the present classification of Artemisia annua and its extracts in New Zealand, are dietary supplements. As such they have not been classified and are not

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able to make any therapeutic claims. This is materially different to the situation in Australia, where products containing Artemisia annua are complementary medicines, and are listed and notified, on the Australian Register of Therapeutic Goods (ARTG).

Due to many years of successive New Zealand governments shying away from the now urgent need to introduce more appropriate legislation in relation to natural health products/complementary medicines in our country, we are now the only 'developed' country in the world, where there is no requirement for natural health products to be manufactured in a GMP environment. Further, there is no definition of a Herbal Medicine or Complementary Medicine in NZ legislation.

While this situation is likely to have limited Medsafe's apparent jurisdiction in this case, it is the role of a responsible medicines regulator, to be confident it can rule out deficits in the products themselves that may have contributed to this cluster of potentially serious AE events, before advocating to reclassify the herb itself, to a prescription only status.

Finally, Phytomed only supplies Artemisia annua extract to practitioners who have had extensive training in herbal medicine, and we are not aware of pharmacists or doctors having had training in the safe clinical usage of this herb. We would therefore advocate for the establishment of a regulatory system that recognises 'registered medical herbalists', as being able to access a small number of herbal extracts that may have certain safety concerns if sold 'over the counter'. In this context, we support the currently application of the New Zealand Association of Medical Herbalists (NZAMH), for statutory regulation under the Health Practitioners Assurance Act, currently being reviewed by Health Workforce NZ.

We are happy to discuss this as appropriate and expand on any aspect required.

Yours sincerely

Mark Callaghan
CEO

Phil Rasmussen
Technical Director

cc Michael Chamberlain, Board Chair, Phytomed

References:

1. Hunt S et al, An open-label six-month extension study to investigate the safety and efficacy of an extract of Artemisia annua for managing pain, stiffness and functional limitation associated with osteoarthritis of the hip and knee. NZ Med J 2016 Oct 28;129(1444):97-102.

2. Stebbings S et al, A pilot randomized, placebo-controlled clinical trial to investigate the efficacy and safety of an extract of Artemisia annua administered over 12 weeks, for managing pain, stiffness, and functional limitation associated with osteoarthritis of the hip and knee. Clin Rheumatol. 2016 Jul;35(7):1829-36.

3. Munyangi J et al, Artemisia annua and Artemisia afra tea infusions vs artesunate-amodiazuine (ASAQ) in treating Plasmodium falciparum malaria in a large scale, double-blind, randomized clinical trial. Phytomedicine 2019; 57:49-56.

4. Mueller MS et al, Randomised controlled trial of a traditional preparation of Artemisia annua L (Annual Wormwood) in the treatment of malaria. Trans R Soc Trop Med Hyg 2004; 98(5):318-321.

5. Kim KE et al, Artemisia annua Leaf Extract Attenuates Hepatic Steatosis and Inflammation in High Fat Diet Fed Mice. J Med Food. 2016 Mar;19(3):290-9.

6. Liu F et al, Determining the protective effects of Yin Chen Hao Tang against acute liver injury induced by carbon tetrachloride using 16S rRNA gene sequencing and LC/MS-based metabolomics. J Pharm Biomed Anal. 2019 Sep 10;174:567-577.

7. Wan X et al, Dietary enzymatically treated Artemisia annua L. supplementation alleviates liver oxidative injury of broilers reared under high ambient temperature. Int J Biometeorol. 2017 Sep;61(9):1629-1636.

8. Blazquez AG et al Novel artemisinin derivatives with potential usefulness against liver/colon cancer and viral hepatitis.Bioorg Med Chem. 2013 Jul 15;21(14):4432-41.

9. Weifeng T et al Artemisinin inhibits in vitro and in vivo invasion and metastasis of human hepatocellular carcinoma cells. Phytomedicine. 2011 Jan 15;18(2-3):158-62.

10. Li Y et al. Induction of apoptosis of cultured hepatocarcinoma cell by essential oil of Artemisia Annul L]. Sichuan Da Xue Xue Bao Yi Xue Ban. 2004 May;35(3):337 9. Chinese.

11. Chen Q et al, Dihydroartemisinin alleviates bile duct ligation induced liver fibrosis and hepatic stellate cell activation by interfering with the PDGF-βR/ERK signaling pathway. Int Immunopharmacol. 2016 May; 34:250-258

12. Kabak B, Dobson AD. Mycotoxins in spices and herbs-An update. Crit Rev Food Sci Nutr. 2017 Jan 2;57(1):18-34.

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13. Do KH et al Nation-Based Occurrence and Endogenous Biological Reduction of Mycotoxins in Medicinal Herbs and Spices. Toxins (Basel). 2015 Oct 14;7(10):4111 30.

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
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5 February 2020

s 9(2)(a)
Nature's Sunshine Products New Zealand
Email: s 9(2)(a)

Dear s 9(2)(a)

Reclassification of Artemisia annua – objection to the recommendation made by the Medicines Classification Committee at the 63rd meeting on 10 October 2019

Thank you for your email, dated 18 December 2019, following a recommendation by the Medicines Classification Committee (the Committee) that Artemisia annua should be classified as a prescription medicine. The Committee is a ministerial advisory committee established under section 8 of the Medicines Act 1981 to advise the Minister of Health on the classification of medicines as prescription, restricted or pharmacy only medicines.

Following the publication of the Committee's recommendations, there is an opportunity to object to the recommendations. The criteria for valid objections are described in the guidance document (www.medsafe.govt.nz/downloads/How_to_change_medicine_classification.pdf).

The information you have provided on the evidence of safety concerns and benefits is not substantially different to that presented to the Committee. Information about the substance, including those that were received from the public and stakeholders during consultation, were taken into consideration by the Committee.

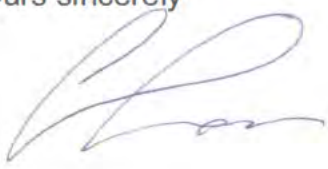
The process that was undertaken is standard for classifying new medicines.
The Committee was presented with a substance that Medsafe regards as a substance intended for a therapeutic purpose and therefore a medicine. The Committee was asked to determine the classification of this substance, to which the Committee recommended that it should only be supplied under the care of an authorised prescriber as a prescription medicine. The Committee was not asked to consider whether the substance was a medicine or not.

Medsafe operates a process where there are consultation opportunities both before and after a meeting of the Committee. As you will be aware, the agenda and items for consideration are made available on the Medsafe website prior to a meeting and Medsafe may also inform parties whom it is aware may have an interest. This is done as a courtesy, however, the expectation is that those interested will proactively engage with the process. I note that you have availed yourself of this process.

To clarify, the decision relates to Artemisia annua extract and this is intended to be clear in the Gazette notice. This will exclude dried, crushed, ground and fresh plant material.

I have reviewed the information that you have provided, and I am satisfied that the grounds on which the objection was raised do not meet the criteria for a valid objection. The Committee's recommendation will not be referred to the next meeting for further consideration.

Yours sincerely



Chris James
Group Manager
Medsafe

NATURE'S SUNSHINE®

Artemisia annua as a prescription medicine

A Response to The Ministry of Health

Nature's Sunshine Products New Zealand

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PO Box 302447, North Harbour, Auckland, 0751
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Website: www.naturessunshine.co.nz

1) Introduction to Nature's Sunshine Products New Zealand

Nature's Sunshine Products New Zealand (NSPNZ) is a company primarily engaged in the importation, manufacturing and marketing of herbal products, vitamin and mineral supplements, personal care and homeopathic products.

Whilst NSPNZ imports much of its products from Nature's Sunshine Products Inc., Utah, USA, we also import product from our Australian counterpart Nature's Sunshine Products of Australia, from Italy and we manufacture some products locally.

The company has been operating in the New Zealand market since 1979. Our products consistently offer the highest quality, and efficacy obtainable and are manufactured under GMP.

NSPNZ remains committed to the principles upon which the company was founded 40 years ago to improve quality of life whilst embracing a business model that provides "Quality, Service, and Integrity." With this in mind our aim is to improve quality of life for all New Zealanders.

Nature's Sunshine Products New Zealand has two products that contain Artemisia annua as part of a proprietary blend of **eight** herbs. These products have been on the market for over 25 years in New Zealand as legal dietary supplements under the Dietary Supplement Regulations 1985, which itself is subject to the Food Act.

The combined sales of these two products are approximately 1,200 units per annum with a customer base of about 2,000 customers. This gives an average use of less than 1 bottle per year per customer. It is not a product used long term by our customers.

To our knowledge, we have never had a complaint or report of an adverse effect following the use of these products.

Nature's Sunshine Artemisia annua products are sold in over 40 countries with no documented product concerns or recalls. Countries include, Austria, Belarus, Canada, China, Colombia, the Czech Republic, Denmark, the Dominican, Republic, Ecuador, El Salvador, Finland, Germany, Guatemala, Honduras, Hong Kong, Iceland, Indonesia, Ireland, Italy, Japan, Kazakhstan, Latvia, Lithuania, Malaysia, Mexico, Moldova, Mongolia, the Netherlands, Norway, Panama, Poland, Russia, Singapore, Slovakia, Slovenia, South Korea, Spain, Sweden, Taiwan, Thailand, Ukraine and the United States.

NSP also market their products through a wholesale model to Australia, Brazil, Chile, Israel, New Zealand, Norway, Peru, Portugal, Spain and the United Kingdom.

2) Background to this response

NSPNZ has very recently been made aware that Medsafe is proposing to classify the herb Artemisia annua as a prescription medicine

We had not been notified of Medsafe's intensions. No doubt Medsafe would say that anyone can make a submission on any proposed classification put to the appropriate committee. NSPNZ sell dietary supplements under the Food Act, not pharmaceutical medicines under the Medicines Act.

NSPNZ management has more than enough to keep itself busy with day-to-day operations without having to bother itself with a regulatory system not related to our products and that appears disinterested in due process.

Medsafe has the emails of a large number of natural health product companies, including ours, so it has no excuse for not notifying us of its intensions.

Medsafe has a legal and moral obligation to consult meaningfully when it intends to take regulatory action that impacts on hitherto lawful activity. It hasn't done so.

There is no legal provision that we are aware of that allows Medsafe to use one Act to prohibit products that are legally sold under another Act.

If Medsafe has determined that Artemisia annua is so dangerous that it should be prohibited, which is what it is doing, then it needs to undertake a robust risk assessment that includes attempts to determine whether any identified risk is related to an individual product or to all products that contain ingredient.

It seems an unusual use of power that Medsafe habitually discounts any adverse reaction report to, say vaccines, on the basis that the adverse effect was "coincidental," but when it comes to a hitherto safe herb it applies a totally different standard in establishing "causality." For example, we are aware of a number of deaths following the use of the vaccine Gardasil that have been deemed "coincidental" by Medsafe with no investigation.

- A toddler died of acute myeloid leukaemia two years after being given Gardasil as a baby by accident. With no formal assessment Medsafe deemed the death coincidental.
- A hitherto healthy young girl died in her sleep of no apparent cause the night after she was given a dose of Gardasil. With no formal assessment Medsafe deemed the death coincidental. The occurance of a sudden death of unknown cause in a healthy teenager is about 1 in 300,000 per year The odds of such a death occuring on a particular day are about 1 in 100 million. Despite such odds of a random occurance, and despite the the odds of 1 in 100 million that a hitherto healthy teenager would die of otherwise unknown causes on the night of a Gardasil vaccination, Medsafe failed to investigate this case further and concluded that Gardasil was not a factor in her death.
- A previously healthy young girl committed suicide two days after a dose of Gardasil. "Nothing to see here; move along," was Medsafe's response.

We are also aware of ACC accepting a case of Limbic Encephalitis following independent assessment of the young girl's medical records. Medsafe deemed the adverse effects as coincidence with no review of the medical records or timeline whatsoever.

NSPNZ is aware of hundreds of legitimate adverse reports to various vaccines that have been deemed "coincidental" and removed from the online database for adverse reaction reports. We are aware that at least four adverse reaction reports recording deaths relating to Gardasil alone that have been reported to CARM/Medsafe and removed from the database that falsely states, "No deaths have been reported."

Medsafe claims that Artemisia annua is dangerous and responsible for adverse reactions causing hepatic failure based on sporadic reports similar to many of those relating to vaccine use. NSPNZ notes that these adverse reaction reports relate almost exclusively to a single product, and that many of the reports followed Medsafe widely publicising safety concerns and requests for further reports of adverse events. It is worth noting that Medsafe itself points out that adverse reaction reports such as those requested and

following publicity can bias their interpretation. No evidence has been provided demonstrating that Artemisia annua causes such adverse events.

As discussed above NSPNZ notes that when adverse reactions are reported regarding pharmaceutical medicines, Medsafe rarely considers those reports to be causal or worthy of regulatory action, especially regarding vaccines. In this case, despite Medsafe itself acknowledging several millennia of hitherto safe use, Medsafe has determined that Artemisia annua is so unsafe that it should be prohibited by stealth.

3) Defining the problem – Medsafe's perspective

Medsafe's proposal, states that according to the International non-proprietary name (INN) of the medicine "Artemisia annua is not classified as a medicine currently." Medsafe says, "it is sold in products as a natural health supplement which are unregulated products."

NSPNZ takes exception to Medsafe's claim that these products are unregulated. They are not unregulated. To make such a claim is not only mischievous it is simply untrue. NSPNZ markets two products containing Artemisia annua under the Dietary Supplement Regulations that, as stated earlier, are regulations under the Food Act. Therefore they are regulated, as are all foods.

Furthermore, it seems somewhat ironic that Medsafe states that they are unregulated when Medsafe itself administers the Dietary Supplement Regulations!

What Medsafe fails to recognise, perhaps deliberately so, is that its raison d'être is to regulate toxic pharmaceutical medicines which are [quite rightly] regulated far more stringently than foods and dietary supplements which have a very long history of safe use and are regulated under quite different legislation.

Not being regulated under the Medicines Act does not make Dietary Supplements unregulated as claimed.

Medsafe also proposes what it terms "Risk mitigating strategies." Medsafe describes the strategies [sic] thus;

> "The classification of *Artemisia annua* as a prescription medicine would remove these products for self-selection and ensure adequate safety monitoring, including effects on the liver, can be implemented. The involvement of healthcare professionals is crucial for this to work and also to ensure patients receive adequate counselling."

This is disingenuous at best. Medsafe knows full well that in classifying Artemisia annua as a prescription medicine it would be attempting to prohibit anyone from accessing the herb for any use as no company would be able to get a product approved for marketing to anyone. As discussed below, that may be a fallacious argument as foods are exempt from the Medicines Act and dietary supplements are foods under the Food Act.

Perhaps surreptitiously, Medsafe's proposal would attempt to prevent access to the herb through qualified medical herbalists. Thus claiming that 'patients' would be able to get product from healthcare professionals so that they get adequate counseling might sound plausible, but it is a sham. The one professional that could provide such advice would be barred from doing so.

Medsafe should know full well that its "Risk mitigating strategies" is simply not going to happen. It won't happen for three reasons. Firstly, the hurdles required are so restrictive and expensive that no company would undertake such an exercise for a generic ingredient. Secondly, Medsafe would never allow the herb to be approved for use as an approved medicine, and thirdly, doctors are schooled in prescribing hazardous pharmaceutical medicines, and are not trained in the use of safe herbal products.

In its discussion Medsafe acknowledges that *Artemisia annua* (Sweet wormwood, Sweet Annie, Qing hao) has been used in traditional Chinese medicine for more than 2000 years, but does not include that in any formal risk assessment.

See Fig 1, for an infographic showing relative risks in New Zealand. Note how dangerous pharmaceutical medicines are and the extremely small risks associated with natural health products. We have consulted with herbal associations around the world who are not aware of any significant issues with Artemisia annua per se. There may be an issue with the product that has raised a red flag, but there is certainly not an issue with our products.

If this is the summation of Medsafe's Modus Operandi; that Medsafe proposes to ban something "...due to its perceived safety profile" then NSPNZ asks, on what legal or objective basis does it operate under?

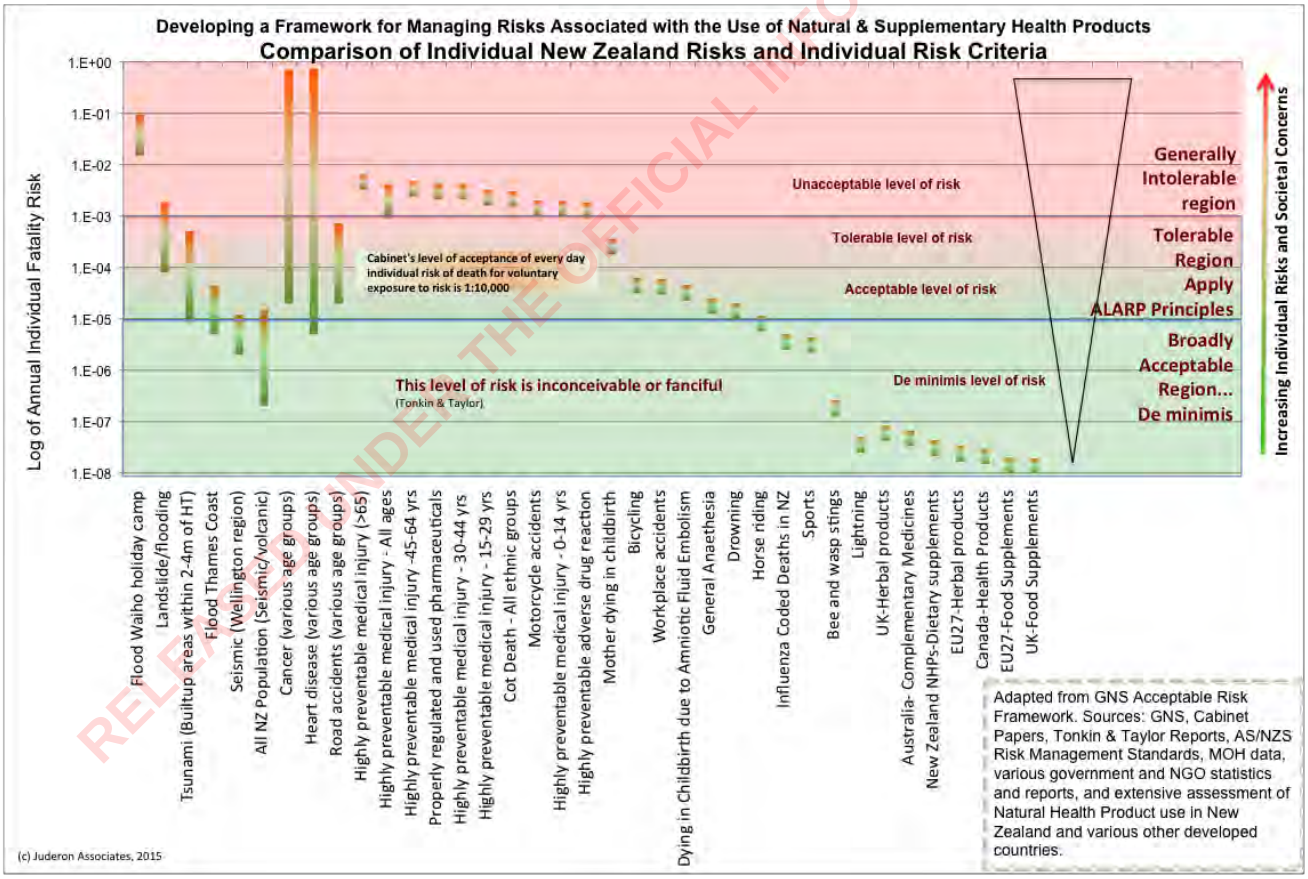

Figure 1: Relative Risks of common activities and substances

4) Artemisia vs Artemisinin – There is a difference!

Medsafe refers to derivatives of Artemisia annua being used in antimalarial drugs without appreciating that derivatives are not the herb itself. They are not even extracts…. they are derivatives. In chemistry, a derivative is a compound that is derived from a similar compound by a chemical reaction. We can't speak for other companies' products, but our products are not made from derivatives of Artemisia annua; they contain Artemisia annua itself.

In early 2009 the World Health Organization (WHO) announced the discovery of malaria parasites along the Thai-Cambodia border that were proving resistant to commonly used derivatives of artemisinin called artesunate and anthemeter.

In its WHO position statement: Effectiveness of non-pharmaceutical forms of Artemisia annua L. against malaria, in June 2012, WHO does not recommend the use of *A. annua* plant material, in any form, including tea, for the treatment or the prevention of malaria.

They note an emerging resistance to artemisinin which is partly due to the complexity of the parasite and the unstoppable nature of its ability to evolve. But it is also the direct result of greed, for which there is no drug or vaccine. That said, the problem is with a derivative of Artemisia annua, not Artemisia annua itself.

5) Defining the problem – An industry perspective

NSPNZ does not dispute that adverse reactions associated with the liver have been reported in conjunction with Artemisia Annua. We know that because Medsafe has publicised that widely, although NSPNZ notes that, despite Medsafe's rhetoric, Medsafe appears not to consider these of significance as the summarised reports have not been made available for public purview on their public SMARS database.

Not only has Medsafe not made an objective case for prohibiting Artemisia annua, but also it is perhaps acting illegally by using the Medicines Act to prohibit a food product. If Artemisia annua is a food ingredient, which it is when sold as a dietary supplement, then if there are any risk issues they should legally be dealt with under the Food Act. Medsafe has no authority to recall product under the Food Act, nor to prohibit foods under the Food Act. It is worth noting here also that Medsafe used the 'Privileged statement' section in the Medicines Act when making a public statement about a food. Is that even legal?

Medsafe has made a number of attempts over the past 35 years to regulate Dietary Supplements as a sub-set of medicines and failed each time. There is a great deal of lack of trust within the wider natural health product industry regarding Medsafe as a fair and reasonable regulator of that industry. Cases like this only increase that lack of confidence.

6) Perceived risk

We accept that Medsafe has created a perceived risk regarding Artemisia anuua and adverse effects on hepatic function. However, it has failed to establish causality, and has attempted to tar an entire industry based on perceived problems with a single product.

Modern Good Regulatory Practice does not prohibit access to hitherto safe products by stealth. Modern Good Regulatory Practice does not prohibit access to hitherto safe products as a result of an inflammatory response to a cluster of adverse events. It is worth noting here that Medsafe first became aware of this perceived risk nearly two years ago and other than trying to destroy the company marketing the "problem" product, it has made no regulatory attempt to have the product recalled. One can only assume that this is because Medsafe has been unable to convince the person with the

power to undertake such a recall, the administrator of the Food Act, that there is a genuine risk to consumers.

7) NSPNZ is an affected party - but not consulted

As noted, NSPNZ was made aware by a third party of Medsafe's perhaps illegal intensions very recently.

- We sell two products containing Artemisia annua.
- We will be adversely affected.
- We are an affected party.
- Our customers will be denied access hitherto safe product.
- We were not consulted as required by law.
- We object in the strongest terms to Medsafe's actions.

8) Wider industry is an affected party – but not consulted

We don't speak on behalf of the wider industry, however we do note that Medsafe failed to use the email list it gathered over several years of consultations during its failed attempts to align the regulation of Natural Health Products more closely with pharmaceutical medicines.

This underhand proposal by Medsafe to use the Medicines Act to prohibit a food ingredient, Artemisia annua, and therefore deny customers the right of access to what are legally regulated food products appears to be immoral if not illegal. That and the lack of consultation will only further alienate and antagonise industry due to distrust of Medsafe's modus operandi.

We understand that the industry group NPNZ became aware of the proposal and chose not to make a formal response. If that is true then it highlights their lack of concern for process and smaller businesses such as ours. Not all Natural Health Product companies belong to NPNZ.

9) When is there a need to regulate?

The information provided by Medsafe shows that in those cases reported to have had an adverse event, the symptoms resolved following withdraw of the product. That does not establish causality, as liver problems are often idiosyncratic and often resolve spontaneously.

If there has been no serious harm, especially irreparable harm, then prohibition is not a rational risk management response. Education and labeling are. If the problem is related to a single [new] product then education and labeling should be targeted to that product, assuming that causality has been established.

Based on several thousand years of use, and no deaths or irreparable harm, and given that consumption of Artemisia annua is a voluntary activity, then there are no objective grounds for prohibiting the herb.

10) What is the actual risk?

Given the several thousand years of use and the marked lack of evidence of harm from consumption of Artemisia annua, as opposed to pharmaceutical derivatives, it seems, on the balance of probabilities, that the problems that Medsafe has used to justify its proposal is either a red herring (as Medsafe would say if this was a vaccine, a "coincidence") or it relates to a new product perhaps utilising a new extraction method.

Given our over 25 years of sales of Artemisia annua with no adverse effects reported, and given the several thousand years of hitherto safe use, on the balance of probabilities, causality has not been established. This is a product with an extremely safe record.

11) Single brand, not Artemisia annua herb

As mentioned above, if there is a risk issue, it relates to a single brand's product, not the herb Artemisia annua per se.

12) Biased assessment of risk compared to pharmaceutical products

As discussed above, Medsafe clearly operates to pre-determined mindsets. One turns a blind eye to pharmaceutical medicines, and particularly vaccines, where deaths with odds of several millions to one are deemed to be 'coincidence.' In the case of Artemisia annua, Medsafe has done nothing to recall a product of concern, but then finds a hitherto safe herb guilty without sound evidence and proposes prohibiting it by stealth. This highlights a biased regulator not fit to regulate products it has no interest in.

13) Definition of a medicine

The Medicines Act defines a medicine;

Meaning of medicine, new medicine, prescription medicine, and restricted medicine

(1) In this Act, unless the context otherwise requires, *medicine*—
(a) means any substance or article that—
(i) is manufactured, imported, sold, or supplied wholly or principally for administering to 1 or more human beings for a therapeutic purpose; and
(ii) achieves, or is likely to achieve, its principal intended action in or on the human body by pharmacological, immunological, or metabolic means; and
(b) includes any substance or article—
(i) that is manufactured, imported, sold, or supplied wholly or principally for use as a therapeutically active ingredient in the preparation of any substance or article that falls within paragraph (a); or
(ii) of a kind or belonging to a class that is declared by regulations to be a medicine for the purposes of this Act; but
(c) does not include—
(i) a medical device; or
(ii) any food within the meaning of section 2 of the Food Act 1981; or
…
(vi) any substance or article of a kind or belonging to a class that is declared by regulations not to be a medicine for the purposes of this Act.

NSPNZ's Artemisis annua products are not manufactured, imported, sold, or supplied wholly or principally for administering to 1 or more human beings for a therapeutic purpose;

NSPNZ's Artemisis annua products are not medicines, as defined in the Medicines Act, as they are classified as foods.

Therefore, despite Medsafe's stated intent to make products containing Artemisis annua prescription only medicines, NSPNZ has difficulty understanding Medsafe's legal basis for doing so.

14) Jurisdiction

As mentioned previously, Medsafe does not administer the Food Act so therefore it has no legal basis to prohibit a dietary supplement.

As mentioned previously, foods are excluded from the gambit of the definition of a medicine.

To be able to classify a substance as a prescription medicine it must first declare it to be a medicine; Medsafe has not done that.

We cannot see that Medsafe has any legal basis to undertake what it is proposing.

Therefore, our understanding is that what Medsafe is proposing would be ultra vires. In other words it would be an error of law as Medsafe has no legal authority to do what it is proposing.

15) Further evidence that Medsafe is not a fit for purpose regulator of Natural Health Products

The above comments provide further evidence that Medsafe is not a fit for purpose regulator of products and ingredients that it has no interest in, nor does it understand.

It would be in Medsafe's best interests going forward to abandon its proposal if it wants to avoid further damage to its already tarnished reputation.

16) Summary

As noted, NSPNZ has marketed two Artemisis annua products for a number of decades with no safety concerns. Artemisis annua products have been sold and consumed safely worldwide for thousands of years. NSP products have been sold and consumed safely in over 40 countries with no safety concerns.

We have only recently been made aware of Medsafe's attempt to effectively prohibit the sale of Artemisis annua based on apparent problems of concern with a single new product manufactured using novel extraction methods.

Medsafe has not established causality, and has applied a double standard compared to the way it manages adverse events following vaccine use.

Medsafe's proposal further enhances the views of many within the Natural Health Product industry that Medsafe has a biased view of Natural Health Products and is not a fit and proper regulator for this industry.

Medsafe's proposal is not objective, is not a rational response, and will be challenged if progressed.

Document 10

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Wellington
New Zealand 6011

DDI s 9(2)(a)
E rene@promisia.com

PROMISIA.COM

17 December 2019

Medsafe
s 9(2)(g)(ii)

Medsafe
Ministry of Health
WELLINGTON

Objection to the recommendation to reclassify Artemisia Annua as a prescription medicine

Dear s 9(2)(g)(ii)

This letter is to record the formal objection of Promisia Integrative Limited to the recommendation of the Medicines Classification Committee to the Minister of Health to have the herb Artemisia Annua declared a prescription medicine.

Artemisia Annua is a herb that has been used by the Chinese for over 2,000 years. It is not a medicine but a food. It can be found in many products and it is added by manufacturers globally for any number of reasons.

In New Zealand, Promisia developed Arthrem as a dietary supplement for joint support and mobility. Arthrem's key ingredient is Artemisia Annua, along with grape seed oil, in a soft shell capsule. Arthrem has only ever been advertised as a dietary supplement in New Zealand and all forms of advertising were approved by TAPS.

Medsafe has taken action due to reported adverse reactions collected by the Centre for Adverse Reaction Monitoring (CARM). The accuracy of these reported adverse reactions is questionable as both CARM and Medsafe have refused to provide details of each reported reaction and refuse to enter into any discussion on the accuracy of these reports. Their reaction can only raise the suspicion that their claims cannot be sustained under close examination and thus a cone of silence has descended.

Some claims made by Medsafe, such that Artemisia Annua caused hepatic cirrhosis, were made without any extensive investigation undertaken to support the claim. Despite this lack of evidence, Medsafe has made this statement in a public forum as if it were a fact. This can only be described as regulatory overreach and bullying of producers of products containing Artemisia Annua. We cannot not find any international evidence of hepatic cirrhosis caused by Artemisia Annua.

Even if all of the adverse reactions, particularly those reporting a liver related adverse reaction, were attributable to Artemisia Annua it would still represent fewer than 0.007% of users. This level of reaction is considered to be very rare by World Health Organisation standards.

The facts just do not support Medsafe's actions against Arthrem and the ingredient Artemisia Annua. CARM has confirmed that its system of collection is over 50 years old and does not provide complete information. The views generated from its data, by its own admission, are only suspicions. Medsafe have taken these suspicions as facts.

We also wish to highlight what can only be described as a deliberate misstatement by Medsafe in relation to this company's product known as Arthrem and Australia. Arthrem entered the Australian market in January 2018. Prior to being sold in Australia it received complimentary medicine status in Australia, a status that is not available in NZ.

The Medsafe review suggests Arthrem was removed from the Australian market due to adverse reactions. This is incorrect. Arthrem has not had a single adverse reaction in Australia in the 18 months that it was on the market. To suggest that it did is untrue.

Medsafe submitted a paper to the TGA suggesting that Arthrem was not safe. The evidence supplied was inaccurate and not supported by any investigation that would generate anything other than suspicions.

s 9(2)(b)(ii) [redacted]

Apart from the distortions propagated by Medsafe there is also the question of why or how Medsafe believes that it has jurisdiction over the natural world. The Medicines Classification Committee was established to regulate medicines, not natural products. Where will it end?

At the recommendation of Medsafe the Committee has deemed that Artemisia Annua has a therapeutic purpose and that it should be classified as a medicine. Will Medsafe ask the Committee to classify any other herb that may be used for a therapeutic purpose? The use of plants for therapeutic purpose has been part of the human experience well before any pharmaceutical products were developed. This action by Medsafe is overreach by a regulator, is unnecessary, and sets a very bad precedent for any other natural product.

We also question why Medsafe has taken this action. Is it an attempt to snuff out the significant natural health sector? Is it being undertaken at the behest of the pharmaceutical industry?

We understand the need for safety of the public and the need to prevent unscrupulous operators selling products without proven efficacy. The use of the catch all 'public safety' to regulate plants,

which are really foods, is unreasonable, removes choice and reinforces the status quo and vested interests of pharmaceutical manufacturers.

The reality is that nothing is 100% safe. We have been contacted by a person who was allergic to their mother's milk from birth. There is no doubt that breast milk is therapeutic but does a low percentage of adverse reactions, some undoubtedly serious and possibly life threatening, justify making it a prescription medicine? We appreciate that the committee is not considering breast milk but the principle is the same. Why are some herbs treated differently from others? Why has Medsafe not taken action against St John's Wort which is known to have serious adverse reactions in some people and may counteract licensed medicines in others?

We note that there are many licensed medicines that have resulted in far more serious adverse reactions, including death, but they seem to be of little interest to Medsafe. The view appears to be that if a product is a licensed medicine then deaths are 'unfortunate' and must be caused by misuse by the user rather than an inherent problem with the product. Please see for the drug related causes of death in Australia in 2016.
https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2016~Main%20Features~Drug%20Induced%20Deaths%20in%20Australia~6

We also refer you to a New Zealand Herald article 'How dangerous is your painkiller?
https://www.nzherald.co.nz/lifestyle/news/article.cfm?c_id=6&objectid=12001230 Dated 24 February 2018.

The lack of action by Medsafe to deaths by licensed medicines and the damage and injury caused by pain killers is in stark contrast to its strenuous efforts to ban a naturally occurring herb, a food that has been used successfully by many millions and is now the only alternative treatment to chloroquine for malaria. It can only be described as rank hypocrisy.

The 'evidence' gleaned from the minimal CARM reports of adverse reactions in New Zealand to Artemisia Annua indicates that dosage could be an issue in the level of adverse reaction. Promisia has attempted to engage with Medsafe on many occasions to discuss options like lowering the dose of Artemisia Annua in Arthrem. Medsafe has refused to even consider options that we have attempted to discuss with its staff.

In closing we repeat our opposition to the Committee's decision to recommend to the Minister of Health that Artemisia Annua, in all its forms, be classified as a prescription medicine. The reason for this opposition are:

- It is based on suspect information concerning reported adverse reactions
- The substance is a natural product that has been used for at least 2,000 years as a natural health remedy without any concerns
- It is over reaching by an industry regulator
- It is an abuse of the Medicines Act
- It sets a dangerous precedent to impose what is effectively a ban on all natural products

Accordingly, we request that you reverse your decision of 10 October 2019 to recommend to the Minister of Health that Artemisia Annua be classified as a prescription medicine.

Yours faithfully

s 9(2)(a)

s 9(2)(a)

Web: www.arthrem.co.nz

Cc Right Hon Winston Peters, Deputy Prime Minister
Hon David Clark, Minister of Health

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

133 Molesworth Street
PO Box 5013
Wellington 6140
New Zealand
T +64 4 496 2000

5 February 2020

s 9(2)(a) [redacted]

Dear s 9(2)(a) [redacted]

Reclassification of Artemisia annua – objection to the recommendation made by the Medicines Classification Committee at the 63rd meeting on 10 October 2019

Thank you for your email, dated 17 December 2019, following a recommendation by the Medicines Classification Committee (the Committee) that Artemisia annua should be classified as a prescription medicine. The Committee is a ministerial advisory committee established under section 8 of the Medicines Act 1981 to advise the Minister of Health on the classification of medicines as prescription, restricted or pharmacy only medicines.

Following the publication of the Committee's recommendations, there is an opportunity to object to the recommendations. The criteria for valid objections are described in the guidance document (www.medsafe.govt.nz/downloads/How_to_change_medicine_classification.pdf).

The information you have provided on the evidence of safety concerns and benefits is not substantially different to that presented to the Committee. Information about the substance, including those that were received from the public and stakeholders during consultation, were taken into consideration by the Committee.

The process that was undertaken is standard for classifying new medicines.
The Committee was presented with a substance that Medsafe regards as a substance intended for a therapeutic purpose and therefore a medicine. The Committee was asked to determine the classification of this substance, to which the Committee recommended that it should only be supplied under the care of an authorised prescriber as a prescription medicine. The Committee was not asked to consider whether the substance was a medicine or not.

To clarify, the decision relates to Artemisia annua extract and this is intended to be clear in the Gazette notice. This will exclude dried, crushed, ground and fresh plant material.

I have reviewed the information that you have provided, and I am satisfied that the grounds on which the objection was raised do not meet the criteria for a valid objection.

The Committee's recommendation will not be referred to the next meeting for further consideration.

Yours sincerely

Chris James
Group Manager
Medsafe

Document 12

Sent by: s 9(2)(g)(ii)
21/01/2020 02:42 pm

To: Andi Shirtcliffe/MOH@MOH, s 9(2)(a) "Les Toop" <les.toop@otago.ac.nz>
cc: s 9(2)(a)
bcc:

Subject: MCC63 - clarification about Artemisia annua extract

Dear members of the Medicines Classification Committee

We are currently reviewing objections to the recommendation from the 63rd meeting that Artemisia annua should be classified as a prescription medicine (agenda item 7.2e).

For avoidance of doubt, Medsafe wishes to clarify with the Committee that the recommendation relates to "Artemisia annua extract", and not the plant itself.

The paper put before the Committee discussed how products containing Artemisia annua extract are sold as natural dietary supplements for maintaining and supporting joint health and mobility. Medsafe identified a potential risk of harm to the liver and a QT prolonging effect with the use of products containing Artemisia annua extract following reports to the CARM. The paper can be found here: https://medsafe.govt.nz/profs/class/Agendas/Agen63/MCC63_72e_artemisiaannua.pdf

During deliberations, the Committee had discussed how the terminology used in the classification wording would require consideration because "Artemisia" includes many different species. The minutes can be found here: https://medsafe.govt.nz/profs/class/Minutes/2016-2020/mccMin10Oct2019.htm

Medsafe has reviewed potential terminology and recommends describing what we are scheduling as "Artemisia annua extract". Describing it as an extract would exclude the plant material (and so would exclude dried, crushed and fresh plant material). Artemisia annua has been used in traditional Chinese medicine for centuries, and it is understood that these remedies contain plant material, rather than the extract.

In the interests of meeting deadlines, can you please respond to this email as soon as possible (latest 24 Jan).

With many thanks

s 9(2)(g)(ii)
s 9(2)(g)(ii) | s 9(2)(g)(ii) | Medsafe | Ministry of Health s 9(2)(g)(ii)
s 9(2)(g)(ii) |

MEDSAFE
New Zealand Medicines and Medical Devices Safety Authority

Secretary
Medicines Classification Committee
Ministry of Health
c/o committees@health.govt.nz

2 March 2020

Subject: Artemisa annua – Scheduling considerations

Dear Medicines Classification Secretary,

We are writing to you in regards to the proposed reclassification of *Artemisia annua* as a Schedule 4 (Prescription level medicine).

Complementary Medicines Australia (CMA) represents is committed to a vital and sustainable complementary medicines sector, and represents stakeholders including manufacturers, raw material suppliers, distributors, consultants, retailers and allied health professionals. Over the last few decades the Australian complementary medicines sector has evolved into a world class industry supporting domestic skilled jobs, research, manufacturing and exports. CMA has members based in New Zealand, as well as Australian businesses who import into NZ.

CMA supports the appropriate and safe classification and use of herbal medicines used in complementary medicines / dietary supplements.

We are concerned at the scheduling of *Artermisia annua* as a herb. The associated issues could be considered idiosyncratic and those that occurred were largely related to a specific extract/preparation type of the herb – a supercritical carbon dioxide extract, suspended in an oil matrix. This does not equate to a predictable reaction related to the herb generally. We propose that in this scenario, there are likely to be more suitable regulatory alternatives that are more in accordance with international approaches.

As a comparison, Australia currently includes 62 medicines (as at 2 March 2020) on the Australian Register of Therapeutic Goods[1], and the Database of Adverse Event Notifications contains an extremely limited number of liver adverse events related to products containing this herb. The search conducted from the full available search range of 1 Jan 1971 to 2 Dec 2019, showing reactions to all products with "Artemisia" is attached at the end of this letter.

Scheduling, at least in Australia, relates to a predictable toxicity, rather than a rare or idiosyncratic reaction. We are concerned that the NZ course of action sets a precedent in respect of international Scheduling actions that is not commensurate with the case for action.

The proposed Scheduling removes an otherwise frequently used (but infrequently problematic) herb from the population. The key word here is 'herb' and not 'extract', 'preparation', or 'product'. *Artemisia annua* as a herb

[1] https://www.ebs.tga.gov.au/

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is not only used in relation to joint or arthritic conditions, but is used for fever, inflammation, parasitic conditions, and as a part of Traditional Chinese Medicine formulations.

Comparable regulatory actions taken within Australia for idiosyncratic liver reactions: The TGA took regulatory actions[2] in relation to Arthrem due to the NZ reactions (although similar reactions were not identified in Australia), and subsequently required related to advice for consumers and health care professionals to be aware of potential adverse reactions for this product:

- updating all medicine labels with the following caution – 'in rare circumstances *Artemisia annua* may be associated with liver harm'
- providing an update to all pharmacies that stock Arthrem capsules
- updating their website to note the risk of liver harm and the symptoms to look out for, as well as instruction that, in the event of these symptoms being observed, to stop taking Arthrem capsules and consult a doctor
- amending messaging on labels, point-of-sale material and so on to stress that the product must be taken strictly as directed.

This action is consistent with required label advisories[3] for other herbs which have been associated with idiosyncratic liver reactions:

> ACTAEA RACEMOSA (Black cohosh) - 'Warning: In very rare cases - black cohosh has been associated with liver failure. If you are experiencing yellowing of the skin or whites of the eyes - dark urine - nausea - vomiting - unusual tiredness - weakness - stomach or abdominal pain - and/or loss of appetite - you should stop using this product and see your doctor.'
>
> CHELIDONIUM MAJUS (Greater celandine) – 'WARNING - Greater Celandine may harm the liver in some people. Use only under the supervision of a healthcare professional'.
>
> FALLOPIA MULTIFLORA - 'Warning: Fallopia multiflora may harm the liver in some people. Use under the supervision of a healthcare professional.'
>
> KHAYA SENEGALENSIS - 'Not for prolonged use. May harm liver';
>
> LARREA TRIDENTATA (Chaparral) - WARNING: Chaparral may harm the liver in some people - use only under supervision of a health care professional'.
>
> PIPER METHYSTICUM (Kava) - May harm the liver

We support in-principle the following types of measures:

- Label warning statements to allow the educated and informed use of a herbal preparation, such as those outlined above.

- Regulatory restriction, where justified, of a specific type of herbal preparation that is associated with a pattern of non-minor adverse reactions. In this case, it appears that the reported reactions are in relation to a particular super-critical carbon dioxide extract suspended in an oil matrix.

[2] https://www.tga.gov.au/alert/arthrem-capsules
[3] Therapeutic Goods (Permissible Ingredients) Determination (No. 1) 2020 https://www.legislation.gov.au/Details/F2020L00150

- Regulatory comparison: Australia no longer permits the sale of Kava extracts as a medicinal herb in solvents other than water, due to a pattern of reactions specifically associated with non-water extracts *(When for oral use, the medicine may only contain dried whole or peeled root or rhizome or aqueous dispersions or aqueous extracts of whole or peeled root or rhizome.)*

- GMP appropriate for herbal, traditional, and complementary medicines, and other appropriate regulatory controls at the manufacturing level.

Thank you for your consideration of the above and please do not hesitate to contact us in relation to the above.

Yours sincerely,

s 9(2)(a)
[redacted]
Complementary Medicines Australia
s 9(2)(a)
[redacted]

Australian Government
Department of Health
Therapeutic Goods Administration

Database of Adverse Event Notifications - medicines

Medicine summary

You searched for the following **7 medicines** between **01/01/1971 – 02/12/2019**:

- Artemisia Compound (Andrographis paniculata; Artemisia annua; Citrus X paradisi; Echinacea purpurea; Fennel Oil; Glabridin (of Glycyrrhiza glabra))
- Arthrem capsules - AUST L 287611 (Artemisia annua)
- Detox 1-2-3 (Artemisia absinthium; Berberis vulgaris; Thyme Oil; Thymus vulgaris)
- Nature's Own Digestive Cleanser Tablets Rapid Clense 10 Day Detox Plan (Artemisia annua; Berberis vulgaris; Matricaria chamomilla; Mentha X piperita; Olea europaea)
- Quick Cleanse - Ultimate Internal 15-Day Detox Program (Angelica polymorpha; Artemisia annua; Berberis vulgaris; Bupleurum falcatum; Carica papaya; Choline bitartrate; Citrus bioflavonoids extract; Clove Powder; Cynara scolymus; Foeniculum vulgare; Gentiana lutea; Guar Gum; Hydrastis canadensis; Inositol; Inula britannica; Inulin; Juglans nigra; magnesium chloride hexahydrate; Mentha X piperita; Pectin; Plantago afra; Rhamnus purshianus; Rheum palmatum; Salvia officinalis; Schizandra chinensis; Taraxacum officinale; Taurine; Uncaria tomentosa; Zingiber officinale)
- Quick Cleanse The Intestinal Broom 15 Day Detox Program (Angelica polymorpha; Artemisia annua; Berberis vulgaris; Bupleurum falcatum; Carica papaya; Choline bitartrate; Citrus bioflavonoids extract; Clove Powder; Cynara scolymus; Foeniculum vulgare; Gentiana lutea; Guar Gum; Hydrastis canadensis; Inositol; Inula britannica; Inulin; Juglans nigra; magnesium chloride hexahydrate; Mentha X piperita; Pectin; Plantago afra; Rhamnus purshianus; Rheum palmatum; Salvia officinalis; Schizandra chinensis; Taraxacum officinale; Taurine; Uncaria tomentosa; Zingiber officinale)
- Quick Cleanse Ultimate Internal 7-Day Detox Program (Angelica polymorpha; Artemisia annua; Berberis vulgaris; Bupleurum falcatum; Carica papaya; Choline bitartrate; Citrus bioflavonoids extract; Clove Powder; Cynara scolymus; Foeniculum vulgare; Gentiana lutea; Guar Gum; Hydrastis canadensis; Inositol; Inula britannica; Inulin; Juglans nigra; magnesium chloride hexahydrate; Mentha X piperita; Pectin; Plantago afra; Rhamnus purshianus; Rheum palmatum; Salvia officinalis; Schizandra chinensis; Taraxacum officinale; Taurine; Uncaria tomentosa; Zingiber officinale)

Important information

The TGA uses adverse event reports to identify when a safety issue may be present. An adverse event report does not mean that the medicine is the cause of the adverse event. If you are experiencing an adverse event, or think you may be experiencing one, please seek advice from a health professional as soon as possible. The TGA strongly advises people taking prescription medicines not to change their medication regime without prior consultation with a health professional.

About the Database of Adverse Event Notifications (DAEN) - medicines

- The DAEN - medicines contains information from reports of adverse events that the TGA has received in relation to medicines including vaccines used in Australia.
- The DAEN - medicines does not contain all known safety information about a particular medicine. Please do not make an assessment about the safety of a medicine based on the information in the DAEN - medicines.

The TGA medicine safety monitoring program

More information about the DAEN - medicines and the TGA medicines safety monitoring program is available at:

- About the DAEN - medicines <http://www.tga.gov.au/safety/daen-about.htm>
- Medicines safety <http://www.tga.gov.au/safety/information-medicines.htm>

You are encouraged to report an adverse event suspected of being related to a medicine used in Australia. Reports of adverse events in relation to medicines and vaccines can be reported using the 'blue card' reporting form, by phone and online <http://www.tga.gov.au/safety/problem.htm>.

Other useful sources of information on Australian medicines

More information about a medicine is available from the Product Information (PI) <http://www.tga.gov.au/hp/information-medicines-pi.htm> and Consumer Medicine Information (CMI) <http://www.tga.gov.au/consumers/information-medicines-cmi.htm> leaflet or the labelling of the medicine. Australian Public Assessment Report for Prescription Medicines (AusPARs) <http://www.tga.gov.au/industry/pm-auspar.htm> for some prescription medicines, are also available from the TGA website. <http://www.tga.gov.au>
Your health professional can also provide help and assistance on how to use medicines.
Information on medicines used in Australia is available from NPS MedicineWise <http://www.nps.org.au/>.

About the release of this information

While reasonable care is taken to ensure that the information is an accurate record of the adverse events reported to the TGA, the TGA does not guarantee or warrant the accuracy, reliability, completeness or currency of the information or its usefulness in achieving any purpose.
To the fullest extent permitted by law, including but not limited to section 61A of the Therapeutic Goods Act 1989, the TGA will not be liable for any loss, damage, cost or expense incurred in or arising by reason of any person relying on this information.

Results

Number of reports (cases): 15

(Multiple adverse events have been reported for some patients)

Number of cases with a single suspected medicine: 13

(The TGA thinks there is a possibility that the medicine caused the adverse event)

Number of cases where death was a reported outcome: 0

(These reports of death may or may not have been a result of taking a medicine)

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Gastrointestinal disorders	Diarrhoea	4	4	0
Gastrointestinal disorders	Vomiting	3	3	0
Gastrointestinal disorders	Abdominal pain	2	2	0
Nervous system disorders	Seizure	2	2	0
Gastrointestinal disorders	Nausea	2	2	0
Skin and subcutaneous tissue disorders	Urticaria	2	2	0
Gastrointestinal disorders	Gastrooesophageal reflux disease	2	2	0
Nervous system disorders	Headache	2	2	0
Gastrointestinal disorders	Ascites	1	1	0
Renal and urinary disorders	Urinary incontinence	1	1	0
Respiratory, thoracic and mediastinal disorders	Dyspnoea	1	1	0
Eye disorders	Eye oedema	1	1	0
Hepatobiliary disorders	Hepatitis fulminant	1	1	0
Hepatobiliary disorders	Hepatomegaly	1	1	0
Nervous system disorders	Neurological symptom	1	1	0
Hepatobiliary disorders	Hepatic steatosis	1	1	0
Skin and subcutaneous tissue disorders	Pruritus	1	0	0
Nervous system disorders	Lethargy	1	1	0
Psychiatric disorders	Restlessness	1	1	0
Nervous system disorders	Tongue biting	1	1	0
Skin and subcutaneous tissue disorders	Rash erythematous	1	0	0
Hepatobiliary disorders	Hepatic function abnormal	1	0	0
Skin and subcutaneous tissue disorders	Rash pruritic	1	1	0
Skin and subcutaneous tissue disorders	Rash macular	1	1	0

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
Eye disorders	Eye swelling	1	0	0
General disorders and administration site conditions	Pain	1	1	0
Skin and subcutaneous tissue disorders	Rash	1	1	0
Gastrointestinal disorders	Colitis	1	1	0
Hepatobiliary disorders	Jaundice	1	1	0

Footnotes

[i] A description of what, in general terms, was affected by the adverse event, as described by the Medical Dictionary for Regulatory Activities MedDRA (for example 'cardiac disorders')

[ii] A description of the adverse event as defined by MedDRA; these adverse events are grouped by system organ class. You can use the MedlinePlus medical dictionary <http://www.nlm.nih.gov/medlineplus/mplusdictionary.html> to look up terms.

[iii] The number of cases for which each type of adverse event was reported

[iv] Results show where a medicine is the only medicine suspected to be related to the adverse event

[v] These reports of death may or may not have been the result of taking a medicine

MINISTRY OF HEALTH
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31 July 2020

s 9(2)(a)
National Committee of the New Zealand Association of Medical Herbalists (NZAMH)

Email: s 9(2)(a)

Dear s 9(2)(a)

Reclassification of *Artemisia annua* extract

Thank you for your letter dated 8 July 2020 to Ms Andi Shirtcliffe and Mr Chris James, in response to their letter of 23 June 2020. I note your concerns regarding several aspects of that response, and I am responding as your letter covers a range of Ministry-wide activities.

You request a redefinition of the classification of *Artemisia annua* extract by the Medicines Classification Committee. I am advised that Phil Rasmussen, President of the New Zealand Association of Medical Herbalists (NZAMH), met with Medsafe in June and there was agreement that Mr Rasmussen would collate further evidence for a submission to the Medicines Classification Committee to review the classification decision.

The Ministry of Health is working on a replacement for the Medicines Act 1981 and on options to regulate natural health products. As you are aware, the Ministry has engaged with you and the sector on the development of natural health products regulation and will continue to do so in the future. We will be looking to advise the Government post-election of the importance of proceeding with this work and proposed engagement with the sector and public more widely on a new natural health products regulatory regime. Accordingly, at this time, we do not have a timeframe for that engagement to share.

I acknowledge the NZAMH desire for the profession to be regulated under the Health Practitioners Competence Assurance Act 2003 (HPCA Act). The primary criteria in determining the suitability of a profession to be regulated under the Act is based upon risk of harm in order to ensure public safety, and the application for Western Herbal Medicine as with all applications will be considered, in accordance with these criteria. It is important to note that any request for regulation under the Act is considered necessary only where no alternate regulatory methods are appropriate or suitable to mitigate the risk posed to the public by the profession. Alternate methods typically include voluntary or self-regulation and may be complemented by product regulation. Dual regulation of products and the profession that utilises said products, is not necessarily required or warranted in many cases in order to manage risk.

Health Workforce cannot provide a time frame for a determination to be made on the application submitted for Western Herbal Medicine to be regulated under the HPCA Act. Whilst an application has been submitted, this in no way guarantees that regulation of Western Herbal Medicine will be successful, rather it will be considered in due course in line with a number of other applications, which are prioritised by date of submission.

With regard to the details of the new Classification Committee under the draft Therapeutic Products Bill, the draft Bill that you have reviewed clearly states that it is enabling legislation. That is, it provides high level permissions rather than providing details which will come later in the Regulations. One such example is the expert advisory committee requirements, where the Act will enable expert committees to be set up but does not provide any details on their area of expertise or membership. Work to define these committees will be undertaken once the Bill has been finalised and the details of any natural health product regulatory scheme are known.

In relation to your concerns about public safety, as you are aware, on receipt of reports of adverse reactions in relation to Arthrem, Medsafe arranged for the Director-General of Health to issue warnings in relation to the issue, conducted testing to detect any adulterant substances that may have been present and raised the matter with the company concerned. Medsafe laid charges against Promisia in relation to the selling of Arthrem as a medicine because it was Medsafe's opinion that the product was a medicine. Medsafe also took a precautionary measure and proposed to the Medicines Classification Committee that access to the claimed active substance in question should be restricted. These were all actions taken, to protect the health and safety of consumers. Our understanding is that the volume of Arthrem sold decreased substantially as a result of our early actions and has remained so.

I would like to be clear about Medsafe's regulatory role and the testing it performs. Medsafe considers each significant issue reported and can, depending on the circumstances of a particular case, submit a product for testing. In some cases, there is no need to conduct testing because, for instance, an adverse reaction may be recognised for the type of product in question or because some other feature of the product may allow regulatory action to be initiated. Medsafe takes actions consistent with ensuring public health and safety and while some testing may be warranted in some circumstances, if information / evidence about a product allows regulatory steps to be taken without comprehensive testing, this course of action will be taken.

You may be interested to know that Medsafe has conducted comprehensive testing on natural products that have been reported to result in adverse reactions, unexpected therapeutic activity or have been suspected of being adulterated. Adulterants detected have included steroids, weight loss prescription medicines (including sibutramine) and PDE5 inhibitor substances (to treat erectile dysfunction). Many of these cases have been prosecuted.

Thank you again for writing. I hope this information is useful, and I wish you well.

Yours sincerely

Clare Perry
Acting Deputy Director-General
Health System Improvement and Innovation

Memo

MINISTRY OF HEALTH
MANATŪ HAUORA

Date:	20 January 2019
To:	Minister's delegate, Chris James, Group Manager, Medsafe
Copy to:	Andi Shirtcliffe, Chair of the Medicines Classification Committee
From:	s 9(2)(g)(ii) Secretary, Medicines Classification Committee
Subject:	**Objections to recommendations made at the 63rd meeting of the Medicines Classification Committee held on 10 October 2019**
For your:	Action and Decision

Background
The closing date for intentions to object to a recommendation made at the 63rd meeting of the Medicines Classification Committee (the Committee), together with a statement of the grounds on which the objection will be made, was 18 December 2019.

Summary
This memo seeks a decision on whether these objections are valid, and if so, to defer implementation of the recommendation pending the Committee's consideration of the objections at the next meeting.

The criteria for valid objections are:
- the Committee did not consider the safety issues correctly (for example a new safety concern may have been identified since the start of consultation)
- the Committee did not consider the benefits
- there was a breach of appropriate process.

A total of six objections were received regarding three recommendations. One objection was received for codeine (another was withdrawn after they realised their medication did not contain codeine), one objection was received for octodrine, and four objections were received for Artemisia annua.

It is recommended that you agree that none of the objections received met valid objection criteria and that you agree to support all the classification recommendations from the 63rd meeting of the Medicines Classification Committee. Following your agreement, letters to the objectors informing them of your decision will be drafted for your signature.

Action

The following objections were received:

1. **Agenda item 5.3a reclassification of codeine**

Out of scope

[redacted]

2. **Agenda item 7.2c octodrine (synonyms include 1,5 – dimethylhexylamine, DMHA and 2,-amino-6-methylheptane)**

Out of scope

[redacted]

3. **Agenda item 7.2e Artemisia annua**

Four objections have been received to one of the Committee's recommendations regarding agenda item 7.2e that Artemisia annua should be classified as a prescription medicine. None of the objectors have identified on which grounds (safety, benefits or process) they have raised their objections. The objections have been summarised below:

1. Promisia Ltd, a supplements company selling a product containing Artemisia annua, has raised an objection and has described reasons that include: that the reported adverse reactions are suspect, that the substance is a natural product with an established use, that the recommendation is an overreach by Medsafe and that it sets a precedent to impose a ban on natural products.

2. s 9(2)(a) a barrister, has raised an objection on behalf of New Zealand Health Trust, a trust that has been active in lobbying for natural health products. Reasons for the objection include: that the Committee has acted outside its jurisdiction, that consultation was not wide enough, and that there is no evidence of liver safety issues arising from the use of Artemisia annua.

3. s 9(2)(a) Director of Herbal Ltd, has raised an objection and has described reasons that include: that Artemisia annua has established Chinese research and that the alcohol industry uses Artemisia in manufacture of gin and vermouth.

4. Nature's Sunshine Products New Zealand, a supplements company, has raised an objection and has described reasons that include: lack of consultation, that their products are dietary supplements and not medicines, and there is no scientific evidence regarding harm related to the herb Artemisia annua.

The reasons described in the objections does not appear to be new information and does not meet valid objection criteria. The consultation process was standard and while consultation is expected to reach most affected stakeholders, it is not possible to reach all interested parties. Objectors have also contested the safety risks identified by Medsafe and the potential for Artemisia annua to cause harm, especially to the liver. Medsafe's position on the safety of products containing Artemisia annua extract and the risk of harm to the liver remains unchanged.

A legal review of the legal aspects raised in the objection by s 9(2)(a) on behalf of the New Zealand Health Trust has not highlighted any issues.

There appears to be a common misunderstanding raised in the objections that the Committee had made a recommendation on whether Artemisia annua is a dietary supplement or medicine. It is recommended that it should be made clear that the Committee was presented with a substance that Medsafe regards as a medicine and the Committee was asked to determine its classification. The Committee was not asked to decide whether the substance was a medicine or not. Further clarification from the Committee has been sought and the Committee has confirmed that the recommendation related to Artemisia annua extract, rather than the plant itself. It is recommended that Medsafe provide clarification on these points in the letters to the objectors and the minutes.

It is recommended that the objections raised by Promisia Ltd, s 9(2)(a) on behalf of New Zealand Health Trust, s 9(2)(a) and Nature's Sunshine Products do not meet objection criteria and are able to be resolved by Medsafe. Letters informing these objectors of your decision will be drafted for your signature.

Recommendations

It is recommended that you:

1.	**agree**	Out of scope
2.	**agree**	Out of scope

3.	**agree**	that the response made by Promisia Ltd regarding agenda 7.2e Artemisia annua, is not a valid objection and can be resolved by Medsafe.	Yes / No
4.	**agree**	that the response made by s 9(2)(a) on behalf of the New Zealand Health Trust regarding agenda 7.2e Artemisia annua, is not a valid objection and can be resolved by Medsafe.	Yes / No
5.	**agree**	that the response made by s 9(2)(a) regarding agenda 7.2e Artemisia annua, is not a valid objection and can be resolved by Medsafe.	Yes / No
6.	**agree**	that the response made by Nature's Sunshine Products New Zealand regarding agenda 7.2e Artemisia annua, is not a valid objection and can be resolved by Medsafe.	Yes / No
7.	**support**	all the classification recommendations made at the 63rd meeting of the Medicines Classification Committee.	Yes / No

Couple of things:
① Is HL advice written - can I have a copy?
② Reactive Comms required + I need a heads up before these letters go out.
Thanks

Signature s 9(2)(g)(ii) Date: 22/01/20

s 9(2)(g)(ii)
Secretary, Medicines Classification Committee

Signature _____ Date:

Chris James
Group Manager, Medsafe

Attachments

Attachment 1: Objection raised by s 9(2)(a)
Attachment 2: Objection raised by
Attachment 3: Objections raised by Promisia Ltd, s 9(2)(a) on behalf of the New Zealand Health Trust, s 9(2)(a) and Nature's Sunshine Products