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For Information

Item 5.1
OICG 11
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COMPOSITIONAL MONOGRAPHS FOR COMPLEMENTARY MEDICINE INGREDIENTS

Background

Default material standards

Current Australian legislation frames the *British Pharmacopoeia* (incorporating the *European Pharmacopoeia*) (BP) as the sole mandatory source of material standards applicable to ingredients in medicines.

Proposed legislative changes under the Australia New Zealand joint therapeutic scheme and the Australia New Zealand Therapeutic Products Authority (ANZTPA) will see the *United States Pharmacopeia – National Formulary* (USP-NF) joining the BP as a default standard for ingredients in Class 1 and Class 2 medicines.

It is also proposed that ANZTPA will hold the legislative capacity to create mandatory monograph(s) as a Managing Directors Order (MDO) for controlling the definition / composition / quality of ingredient(s) for use in complementary medicines where there is no appropriate default standard. The MDO will override other standards for that ingredient if the circumstances arise. The standards will be known as a Compositional Monographs (CMs).

Compositional Guidelines

The current concept of 'Compositional Guidelines' was introduced in 1999 by the (then) Complementary Medicines Section of the TGA. Compositional Guidelines (CGs) were introduced in an attempt to overcome problems associated with characterising ingredients approved for use in Listed medicines and applied where the ingredient was not covered by the BP.

Prior to the introduction of CGs, information on the definition / control / composition of new Listable ingredients remained within the body of evidence retained as confidential application information. It was assumed at that time, that the Australian Approved Name (AAN) was sufficient for stakeholders to select the 'correct' ingredient consistent with the composition of that approved. However, given the complex and variable nature of some complementary medicine ingredients (particularly those derived from botanical or biological sources), there was concern as to whether commercially available complementary medicinal ingredients were, indeed, consistent in composition with those approved for use in Listed medicines.

CGs provide a primary compositional reference for stakeholders, to ensure ingredients used in product formulation are consistent in composition with the ingredient approved for use in Listed medicines. CGs provide a clear regulatory linkage between the:

- Key compositional parameters / properties defining an ingredient and controlling the potential variance thereof; and

- Evidence supporting the safety of the ingredient and that approved for use in Listed medicines.

Furthermore, the CG provided assurance that a consistent AAN was used for ingredients covered by the CG. The implication for quality and safety arising from the use of an ingredient that departs from a CG is assessed on a 'case-by-case' basis, and is dependant on the nature and magnitude of the departure.

The OCM is receptive to comments on all CGs. A web-address (on the TGA website) is maintained for stakeholders to comment on draft and non-draft CGs.

Since the introduction of CGs in 1999, the number of requests for the alteration of (draft and non-draft) CGs has reduced to one, or two, annually. Similarly, inquiries relating to the approval of materials that depart from a relevant CGs has essentially stopped.

Compositional Monographs

In 2005, the Government resolved to introduce 'mandatory compositional standards' in response to Recommendation 2 of the *Expert Committee on Complementary Medicines in the Health System* (p.10; Attachment 2 – Government Response).

Consistent with this resolution, it is intended that CGs will be replaced by CMs; the important difference being that CMs will be presented in the form of an MDO and will therefore be mandatory default material standards applicable to ingredient(s). However, it is arguable that the introduction of CMs will not greatly impact on the current regulatory arrangements for complementary medicines. Compositional Guidelines are generally perceived as a pseudo 'standard' by stakeholders, and appear to be treated, on the whole, in a manner similar to that of a BP or USP monograph(s) by ingredient suppliers, complementary medicines manufacturers and sponsors; as suggested by the following:

- it is commonly found that complementary medicines manufacturers generate ingredient acceptance specifications by adopting (verbatim) the relevant CGs from the TGA website.
- feedback from material suppliers indicates that medicine manufacturers will generally discriminate against ingredients that depart from an applicable CGs.

The introduction of CMs will allow a greater degree of flexibility than allowed currently. For example, in circumstances where an ingredient is unable to meet specific requirements of a default pharmacopoeial monograph, or the latter is considered to be inappropriate, or additional material requirements need to be imposed in the interests of consumer safety, the TGA can replace a BP/Ph Eur/USP-NF standard by a CM through Managing Director's Orders.

The OCM also anticipates that the CMs will provide Industry and stakeholders with a greater depth of applicable analytical methodology, compared to the information currently provided in existing CGs (in particular, the CGs generated in the early years of the OCM). The OCM advocates a policy of evolving the CMs to reflect contemporary or changing requirements / controls applicable to such ingredient(s).

Identification of Listable ingredients to which default material standards will apply

The OCM will review the list of ingredients (eligible for use in Listed medicines) and identify ingredients that are the subject of an applicable pharmacopoeial standard. This will also include ingredients that are the subject of a current CG.

The OCM will develop a strategy, in consultation with Industry and stakeholders, that will:

- explain the new strategy of default material monographs under ANZTPA;
- communicate the process where a CG is to be replaced by a default material standard;
- provide a workable time period in which Industry can achieve transition to the use of ingredients that are compliant with default material standards; including CMs.

Summary

Upon implementation of the Australia New Zealand joint therapeutic scheme, it is proposed that ingredients that are eligible for use in medicines will be subject to a revised regulatory framework, as follows:

- Introduction of additional mandatory pharmacopoeial material standards for ingredients;
- Current CGs will be replaced by mandatory CMs and will include greater depth of analytical and descriptive information compared to the current CGs;
- In particular circumstances, a CM can replace a default material standard where this is directed in the Managing Directors Orders.

In preparation for these reforms:

- The current list of ingredients eligible for use in Listed medicines will be reviewed to determine if an ingredient is covered by a proposed default pharmacopoeial material standard (for example, the upcoming BP monograph for Chondroitin sulphate (bovine and marine) will supersede the current CGs for those ingredients);
- Where an ingredient is the subject of a current CG and requires a CM under the Australia New Zealand joint therapeutic scheme, the OCM will work with stakeholders in the change-over process.

Recommendation

That the OICG note the approach to the introduction of new pharmacopoeial and CM standards for ingredients proposed for use in complementary medicines under the Australia New Zealand joint therapeutic scheme.