Technical Alert

Clarifications: 1. Using Herbal Components; 2. Using Biological Components

1. Using Herbal Components

In 2018, the TGA ran a consultation to remove (non-mandatory) herbal component names (HCNs) and quantities from the ARTG as an administrative change. The reasons communicated were to free TGA evaluation resources to more efficiently process pre-market applications, including new substances and pre-assessed complementary medicines, as well as to allow industry more flexibility and speed when voluntarily using non-mandatory components as part of product labelling.

They subsequently removed the ability for herbal ingredients to include herbal component names (HCNs) from the ARTG record, except for those components that are mandatory for safety reasons. "Mandatory" components have a restriction in the Permissible Ingredients Determination for a particular safety reason, and therefore must be included in the ARTG listing and finished product specifications (label declaration is optional unless stated otherwise in the Permissible Ingredients Determination).

"Non-mandatory" herbal components do not have a TGA restriction applicable to them, and are therefore a voluntary feature of the product through the standardisation of a herbal extract generally for quality and/or efficacy purposes. However under the change in 2018, there is no longer the function to include them on the ARTG. A non-mandatory standardised component may still be included on product specifications and labels, and a sponsor will need to produce documentation that demonstrates the presence and quantity of the component during a medicine review if needed to substantiate any associated label or evidence claims.

A fuller outline of the requirements are included on the TGA website here. Additional information on the background is available in CMA's prior technical alert 28 Aug 2018: Changes to Herbal Component Names.

Key issue

The removal of HCNs has created some ongoing issues for industry as to how to manage the interface between the ARTG and the finished product specifications as well as other manufacturing documentation and records. **There have been questions from industry as to whether the removal of non-mandatory HCNs from the ARTG requires manufacturers to remove them from finished product specifications (FPS), because the FPS would no longer match the ARTG.** Further, there has been concern that this removal of the HCN from the FPS and ARTG would have resulting adverse effects on labels and evidence for sponsors.

In summary, the TGA have confirmed advice that:

- **Non-mandatory HCNs from standardised herbal extracts may remain on FPS, even though they cannot be entered onto the ARTG record.**

A summary table is included on the next page.

No difference between TGA approach to biological and herbal components

As far as we are aware, the TGA's regulatory approach for biological components and herbal components each described in part 1 and 2 apply equally to each other. CMA have not been able to detect any difference in the regulatory approach whether a component of a parent ingredient is of herbal or biological origin, and have therefore submitted a request for this to be better reflected in TGA website guidance.

IS THE HERBAL COMPONENT MANDATORY?

A herbal component is mandatory if is included in the Permissible Ingredients Determination; for example:

Iodine is a mandatory component of *Alaria esculenta*.

Arbutin is a mandatory component of *Turnera diffusa*.

When for oral or sublingual use, **Hydroxyanthracene glycosides calculated as sennoside B** is a mandatory component of *Senna alexandrina*.

Caffeine is a mandatory component of *Camellia sinensis* for oral use.

Steroidal alkaloids calculated as solanine is a mandatory component of *Lycopersicon esculentum.*

Menthol is a mandatory component of *Mentha x piperita*.

MANDATORY HCNs *are herbal components that are included in the Permissible Ingredients Determination to control a safety aspect.*	***NON-MANDATORY HCNs*** *do not have a TGA safety restriction and can't be entered into the ARTG. They may still be included on Finished Product Specifications, and have associated label or evidence claims or be present as a quality marker.*

Herbal Component - Name & Quantity

FPS	ARTG	FPS	ARTG
☑ MUST INCLUDE herbal component and quantity on FPS & ARTG entry.		☑ CAN INCLUDE on FPS as part of standardised extract.	⊗ UNABLE TO INCLUDE on ARTG. See note below.

Extract type

☑ MAY USE '*extract concentrate standardised*' if standardised extract used.	☑ MAY USE '*extract concentrate standardised*' if standardised extract used.	⊗ UNABLE TO ENTER '*extract concentrate standardised*'. ☑ MAY USE '*extract concentrate*' for standardised extracts.

'Since mandatory components must be included in the ARTG record, the manufacturing process must be able to support the identification and quantification of the mandatory component to demonstrate compliance with the Determination. As such, mandatory components must be present in the finished product specification (FPS).'

'If a sponsor chooses to make a quantitative claim about a non-mandatory component or make an indication/claim related to it on the product label, the sponsor must be able substantiate this by verifying its presence and concentration. To achieve this, the quantity of the non-mandatory component may be specified in the FPS, and quantified in the finished good and/or raw materials. The declaration of a non-mandatory herbal component on the product label is optional.

Discordance between ARTG summary and the finished product specification/ label in such instances would not be considered a non-compliance issue, and it is recognised that this issue is due to a system limitation.'

TGA advice Sep 2019.

Further information is available on the TGA website; the Complementary Medicines and OTC Branch have recommended referring GMP inspectors to the FAQ in the event that questions arise during inspections:

tga.gov.au/discontinuing-pre-market-evaluation-herbal-component-names-frequently-asked-questions-faqs

2. Biological Components

Like herbal components, biological ingredients can be comprised of multiple constituents or components that are often not individually assessed or named by the TGA.

Biological components of 'parent' biological ingredients are treated in the same way to herbal components for 'mandatory' and 'non-mandatory' components, although this is not currently reflected on the TGA's FAQ document, industry queries have confirmed this approach, as described below.

Mandatory biological components

- When a component is specified in Therapeutic Goods (Permissible Ingredients) Determination (the Determination) as a mandatory component of an ingredient, it must be included in the ARTG record. These mandatory components are identified in the Determination, and are mandated by the Poisons Standard or for safety reasons. The declaration of these components on the ARTG is made in addition to the listing of the parent biological ingredient, and the components must also be included on the Finished Product Specification.

Non-mandatory biological components

- Where a component is not a mandatory component in the Permissible Ingredients Determination, there are no legislative requirements for the listing of that component to be in the ARTG record. The declaration of a non-mandatory biological component on the product label is optional.

However where a sponsor chooses to make a label claim regarding a non-mandatory biological component, the sponsor must:

- Hold evidence that the individual component is known to be present in the variant of the biological ingredient used;
- Hold evidence to support any claims (and/or indications) made for that component; and
- Where the label includes a quantitative claim, be able to quantify the component. If the ingredients in the finished good are quantified by input for robust scientific reasons, then alternative quantification approaches such as in the raw materials must be in place.
- Supply evidence to the TGA if requested during a compliance review.

Member Questions and Comments

If you have any general questions or comments about the regulatory approach, please contact CMA directly Lucy.Lang@cmaustralia.org.au as we are coordinating industry clarification on this issue.

ENDS