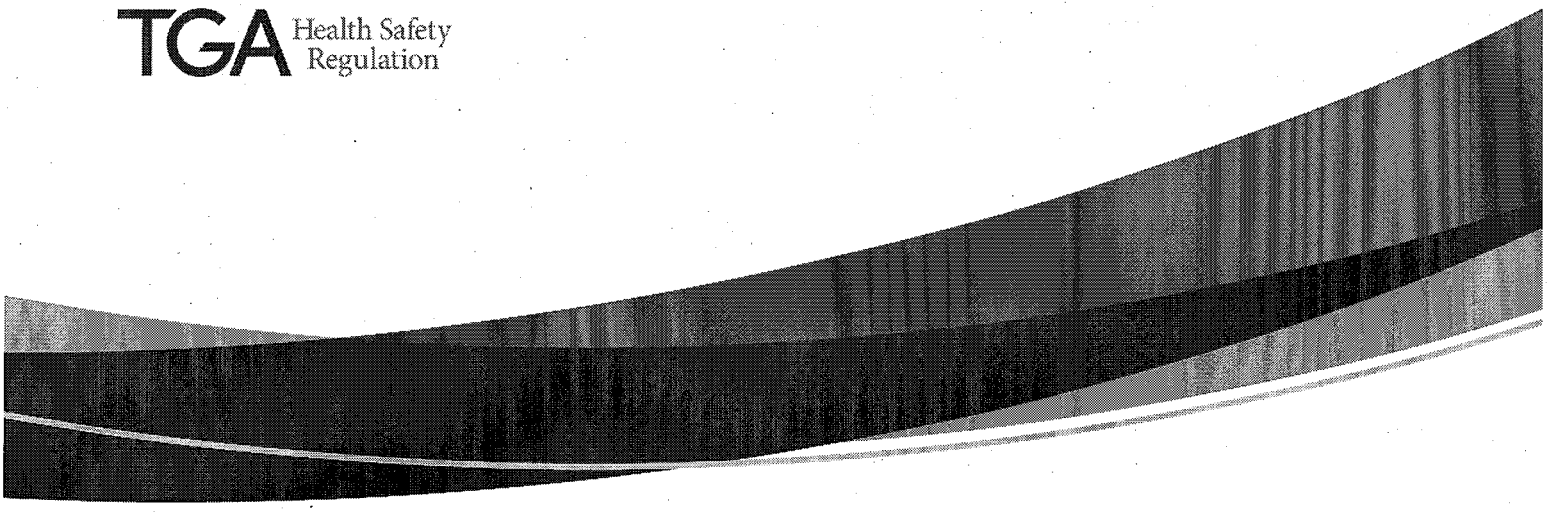
Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

ACCM 13th Advisory Committee on Complementary Medicines

Ratified Minutes

1st March 2013

TGA Health Safety Regulation



Abbreviations

ACCM	Advisory Committee on Complementary Medicines
ARGCM	Australian Regulatory Guidelines for Complementary Medicines
ARTG	Australian Register of Therapeutic Goods
BP	British Pharmacopoeia
CG	Compositional Guideline
CMEC	Complementary Medicines Evaluation Committee
CSU	Committee Support Unit
FSANZ	Food Standard Authority Australia and New Zealand
ICP-AES	Inductively Coupled Plasma Atomic Emission Spectroscopy
MAG	Marketing Authorisation Group
NOAEL	No Observable Adverse Effect Level
OCM	Office of Complementary Medicines
OPR	Office of Product Review
TGA	Therapeutic Goods Administration
USP-NF	United States Pharmacopeia and National Formulary

The Advisory Committee on Complementary Medicines (ACCM) held its thirteenth meeting at the Therapeutic Goods Administration from 9:45am to 3:45 pm on 1 March 2013.

Members of ACCM present

Professor Alan Bensoussan (ACCM Chair)

[redacted]

Present from the Therapeutic Goods Administration

Ms Jenny Burnett (ACCM Secretary)
Dr Anthony Hobbs (Principal Medical Adviser)
Ms Susan Coates
Mr David Blick
Dr Kaylene Raynes
Dr Linda Lenton
Ms Meenu Mathur
Ms Leisa Dee Scholes

1. Procedural matters

1.1 Opening of meeting

The Chair opened the meeting at 9:40am, welcoming ACCM members, particularly those attending their first meeting, and TGA staff. An overview of the induction program held on the previous day (28 February 2013) was given for the benefit of members who had not been able to attend.

The new TGA Principal Medical Adviser, Dr Anthony Hobbs, was introduced to the committee.

As part of the induction program, the Secretary provided all members with information on committee processes and associated timelines.

1.2 Apologies

Nil

1.3 Meeting declaration of interest

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

2. Minutes of previous meetings

2.1 Ratification of ACCM 12th minutes

Members noted that the minutes of the previous ACCM meeting had been ratified out of session.

3. Action arising from previous meetings

Nil

4. Regulatory updates

Members were provided with an update on the complementary medicines regulatory reforms and business processes within each section of the Office of Complementary Medicines (OCM).

4.1 Listing and Operations

A TGA officer gave a presentation outlining the roles and responsibilities of the Listing and Operations Section of the OCM.

The committee noted the number of listed medicines on the Australian Register of Therapeutic Goods (ARTG) and the manner in which they can be removed, that is by sponsor initiated cancellation or TGA cancellation or suspension.

Members raised the issue of identification of medicines that may require assessment to determine whether the goods were actually foods rather than medicines. It was noted that this can occur via OCM receipt of complaints from external stakeholders, information from other government bodies (such as Food Standard Authority Australia and New Zealand [FSANZ] or Australian State/Territory Health Authorities) or the TGA Regulatory Compliance Unit. Members recalled previous committee discussion on the food/medicine interface and how the presentation of the goods is a critical factor in making determinations in this area. The FSANZ list of 'novel foods' was noted by a member and the on-going collaboration between FSANZ and the TGA was discussed.

4.2 Listing and Compliance Section

A TGA officer gave a presentation outlining the roles and responsibilities of the Listing Compliance Section of the OCM and some case studies of recent listing compliance reviews.

A member raised the issue of the current high media profile of listed medicines, particularly complaints regarding advertising of these goods. A TGA officer outlined the processes related to approval of advertising of medicines and the review of medicine labels conducted by the TGA.

The committee discussed various aspects relating to the new draft 'evidence requirements' for listed complementary medicines, including traditional use held in oral records rather than written and the identification of authoritative texts, particularly the committee's concerns that the list previously provided was not sufficient. It was confirmed that the committee would be able to provide comment on the revised draft document.

Members discussed the difference between cancellation of a medicine from the ARTG and recall of goods from the marketplace and the concern that this difference is not understood by consumers. It was noted that, for example, medicines may be cancelled due to lack of evidence to support claims but in the absence of a safety concern the goods may not be removed from retail outlets.

A TGA officer outlined the different types of evidence that a sponsor may hold to support the claims made for their medicine and proposed that there is some misconception about the level of evidence needed and the quality of the evidence. Situations where traditional claims are made but poor quality scientific evidence is held in support of these claims were raised and it was noted that in these instances the evidence is not considered to be sufficient.

This led to discussion on the ability of the TGA to review therapeutic efficacy when evaluating substances for use as ingredients in listed medicines. Committee members' on-going concerns in this regard were noted.

Discussion on the use of the 'free text box' in a listing application, and the associated potential for regulatory non-compliance, identified the potential use of overseas regulators' approval of complementary medicine ingredients with the associated approved indications, the current TGA

review of the 'free text box' field which may be more restrictive and hence encourage sponsors to register their medicines instead of listing.

4.3 TGA Blueprint projects

A TGA officer gave a presentation updating the committee on the status of the regulatory reforms including those affecting complementary medicines.

The committee noted the progress in revision of the Australian Regulatory Guidelines for Complementary Medicines, as well as the 'evidence requirements' previously discussed, and asked that they be kept informed when these documents were published for consultation.

Members briefly discussed the work of the Informal Working Group on Complementary Medicines, particularly potential changes to labelling of listed medicines, and the work being done to improve the transparency of the post-market reviews of listed medicines. They noted that information on implementing the Blueprint recommendations was available on the TGA website.

4.4 Pre-market Assessment

A TGA officer gave a presentation outlining the roles and responsibilities of the Pre-market Assessment Section of the OCM including the outcomes of a recent business process review.

The existence of 'grandfathered medicines', both listed and registered, was noted by members. The fact that many registered medicines comprising 'complementary medicine substances' as active ingredients were grandfathered, meant that the total number of registered complementary medicines was difficult to determine via the ARTG. Members noted that the type of active ingredient was used to decide in which TGA office a new registered medicine would be evaluated, while scheduling in the Poisons Standard or the type of therapeutic indication determined whether a complementary medicine could be listed rather than registered.

The low numbers of applications for new registered complementary medicines was noted by members and possible reasons for this were discussed. A TGA officer outlined the differences between the business processes for registration of prescription medicines, OTC pharmaceuticals and complementary medicines and the number of applications that are withdrawn when it becomes evident that an appropriate dossier has not been submitted. The effect on the timeliness of approvals arising from working with low quality applications for both new medicines and new substances was noted.

A member sought clarification on the level of post-market review of the efficacy of registered medicines in comparison with the review of listed medicines that had been discussed earlier. The role of the Office of Product Review in monitoring adverse event signals for new medicines was discussed and the difficulty in monitoring a changing evidence base was noted.

With regard to evaluation of new substances for use in listed medicines, members discussed the role of TGA compositional guidelines, the difficulty that can arise in determining when a substance is in fact a 'new' ingredient and the lack of legislative backing for these documents.

5. Evaluation of New Substances

[redacted]

[redacted]

5.1 Complex ingredients of natural origin and compliance with the default standards

Background

A TGA officer introduced this item, outlining the current Australian Therapeutic Goods legislation and its recognition of default standards.

Under the current Australian legislation, ingredients used in therapeutic goods must comply with requirements of relevant monographs in the default standards (the British Pharmacopoeia (BP), the United States Pharmacopoeia-National Formulary (USP), the European Pharmacopoeia (Ph Eur).

Many ingredients that are manufactured from substances of natural origin are subjected to processing prior to their inclusion in medicine formulations. This is often undertaken to increase the concentration of constituents with which therapeutic claims are associated and can result in different 'grades' of material being available in the marketplace.

The monographs in the default standards recognise these deliberate variations by allowing either wider than usual or open ended limits for some constituents of the ingredient, for example, 'Not less than 60%' as minimum quality standard. This is in contrast to single chemical entities where the limits are more restrictive, for example '99.0-101.0%'.

The TGA is increasingly being asked to determine the status of ingredients for use in listed medicines that do not meet the requirements of an applicable monograph. That is, whether a 'non-compliant' substance should be considered a separate ingredient identified by a different name and hence not subject to the monograph.

ACCM was asked to consider whether complex substances of natural origin, that are the subject of a monograph in a default standard but do not comply with the requirements of that monograph, should be considered separate substances.

Discussion

Members noted that, prior to considering the matter of compliance with a monograph, there is also sometimes difficulty in determining the actual 'active' therapeutic entity. Placing restrictions or requirements on components within a substance may therefore be problematic. This raises the issue of distinguishing between therapeutically relevant constituents and quality markers and the difficulty in doing so.

With regard to how requirements for the testing of ingredients are determined, members discussed the mechanisms employed by different pharmacopoeial commissions in drafting, consulting, finalising and reviewing monographs. It was noted that suppliers or, in the case of new chemical entities, the innovator, often initiate new monographs. When other suppliers have ingredients that do not comply with requirements or other modifications are needed (for example, up-dated testing methodology), requests can be made to revise an existing monograph. Members agreed that, in general, regulatory agencies would not be involved in seeking amendment to the requirements of a pharmacopoeial monograph.

A member raised the issue of TGA compositional guidelines (CGs), which are created in the absence of a monograph for a new permitted ingredient, and the need for equity in amending these documents in a manner similar to the default standards. A TGA officer confirmed that stakeholders

were able to seek amendment of CGs at any time during the life of the document and that there is an established business process for such requests.

Members agreed that if a relevant specific pharmacopoeial monograph exists (that is, the ingredient meets the definition within the document), and an ingredient does not comply with the requirements of that monograph, it is 'non-compliant' with a default standard according to current Australian therapeutic goods legislation. While it was questioned as to why a supplier would choose a non-complaint ingredient, it was agreed that amendment of the monograph could be sought, if appropriate. Considerations regarding amendment would include confirming that the 'non-compliance' did not compromise the safety of the ingredient. It was further agreed that, in situations where the differences were significant or the substance did not meet the definition of the ingredient specified in the monograph, this would be a new ingredient and it would be more appropriate to generate a new monograph. Members noted the existence of multiple default standards within the current legislation and queried the possible adoption of other pharmacopoeia.

Advice 13.1

ACCM advised the TGA that, if a substance meets the definition of an ingredient in a monograph (in that is it has the same source and undergoes processing as described in the pharmacopoeia), then it must comply with all the requirements of the default standard. The committee noted that requests can be made to pharmacopoeial commissions to revise the requirements of a monograph and that this is not the regulator's responsibility.

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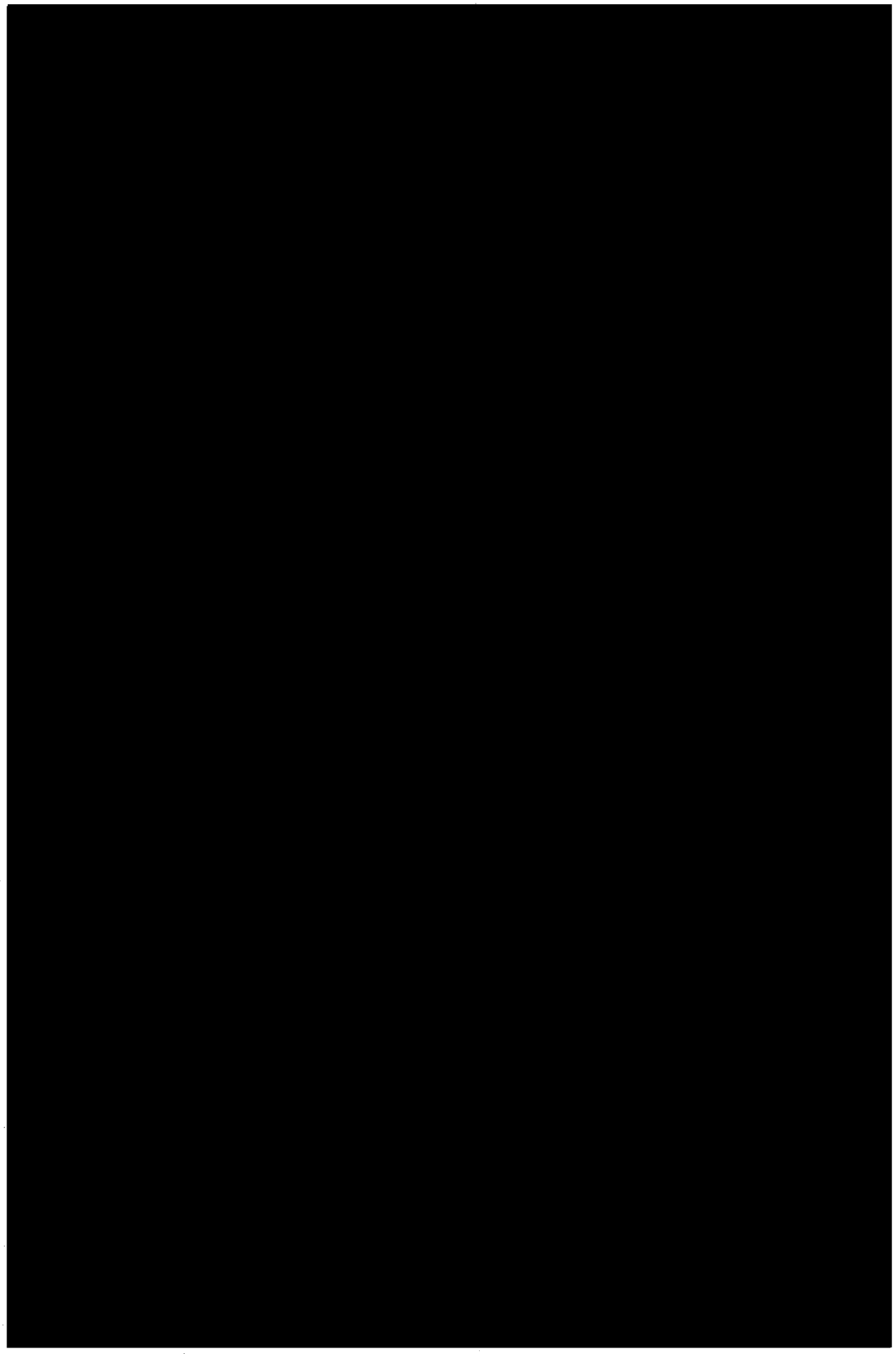

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Advice13.2

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6. Evaluation of new Registered Complementary Medicines

6.1 Nil

7. Reports to ACCM

7.1 Nil

8. Other business

8.1 Outcome of previous ACCM considerations of applications to OCM since March 2011.

A TGA officer introduced this item, advising members of the regulatory outcomes associated with applications that had been considered by the committee since March 2011.

Members highlighted the value of being provided with this information and noted that it would become a standing agenda item.

9. ACCM Committee Advice record

Advice 13.1

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Advice 13.2

[redacted]

Chair's certification

I certify that this is an accurate record of proceedings of the meeting.

Professor Alan Bensoussan

ACCM Chair

2013

Therapeutic Goods Administration

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