



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

CMEC 68
COMPLEMENTARY
MEDICINES
EVALUATION
COMMITTEE

Extracted Ratified Minutes

Sixty-eighth Meeting

15 August 2008

Abbreviations

ADRAC	Adverse Drug Reactions Advisory Committee
ANZTPA	Australian and New Zealand Therapeutic Products Agency
ARGCM	Australian Regulatory Guidelines for Complementary Medicines
ARTG	Australian Register of Therapeutic Goods
AVS	Aortic valve stenosis
BP British	Pharmacopoeia
CAD	Coronary artery disease
CMEC Co	plementary Medicines Evaluation Committee
DGL Deglycyrrh	izinized liquorice
FSANZ	Food Standards Australia New Zealand
GZ Glycyrrhizin	ic acid
GMP	Good Manufacturing Practice
LDL Low-density	lipoprotein
MEC	Medicines Evaluation Committee
NPS	National Prescribing Service
OCM	Office of Complementary Medicines
PPRC	Pharmacopoeia of the People's Republic of China

TCM Traditional	Chinese Medicine
TGA Therapeutic	Goods Administration
TGO Therapeutic	Goods Order
UWS	University of Western Sydney

The Complementary Medicines Evaluation Committee (CMEC) held its sixty-eighth meeting in the Hilton Hotel, Melbourne Airport, Melbourne from 9.30 a.m. to 4.35 p.m. on Friday 15th August 2008.

Members of CMEC present

Emeritus Professor Tony Smith (Chair)
Dr Lesley Braun
Dr Gary Deed
Dr Vicki Kotsirilos
Ms Karen Martin
Professor Stephen Myers
Dr Kevin Ryan
Professor Bill Webster
Dr Hans Wohlmuth

Present from the Therapeutic Goods Administration (TGA)

Dr Ruth Lopert (Acting Principal Medical Advisor)
Professor David Briggs
Ms Michelle McLaughlin
Dr Bogdan Sikorski
Ms Diane Wilkinson
Ms Nicola Powell

1 PROCEDURAL MATTERS

1.1 Opening of Meeting

The Chair opened the meeting at 9:30 am, welcoming CMEC Members and TGA staff.

1.2 Apologies

Professor Alan Bensoussan

Dr Richard Oppenheim

1.3 Conflict of Interest

Members discussed conflict of interest requirements and submitted conflict of interest declarations, specific to agenda items for this meeting, to the Chair.

2 CONFIRMATION OF MINUTES OF CMEC 67 (20 JUNE 2008)

Members accepted the Minutes of the sixty-seventh meeting of CMEC as an accurate record of proceedings, subject to minor amendment.

Members made the following recommendation:

Recommendation 68.1

CMEC confirms that the draft Minutes of its previous meeting (CMEC 67, 20 June 2008), as amended, are a true and accurate record of that meeting.

3 GUIDELINES ON LEVELS AND KINDS OF EVIDENCE TO SUPPORT CLAIMS FOR THERAPEUTIC GOODS (GUIDELINES)

CMEC did not consider any matters under this agenda item.

4 ACTION ARISING FROM PREVIOUS MEETINGS

CMEC discussed three items under this agenda item.

5 EVALUATION OF NEW SUBSTANCES

CMEC discussed one item under this agenda item.

6 SAFETY OR EFFICACY REVIEWS

CMEC did not consider any matters under this agenda item.

7 HERBAL SAFETY REVIEW PROJECT/ PLANT PART PROJECT

7.1 Review of *Glycyrrhiza glabra* and *Glycyrrhiza uralensis*

Background

A TGA Officer introduced this item, advising Members that a potential safety concern had been identified with respect to the use of all plant parts of *Glycyrrhiza glabra* and *Glycyrrhiza uralensis* in Listed medicines. Specifically, the concern was expressed that excessive doses of liquorice preparations should be avoided in cases of hypertension, cardiac insufficiency, kidney insufficiency and oedema.

CMEC noted that the two currently Listable species of *Glycyrrhiza* were considered together in the review, as these two herbal species have a similar composition [particularly with respect to the component of toxicological concern, glycyrrhizic acid (glycyrrhizin)], the

herbs have been traditionally used interchangeably, and the herbs often appear under the same entries for 'liquorice' in the various pharmacopoeias.

The TGA Officer advised that there is currently no restriction on any plant part, or component, for these herbs and that liquorice is used widely in herbal medicine, mostly in combination with other herbs. '*Radix Glycyrrhizae*' is used in Traditional Chinese Medicine (TCM) to reinforce the function of the spleen and replenish 'qi', remove heat and counteract toxicity, dispel phlegm and relieve cough, alleviate spasmodic pain and to moderate drug actions. The plant parts used in the majority of liquorice preparations are the root, rhizome and/or stolon. A relatively small number of products include preparations of the stem of *G. uralensis*.

As at July 2008, there were 153 Listed Medicines in the Australian Register of Therapeutic Goods (ARTG) containing preparations of *G. glabra* as an ingredient; and 503 medicines containing preparations of *G. uralensis*. Therefore, the CMEC noted that any proposed regulatory action would have the potential to impact on a large number of products.

The Officer advised that the review identified safety concerns for the glycyrrhizinic acid (GZ) component of *G. glabra* and *G. uralensis*, and that it is well established that ingestion of liquorice may lead to sodium and water retention, hypokalaemia, hypertension, and suppression of aldosterone and renin levels. These effects are attributable to the GZ component. Reportedly, the dried extracts of the roots of *Glycyrrhiza* species may contain 4-25% glycyrrhizin, though recently published analyses gave a range of up to 8%. Information on the GZ content is available in the ARTG for only a small number of the Listed medicines containing *G. glabra* or *G. uralensis*.

CMEC Members noted that the available evidence indicates that, for most individuals, adverse effects do not arise from repeated exposure of up to 100 mg/day of GZ. However, as some individuals appear to be more sensitive to the effects of GZ, including those with certain health conditions or those taking various medications, and as additional intake from dietary sources is also possible, imposition of a maximum daily dose limit for GZ in Listed medicines containing liquorice may not assure full protection against potential adverse reactions.

A TGA Officer suggested that Members may wish to consider whether a label advisory statement is appropriate to alert individuals with medical conditions such as hypertension, or those taking specific medication, to the potential adverse effects of liquorice. Also, as it is possible that a number of Listed medicines may contain GZ at a level that will not be biologically significant, it may be appropriate to consider a cut-off level for this component below which a label advisory statement should not apply. Further, the Officer suggested that Members may wish to comment on whether the use of *G. uralensis* and *G. glabra* as ingredients in Listed medicines should be limited to certain plant parts.

CMEC was asked to advise if any regulatory controls were required to assure the safety in use of preparations of *G. glabra* and *G. uralensis*, or the component glycyrrhizinic acid, in Listed medicines.

Discussion

Awareness of the hypertensive effects of liquorice

Members considered that the hypertensive effects of *G. glabra* and *G. uralensis* were well described in the clinical literature and clinicians should be aware of these effects. It was expected that clinicians would not usually prescribe the herb to anyone with hypertension. In addition to this, the blood pressure of a patient taking liquorice would usually be monitored.

However, Members acknowledged that, while healthcare practitioners are generally aware of the potential adverse effects of liquorice in patients with hypertension, this was not something that the general public would be expected to be aware of. Members agreed that there is a paucity of public information about the potential effects of liquorice, considering its widespread use, and that any recommendation made by the Committee should address this.

Consumption of liquorice and at risk groups

Members discussed the extensive use of liquorice in herbal medicine, particularly in relation to the herb's use as a flavouring agent (in relatively small doses) to mask the bitterness of other herbs. It was noted that liquorice is a common ingredient in products, such as cough remedies, to improve the palatability of these medicines, and is also commonly used by elderly people as a laxative.

In relation to 'at risk' groups, a Member commented that over 50% of people over 60 years of age have hypertension, and this group of people are more likely to consume liquorice. Another Member expressed concern in relation to those people with diabetes, as even a slight increase in blood pressure can increase the risk of renal impairment.

Label statement

Given that many people may self-prescribe liquorice, Members considered that a label advisory statement for medicines including preparations of liquorice was justified, and discussion ensued in relation to the appropriate wording for such a statement.

Members agreed that the simple statement '*Contains liquorice*' was not sufficiently descriptive and had the potential to encourage misuse of the product as a laxative, without alerting the consumer to the potential adverse effects.

A Member commented that a number of liquorice food products voluntarily display a label advisory statement, and provided an example of a liquorice tea bag that displayed the following statement:

'Not recommended for people with a history of high blood pressure, those who are pregnant or those with kidney disease'.

Members considered this statement informative and concise.

There was some discussion regarding whether or not an advisory statement should appear on all liquorice products, or just those containing a higher quantity of liquorice or GZ. A Member added that duration of use should be taken into account as well as dose. Overall, Members agreed that an appropriate concentration cut-off or an identified safe duration of use

would be difficult to determine, and that it would be more practical to apply the label statement to all products containing liquorice.

A TGA Officer brought to the Committee's attention that currently, medicine labels are required to use the Australian Approved Names of *G. glabra* and *G. uralensis*, which the general consumer may not recognise as liquorice. Members agreed it was appropriate for the advisory statement to include the common name 'liquorice' to clearly indicate the presence of the herb.

Plant part

In relation to whether the use of herbal preparations of *G. glabra* and *G. uralensis* should be restricted to specific plant parts, one Member stated that the *British Pharmacopoeia 2007* (BP) monograph describes use of the root and stolons, whilst the *Pharmacopoeia of the People's Republic of China 2005* (PPRC) describes use of the dried root and rhizome. The Member clarified that stolons are types of stems (runners), and that rhizomes are underground stems. Therefore, the Member considered that the plant parts '*roots, rhizomes and stolons*' would incorporate the traditionally used plant parts, as documented in the BP and PPRC. Members agreed with this approach.

Deglycyrrhizinated liquorice

Members briefly discussed issues in relation to preparations of 'deglycyrrhizinated' liquorice (DGL); including whether preparations of DGL would meet the definition of a 'herbal substance' as included in Schedule 2 of the *Therapeutic Goods Regulations 1990* (the Regulations).

Members queried the benefit of removing GZ from liquorice, noting that there were reportedly less adverse effects associated with DGL, and the material was apparently useful in the treatment of gastrointestinal ulcerations.

Whilst Members considered this matter outside of the current scope of discussion, they agreed that it was a relevant issue, and requested more information and consideration at a future meeting.

Conclusion

CMEC recommended that a label advisory statement for medicines containing herbal preparations of *Glycyrrhiza glabra* and *Glycyrrhiza uralensis* was appropriate.

Recommendation 68.3

CMEC recommends to the TGA that herbal preparations of the root, rhizome and/or stolons of *Glycyrrhiza glabra* and *Glycyrrhiza uralensis* are suitable as ingredients in Listed therapeutic products, subject to labelling advising of the potential for adverse effects in at-risk individuals, with wording to the effect:

"Contains liquorice. Not suitable for people with a history of high blood pressure, or who are pregnant, or have kidney disease".

7.2 Review of *Daemonorops draco* (fruit resin)

Background

A TGA Officer introduced this item, advising Members that a potential safety concern had been identified with respect to the use of the resin of *Daemonorops draco* (*D. draco*), and the subsequent potential for allergic reactions and overdose.

Preparations of *D. draco* are currently permitted ingredients in Listed medicines with no regulatory restrictions. There are three Listed medicines in the ARTG containing *D. draco* as an ingredient; two are topical preparations, one is an oral preparation. Two list the plant part used as 'fruit resin', while one lists 'sap resin' as the plant part.

Members noted that the fruit resin obtained from *D.draco* is commonly known as 'dragon's blood'. The same name also refers to resins obtained from eighteen different plant species, from four plant families. The three plants most commonly referred to in the literature as 'dragon's blood' are *Daemonorops draco*, *Dracaena draco*, and *Croton lechleri*. Of these plants, only *Daemonorops draco* and *Dracaena draco* are permitted for use in Listed medicines.

Medicinal references to *D. draco* almost exclusively pertain to the resin of the fruit (Dragon's blood). Use of other plant parts (fronds and stalks) are only mentioned by two sources and it is unclear if these references specifically refer to *D.s draco*. Commercial application pertains solely to the fruit resin.

The Officer advised that *D. draco* is traditionally used as an astringent, administered orally for diarrhoea and topically for wounds. The PPRC includes indications for "injury with blood stasis and pain" and "unremitting bleeding due to trauma". TCM literature contraindicates the uses of the herb in the absence of "blood stasis".

The current review revealed one text which quoted a case of allergy to the substance 'dragon's blood' but it could not be directly attributable to *D. draco*. No significant potential for toxicity or allergenicity associated with use of the substance was identified in the review.

Members noted that the OCM had recently received, from the University of Western Sydney (UWS), the results of a literature review of the TCM Journal Database system. This report revealed five cases of allergy, reported in Chinese-language journals, resulting from external and internal use of the herb. The case reports primarily involved skin symptoms consistent with urticaria; however, angioedema of the hands and face is also mentioned in the literature. No reports of anaphylaxis were found and no cases of overdose were identified, although it was noted that one of the allergic reactions was at a daily dose of 3 g per day of the decocted herbal substance, which is above the 1-2 g daily dose recommended by the PPRC. The Officer pointed out that a dose of the powdered fruit resin of *D. draco* exceeding 2 g is unlikely to occur in Listed medicines due to the resinous nature of the substance.

The Officer proposed that the information available to date does not appear sufficient to suggest that the incidence or severity of allergy to the herb is greater than those idiosyncratic reactions which may occur with any medicinal substance.

CMEC noted that the Regulations do not impose a restriction on any plant parts of *D. draco* and Members were asked to consider if it was appropriate to restrict the use of *D. draco* to the fruit resin, which is the plant part supported by a history of traditional use.

Discussion

Allergic reactions

Members discussed the fact that resinous substances, such as *D. draco*, have a high allergic potential, and noted that the UWS report included some cases of allergic skin reactions to the herb. Nevertheless, Members considered that these allergic reactions did not appear to differ greatly from a number of other herbal substances in terms of an allergenic response.

Members noted that whilst there did not appear to be any definitive scientific evidence to support the herb's safety, *D. draco* has been used traditionally for a long time with no substantial reports of adverse reactions. Further, there are no official reports indicating any safety concerns.

Traditional use

Members noted that the herb is included in the PPRC and is commonly used in TCM. A Member added that the herb is contraindicated in the absence of blood stasis in TCM and expressed a general concern that terms such as 'blood stasis' are not generally understood by those operating outside the TCM paradigm.

Plant part

Members agreed that the use of the herb in Listed medicine should be restricted to preparations of the plant part on which traditional use is based.

Conclusion

Members agreed that as long as the traditional plant part 'fruit resin' is used, *Daemonorops draco* remains suitable for inclusion as an ingredient in Listed Medicines, subject to input from an absent CMEC Member with expertise in TCM.

Recommendation 68.4

CMEC recommends to the TGA that only herbal preparations of the fruit resin of *Daemonorops draco* are suitable for use as an ingredient in Listed medicines.

8 REGISTRATION APPLICATIONS

CMEC did not consider any matters under this agenda item.

9 VARIATION TO A REGISTERED PRODUCT

CMEC did not consider any matters under this agenda item.

10 MATTERS REFERRED FROM WITHIN TGA

10.1 Adverse Drug Reactions Advisory Committee (ADRAC) Meeting 308

Complementary medicine issues

CMEC discussed adverse drug reaction reports involving complementary medicines and related issues of interest from ADRAC Meeting 308.

Case reports

Members discussed, in detail, case reports of interest from ADRAC Meeting 308.

10.2

Members discussed one matter under this agenda item.

10.3 Medicinal interchange ability of BP/Ph. Eur. monograph herbs

CMEC deferred this item to CMEC 69.

10.4 Label advisory statements for products containing phytosterols

Background

A TGA Officer introduced this item, advising members that a phytosterol-containing ingredient was determined by the Medicines Evaluation Committee (MEC) to be suitable for use as an ingredient in Listed medicines, subject to the following conditions:

- Including the following advisory statement on product labels:

“There is no benefit, in lowering cholesterol, of having more than 3 g/day of phytosterols from all sources. Consult a healthcare professional if you usually eat margarine or other products which claim cholesterol- lowering benefits”.
- Inclusion of a label advisory statement indicating that use is not recommended in children under 5 years, or in pregnant or breastfeeding women.

The Committee further noted that two substances containing phytosterols are already permitted for use as ingredients in Listed medicines: ‘Phytosterol complex - conifer’ (a mixture of phytosterols derived from tall oil), and ‘Phytosteryl macadamiate’ (a mixture of phytosterol esters), which is permitted for topical use as an excipient.

Whilst there have been no concerns raised with respect to the safety of phytosterols or phytosterol esters as part of a normal diet, Members noted that human exposure to phytosterols has increased in Australia due to the dietary intake of functional foods combined with the intake of therapeutic products containing phytosterol ingredients (promoted to reduce cholesterol uptake).

At present these medicines do not require any label advisory statements and Members were asked to consider, in light of the MEC's considerations of the phytosterol-containing ingredient, whether label advisory statements are appropriate for all Listed medicines containing phytosterols as ingredients.

The Officer advised Members of the Australian Heart Foundation recommendation that a daily intake of phytosterols in excess of 2-3g/day does not offer an additional benefit in terms of reducing low-density lipoprotein (LDL) cholesterol. Furthermore, apart from individuals with known metabolic disorders resulting in impaired ability to eliminate dietary phytosterols, and for whom supplementation with phytosterols has been contraindicated on health grounds, there are no therapeutic grounds for limiting absorption of cholesterol during pregnancy, breastfeeding or in young children.

Members were also asked to note the paper by Helske *et al.* (2008), which reports that phytosterols were found to accumulate in diseased aortic valves, suggesting that a relatively high intake of phytosterols may be a health risk in certain individuals, even when serum phytosterols levels are normal.

Discussion

Consideration of MEC Recommendation

Overall, Members concurred with the MEC's Recommendations, considering that they reflected the current available evidence, and agreeing that CMEC and MEC's positions should be consistent.

Dose limit of 3 g/day

Members noted that there was no reported benefit from taking more than 2-3 g of phytosterols/day, and while the Helske *et al.* (2008) paper provides some evidence that phytosterols accumulate in the aortic valves (which could be a concern for a sub-group of the population), it was not possible to establish that consuming more than 3 g/day was detrimental. Members therefore agreed that as there was no benefit from taking more than 3 g/day, limiting intake to this amount could decrease any potential safety concerns.

This led to discussion in relation to whether there should be a cut-off applied to the daily dose of phytosterols in Listed products, with Members noting that the MEC had not recommended a cut-off dose for such use. The issue of collateral dietary intake was raised, with Members questioning the amount of phytosterol consumed in a typical diet, and whether the phytosterol quantity, or advisory statements, are required on food labels. Members discussed that the usual intake of a phytosterol fortified food, such as margarine, would be 3-4 teaspoons a day, delivering approximately 300-400 mg/day of phytosterols. Members noted that the phytosterol content would be disclosed on food labels for marketing reasons, and that as the inclusion of phytosterols significantly increases the cost of the foods, it would be highly unlikely that the amount would not be declared on the food label.

In all, Members agreed that consumers would be taking these products specifically for the phytosterol content and should know how much they are taking. It was therefore considered appropriate that a label advisory statement, rather than a cut-off figure, should be sufficient to control the excessive intake of phytosterols.

Wording of advisory statement

Members agreed that an advisory statement indicating that there is no benefit from taking more than 3 g of phytosterols/day is appropriate, but that the wording of the statement should be considered further.

In particular, Members considered that inclusion of the words ‘in lowering cholesterol’ in the statement (‘There is no benefit, in lowering cholesterol, of having more than 3 g/day of phytosterols from all sources’) was confusing, and preferred the omission of these words.

In addition, in relation to the statement ‘*Consult a healthcare professional if you usually eat margarine or other products which claim cholesterol lowering benefits*’, Members did not consider it necessary for the statement to include a recommendation to see a healthcare professional.

Members also discussed the issue of phytosterol consumption during pregnancy and lactation, or by children, noting that it was theoretically not advisable to lower cholesterol levels in these groups. Members considered that therapeutic goods containing phytosterols would generally not be recommended for children, so the risk of children being exposed to these substances was low. Hence, it was not necessary for the label advisory statement to include wording in relation to children. However, Members considered that including a statement indicating that these products were not suitable for pregnant or lactating women would be beneficial, as there was a potential for these women to be unnecessarily exposed to these products.

Conclusion

CMEC agreed with the MEC recommendation that advisory statements, as amended, were appropriate for Listed Medicines containing phytosterols.

Recommendation 68.5

CMEC recommends to the TGA that Listed medicines containing phytosterols require a label advisory statement with words to the effect:

“There is no benefit from taking more than 3 g/day of phytosterols from all sources”

“Not suitable for pregnant or lactating women”.

11 FOR INFORMATION

11.1 Phytosterol safety concerns

Background

A TGA Officer introduced this item concurrently with Item 10.4, advising Members that phytosterol-containing foods are being promoted as an alternative to prescription medicines for reduction of serum cholesterol levels, an apparent risk factor for coronary artery disease (CAD).

The Committee noted that the presence of phytosterols in a range of functional foods has been progressively increasing and is likely to continue to do so, with Food Standards Authority Australia New Zealand (FSANZ) advising that the range of products containing these ingredients is likely to expand. Overall, exposure to phytosterols from both functional foods and therapeutic products has been increasing over the last decade and is likely to increase even more. This may potentially present hitherto unknown safety concerns.

The Officer drew Members attention to a paper by Helske *et al.* (2008) entitled '*Accumulation of cholesterol precursors and plant sterols in human stenotic valves*'. In this paper, the authors indicate that one of the main features of aortic valve stenosis (AVS) is accumulation of the LDL cholesterol in valve leaflets. Lowering the amount of circulating LDL, and thus also the amount of the LDL potentially entering the valve leaflets, could be beneficial to AVS patients. However, in addition to cholesterol, LDL particles contain non-cholesterol sterols, including phytosterols. Phytosterols compete with cholesterol for intestinal absorption and have been used alone, or with statins, to reduce serum cholesterol concentrations. Importantly, it has been noted that while statins may reduce cholesterol synthesis, this enhances the absorption of plant sterols from the intestine, thus elevating the serum concentration. Despite the fact that beneficial effects of phytosterols on absorption of cholesterol are generally accepted, data supporting their protective effects against cardiovascular diseases are still equivocal.

Furthermore, evidence reviewed by Helske *et al.* (2008) suggests that phytosterols are absorbed into valve leaflets and are thus able to participate in the atherosclerotic process in the general population, which includes individuals with apparently normal absorption of plant sterols. Indeed, in some clinical studies, elevated circulating levels of phytosterols have been associated with the occurrence, severity and positive family history of CAD.

The Officer further advised that results presented by Helske *et al.* (2008) demonstrate that plant sterols do accumulate in aortic valves, even in individuals with normal serum phytosterol levels, and that increased levels of circulating plant sterols result in elevated levels of plant sterols in aortic valves. These findings suggest that increased intake of phytosterols may increase the risk of developing, or accelerating, progression of AVS.

Discussion

Members discussed this item concurrently with Item 10.4.

Members noted that the Helske *et al.* (2008) study demonstrated the presence of plant phytosterols in aortic valves. Members also considered the possible contribution of phytosterols to aortic valve stenosis, particularly in those who have a congenital deficiency in transportation of phytosterols. In general, Members agreed that no casual link could be made at this stage.

OUTCOME

CMEC noted the article by Helske *et al.* (2008) titled '*Accumulation of cholesterol precursors and plant sterols in human stenotic valves*'.

11.2 Regulatory reforms for complementary medicines – verbal presentation

Background

A TGA Officer presented this item, reminding Members that on 16 July 2007, the New Zealand Government announced that it would not be proceeding with the establishment of a joint agency, with Australia, to regulate therapeutic products. Considerable effort, including extensive stakeholder consultation, has been invested in the development of the proposed joint regulatory scheme and refining existing regulatory arrangements. To ensure that this valuable work is not lost, the Australian Government is proposing to move forward, in an Australian-only context, on proposed enhancements that have already undergone extensive consultation.

Members noted that the proposed reforms aim to reduce regulatory burden, increase transparency and access to information, and enhance post-market monitoring. They also include legislative amendments that had been deferred pending establishment of the joint scheme. The Officer outlined reforms under each category, as listed below.

Reducing regulatory burden

The following initiatives are to be implemented in this category:

- the adoption of the *European Pharmacopoeia* (Ph. Eur.) and the *United States Pharmacopoeia-National Formulary* (USP) as default standards, in addition to the BP;
- the implementation of revised Therapeutic Goods Orders (TGOs) related to child resistant packaging, general requirements for tablets and capsules, labelling requirements and grouped medicines;
- legislation to be amended to incorporate the new definition of a complementary medicine;
- public consultation to be undertaken in relation to a range of export reforms;
- the legislation to be amended to provide details of the requirements relating to infringement notices;
- public consultation to be undertaken in relation to licensing and fee changes in relation to Good Manufacturing Process (GMP);
- amendment of the *Therapeutic Goods Act* (the Act) to replace ‘*fit and proper person*’ (in relation to manufacturing licenses) with statutory provisions for suspending, revoking or refusing to grant a licence or a certificate; and
- implementation of the proposal to exempt starting materials for use by a medicine manufacturer from the requirement to be manufactured by a licensed manufacturer.

Transparency

The Officer advised that measures will be undertaken to allow public access to a broader range of information held in the ARTG.

Deferred legislative amendments

The following measures are to be undertaken in this category:

- Expert Committee membership.

Membership of the Adverse Drug Evaluation Committee (ADEC) and the Adverse Drug Reactions Advisory Committee (ADRAC) will be enhanced to ensure that appropriate consumer input is available to the committees. The CMEC membership is to be expanded to include expertise in the manufacture of complementary medicines, and epidemiology.

- Administrative amendments.

To increase transparency and formalise certain Listing requirements, the conditions and requirements of Listing a medicine in the ARTG will be included with other standard conditions under Section 28 of the Act.

- Compositional monographs.

Compositional monographs to be developed to provide legal underpinning for the compositional requirements for ingredients for use in Listed medicines, where no other mandated standard for the ingredient exists.

- Homoeopathic and anthroposophic medicines

A new regulatory framework to be implemented for homoeopathic and anthroposophic medicines.

- Definition of herbal substances

Further consultation to be undertaken in relation to the revised definition of a herbal substance.

- 'Low volume low value'

The requirements for claiming 'low volume low value' to be clarified, including the requirement for evidence to support eligibility.

Enhanced post-market monitoring

The Officer advised that to enhance post-market monitoring, the following measures will be undertaken:

- establishment of a new statutory committee to advise on the safety of medicines;
- new provisions to allow for the suspension of medicines from the ARTG; and
- a proposal to amend the legislation to permit taking samples of any substance or material used in the manufacture of the medicine.

Future directions

The Officer outlined the following future directions:

- The National Prescribing Service (NPS) is undertaking a study on the information and skill needs of consumers and health professionals in relation to complementary medicines.
- Replacing Levels of Evidence Guidelines.
- Incorporating a program of random audits of Good Clinical Practice and ‘for cause audits’, as required.
- Exploring options to regulate Good Distribution Practice, consistent with leading international regulatory agencies.

Discussion

Members acknowledged the considerable regulatory reforms that have, and will be, undertaken. One Member questioned whether the issue of ‘sole traders’ was a consideration in the regulatory reforms. A TGA Officer responded that this has been foreshadowed and would be considered in a future reform package.

12 SPONSOR REPRESENTATIONS TO CMEC

CMEC did not consider any matters under this agenda item.

13 OTHER BUSINESS

CMEC noted an issue raised by a Member regarding a study included in the systematic review and meta-analysis of antioxidant supplements by Bjelakovic *et al.* (2007); 297:842-847. Members agreed that this matter should be considered further at a future meeting.

14 RECOMMENDATION RECORD

Item 2 Confirmation of Draft Minutes of CMEC 67 (20 June 2008)

Recommendation 68.1

CMEC confirms that the draft Minutes of its previous meeting (CMEC 67 20 June 2008), as amended, are a true and accurate record of that meeting.

Item 7.1 Review of *Glycyrrhiza glabra* and *Glycyrrhiza uralensis*

Recommendation 68.3

CMEC recommends to the TGA that herbal preparations of the root, rhizome and/or stolons of *Glycyrrhiza glabra* and *Glycyrrhiza uralensis* **are suitable** as ingredients in Listed therapeutic products, subject to labelling advising of the potential for adverse effects in at-risk individuals, with wording to the effect:

“Contains liquorice. Not suitable for people with kidney disease, a history of high blood pressure or during pregnancy.”

Item 7.2 Review of *Daemonorops Draco* (fruit resin)

Recommendation 68.4

CMEC recommends to the TGA that only herbal preparations of the fruit resin of *Daemonorops draco* are suitable for use as an ingredient in Listed medicines.

Item 10.4 Label Advisory Statements for Products Containing Phytosterols

Recommendation 68.5

CMEC recommends to the TGA that Listed medicines containing phytosterols and/or phytosterol esters require a label advisory statement with words to the effect:

“There is no benefit from taking more than 3 g/day of phytosterols from all sources”

“Not suitable for pregnant or lactating women”.

The Chair closed the meeting at 4:35 pm.