Australian Government
Department of Health
Therapeutic Goods Administration

Consultation: Discontinuing pre-market evaluation of Herbal Component Names (HCNs)

TGA Health Safety Regulation

Introduction

Herbal Component Names (HCNs) are standardised components comprising either a single chemical constituent or a particular group of chemical constituents found in herbal ingredients. An HCN is not a stand-alone name and should only be used when expressing the herbal component equivalence for a herbal ingredient name.

HCNs may be used in medicine applications and on labels, where:

- names are required to identify marker components of standardised herbal ingredients
- therapeutic indications or claims are made about the strength or concentration of components in herbal ingredients
- names are required for the purpose of declaring a component in a medicine application due to restrictions specified in the Standard for Uniform Scheduling of Medicines and Poisons (SUSMP).

The Poisons Standard mandates that certain components are declared in listed medicine applications, due to safety concerns. These components are referred to as 'mandatory' components. Whether these components need to be declared on the medicine label is determined by the relevant Labelling Order.

Non-mandatory components have been made available in the application system to sponsors to include in the listed medicine application. A sponsor may choose to include these HCNs in their application to ensure that marketing or indications match their ARTG entry.

Proposal overview

Listed complementary medicines sometimes utilise Herbal Component Names (HCNs) as a means to communicate information about the content of the product to consumers. At present, the TGA administers processes for the receipt, scientific assessment and approval of applications for new HCNs. Overall, this activity requires significant TGA resources, is not underpinned by legislation, and importantly, does not provide consumers with an assurance that HCNs are applied consistently across products.

Taking these considerations into account, along with feedback over recent years from the regulated industry, we are proposing to discontinue the receipt and pre-market evaluation of HCN applications.

Key features of this proposal include:

- Applications for new HCN applications will no longer be required or accepted from a pre-defined point in time (to be determined in consultation with industry stakeholders);
- Any references to standardised components on medicine labels will remain acceptable provided legislative labelling requirements are met[1];

[1] As is currently the case, sponsors must ensure that they hold evidence to support the validity of the standardised component claim on their label. Claims that are made on a medicine label may be evaluated as part of a post-market compliance review.

- Existing, non-mandatory component HCNs will no longer be available to select in new listed medicine applications;
- Variation applications for existing listed medicines that include a non-mandatory HCN will not be affected by any system changes and
- The listed medicine application system will still require sponsors to declare the quantity of mandatory components in the application as required by the *Permissible Ingredients Determination*.

Purpose

This consultation paper sets out the details of our proposal to discontinue the receipt and pre-market evaluation of HCN applications.

This business process change has been proposed for the following reasons:

- Listed medicines themselves are not required to undergo any pre-market evaluation and comprise the lowest risk class of regulated medicines (i.e. the evaluation of HCNs is not consistent with the risk framework in-place);
- The regulated industry has raised concerns about the length of the evaluation process and the lack of predictability for business planning and the timing of product launches;
- The creation of an approved HCN is not a legal requirement for listed therapeutic goods and
- The HCN approval process is resource intensive and costs are not recovered from applicants at present.

Comments on this proposal are invited and the feedback received will guide changes to our HCN requirements. Specific information relating to any savings made or additional costs borne if this process were discontinued would be appreciated.

Please provide your feedback by **close of business Friday 12 January 2018**.

Any queries can be directed to complementary.medicines@health.gov.au.

Current regulatory requirements

The *Therapeutic Goods Order No. 92- Standard for labels of non-prescription medicines* requires sponsors to include the quantity of any *standardised* constituents(s) in the herbal material or herbal preparation on the product label. Any claims that are made on a medicine label may be evaluated as part of a post-market compliance review, including those relating to HCNs.

Sponsors must hold evidence to support any standardisation claims they make, including:

- the name and chemical structure of the constituent or, where a component consists of a group of constituents, the name and chemical structure of each constituent in the group;
- evidence that the constituent(s) of the component occurs in the herbal species;
- details of the method of analysis used to quantify the constituent(s) of the component;

- where a component consists of a group of constituents, details of the approximate relative proportion of each constituent; and
- information about whether the component is a therapeutic marker (the component has known therapeutic activity) or a quality marker.

Therapeutic Goods Order No. 92

Herbal material means a plant or part of a plant (defined by its botanical scientific name according to the binominal nomenclature system, including author, and the plant part), whether fresh or dried, that is whole, fragmented, cut or ground.

Herbal preparation means an ingredient that is the result of the processing of a herbal material.

Where standardisation of the herbal preparation is claimed on the label, then, the minimum dry or fresh weight of herbal material from which the preparation is derived and the quantity of standardised constituents(s) in the herbal preparation must be included on the product label.

Medicine labels: Guidance on TGO 91 and TGO 92

2.3.6 Where standardisation is claimed

Standardisation is the process in which the content of a specific chemical constituent(s) has been determined in a herbal material or herbal preparation. Where standardisation of the herbal material or herbal preparation is claimed on the label of the medicine, it affects the way that the quantity or proportion of the active ingredient must be expressed.

There is no legislative requirement to include a non-mandatory HCN component in the ARTG entry for a listed product even if that component has been included on the medicine label. The evaluation and approval processes in-place for HCNs is not required by existing therapeutic goods legislation.

At present, sponsors apply to have their HCN (which is often a standardising component) evaluated and approved, after which it is visible in the listed medicine application system and available for inclusion on ARTG entries. A business process has been designed and implemented around such applications, even though they are not a formal legal requirement.

The application form is available online and applicants are asked to complete this form to initiate the evaluation and approval process for HCNs.

The first time an application for a particular HCN is received, the TGA reviews the supportive information provided by the applicant which includes details of the laboratory methods used for the material's analysis, along with validation data. The assessment process also routinely incorporates advice from the Herbal Ingredient Name Committee. While this process is scientifically robust with respect to the individual application, the fact that the 'approved' HCN is

available in ELF for use in all future listed therapeutic products, and no comparative analysis against the original application is required or performed, means that there is no assurance in the market place that a particular HCN will be applied consistently across products.

Consultation Considerations

1. Past industry concerns

- Previous consultations on this topic indicate that industry is dissatisfied with the HCN process and generally supports the discontinuation of the process.
- A paper entitled *Herbal Component Names (HCNs) – Regulatory review* was the subject of an item at the 11th meeting of Complementary Medicines Evaluation Committee (CMEC) in February 1999 (**Attachment A**). The paper included key concerns raised by external stakeholders. The advisory committee at the time recommended that representatives from the regulated industry and the TGA work together to produce a workable mechanism that addresses the all concerns.

Considerable time has passed since this earlier consultation and we are seeking to review the current industry position on this matter.

2. Risk

Once an HCN is evaluated (incorporating a review of the validated analytical methods employed by the applicant), it is made available in the listed medicines application system. Other applicants can then include the available HCN within their ARTG entry without TGA assessment of their methods of analysis. However, such information should be available to TGA upon request during a post-market compliance review. This means that there is no guarantee that all marketed, listed products using the same HCN and making standardisation claims are directly comparable and thereby erodes the impact of this business practice.

3. Cost recovery

The costs borne by the TGA to administer the HCN evaluation process are currently not recovered in a specific manner from applicants but are instead covered by annual fees for listed medicines. If there was strong industry support to continue the HCN evaluation process, a fee for the processing and evaluation of such applications would need to be considered.

4. Applications for new HCNs

The IT system may be amended so that non-mandatory HCNs are not available for new applications. Any new listing will not be able to use a previously available HCN and the option for adding an HCN will not be available.

Potential applicants will be notified that the pre-approval process for HCNs has been discontinued via the TGA website and upon receipt of any new applications. Claims made on a label or advertising material about existing or new components will be acceptable without pre-approval of the HCNs or inclusion of the HCN on the ARTG entry provided they meet other regulatory requirements. Evidence to support any label claims made about components must

still be held and available upon request. Any claims that are made on a medicine label may be evaluated as part of a post-market compliance review.

Regulatory Options

We are proposing two options to address the proposal to discontinue the receipt and pre-market evaluation of HCN applications.

Option 1

Maintain the status quo.

Consistent with the cost recovery arrangements in place, a fee for such applications may be considered in the future.

Option 2

Industry and the TGA to work together to produce a workable mechanism that allows for discontinuing pre-market evaluation of HCN applications.

Proposed next steps

1) Seek feedback on this proposal through the publication of this consultation paper on the TGA website.
2) Publish an explanatory web statement with related news item on the TGA website to announce the outcome of the consultation.
3) Pending the outcome of consultation, if positive, the availability of HCNs in the Ingredient Repository will be removed from the system and the option for selecting an HCN will not be available.
4) Amend the business process by archiving the existing HCN forms and guidance from the TGA website.
5) Develop a series of frequently asked questions for use in stakeholder communication if required.

Feedback sought

1. Do you support Regulatory Option 1 or 2 as outlined in this paper or would you like to propose an additional option for consideration?
2. Do you have any specific concerns regarding discontinuation of the HCN evaluation process?

Item 8.1

CMEC 11

February 1999

For Advice to TGA

Herbal Component Names (HCNs) - Regulatory review

Advice requested from CMEC:

CMEC is asked to consider whether or not herbal component names (HCNs) are necessary in the naming of standardised herbal ingredients, and, if they are necessary, whether the naming of such components should be retained with the TGA, or could be administered by Industry.

Background

Australian Approved Herbal Component Names, or HCNs, are Australian Approved Names allocated to identified chemical constituents, or groups of constituents, present in herbal material. They are used to correctly express standardised herbal ingredients in the Australian Register of Therapeutic Goods (ARTG), where the complete expression of the quantity of the ingredient must include a statement of the quantity of the standardised component.

The TGA approval process for HCNs is similar in many ways to that in place for other Australian Approved Names (AAN), such as chemical-AAN, ABN (Australian Biological Names) and AHN (Australian approved Herb species Names). Australian approved names have been developed to give accuracy and consistency to ingredient names used on labels and entered onto the ARTG.

HCNs are not necessarily active components of herbs, but they do form part of the active ingredient – the herb. TGO48, Clause 3(2)(b) indicates that all active ingredients are required to be named with Australian approved names, and in the case of an herbal ingredient, the Australian approved name consists of the plant species name, the plant part and the plant preparation. A HCN is currently required to correctly express a standardised preparation.

When submitting an application for a HCN, applicants are requested to:

- provide a chemical structure (or structures) and proof of the name (eg MERK reference),
- demonstrate that the compound(s) exist in the herb,
- in the case of groups of components, describe the relative proportions of the different components in the group, and
- where the component(s) are calculated as another marker, name that marker.

The allocation of HCNs is not always straightforward. Whilst identification of a single chemical constituent is usually quite simple, the naming of groups of constituents is not always so. The individual constituents in a group of isoflavones for example, may differ not only from species to species, but may also vary in different plant parts. Hence the term

"isoflavones" is representative of a number of different chemical profiles. The issue of how the component(s) are measured also affects the term chosen to represent the group.

In mid 1997, and again in early 1998, the TGA was approached by the Nutritional Foods Association of Australia (NFAA), who expressed concern at the lengthy delays in gaining approval of new herbal component names, or HCNs. They were also concerned with the amount of TGA staffing resources committed to this approval process, as they felt that these staff might be better utilised in other areas. Industry put forward the option of approving HCNs themselves.

In response to the matter of time taken to approve HCNs, the Herbal Ingredient Names Committee (HINC), the committee responsible for the approval of Australian Approved Names (AANs) relating to herbal ingredients, reviewed the then current approval process.

At the time these concerns were raised, the HINC was meeting on an ad hoc basis, dependent upon the number of applications received and the availability of staff. This practice was discontinued, and regular monthly meetings of the HINC were introduced. The process was further streamlined around mid 1998, to further improve the notification process to applicants

The NFAA agreed that the matter should be taken to CMEC for advice.

At the end of July 1998, the NFAA put forward a paper to go to CMEC (Attachment 1), proposing that HCNs were not necessary, and should be "scrapped". The paper entitled "Herbal Component Names – Are they really necessary?" compiled was by the Industry Members of the Herbal Task Force.

The TGA was concerned with some of the points raised in the Task Force paper. In an attempt to address what it considered to be misconceptions and misunderstandings surrounding the use and approval of HCNs before it would be ready to be taken to CMEC, TGA responded to this paper on two fronts.

Firstly, the issues were raised at a meeting of the Herbal Task Force held on 28 August 1998. This was followed up with a letter on the 11 November 1998 (Attachment 2), the basis of which was the draft position paper on HCNs. This letter also invited the Task Force to submit another draft of their proposal concerning the abolition of HCNs, taking into account the additional information supplied, with the intention of presenting that paper to the CMEC.

On 5 February 1999 the TGA received a response from the Complementary Healthcare Council of Australia (CHC) (Attachment 3) - formerly the NFAA This response primarily consisted of comments directed at particular paragraphs of the TGA letter dated 11 November 1998, claiming that the TGA response was more a justification of the status quo rather than a response to the problems raised in the NFAA paper. A summary of the CHC response to TGA has been prepared (Attachment 4).

In general, the CHC response was apparently based on the belief that the TGA thinks that standardised components are active, and that the TGA do not accept that the Electronic Lodgment System (ELF) is changing. The CHC also claim that an herbal component name can apply to many herbs. The response concluded that HCNs serve little or no purpose and might usefully be discarded. No alternative mechanism to deal with expression of standardised ingredients was provided.

Industry position

Industry, via the CHC, states that they are not happy with the current situation relating to the use and approval of HCNs. The reasons given for this dissatisfaction include:

- Time taken to approve a HCN, hence market advantage may be lost,
- Unnecessary workload for both TGA and the sponsor,
- Claim that HCNs are not a legal requirement for the listing of therapeutic goods,
- HCNs not a measure of safety,
- Use on labels is really a Trade Practices issue,
- Current HCN list is prescriptive,
- Control and detail required is not reflected in the ELF system.

Industry, via the CHC, state that they want HCNs "discarded", in order to:

- Give sponsors more freedom with the placement and description of components,
- Save TGA resources currently tied up in approval of HCNs (for which no fee is charged), and free staff up for more relevant and important tasks,
- Be able to use component names for any relevant herb.

TGA position

The TGA believes that component names are necessary, in order to properly express standardised ingredients. It is preferable that these names, like other Australian Approved Names, be accurate and consistent. The component name used should correctly characterise the constituent or constituents being referred to.

The HCN approval process has been streamlined in the past year in an attempt to meet the needs of Industry. The HINC now meet on a monthly basis, applicants are notified of the approved HCN within 2 working days, and an alternative procedure to deal with urgent HCN applications is currently in place.

There are, however, problems with the current system, and these should be addressed. These include:

- The approval process does take time, and whilst names for single components are generally straight forward, names for groups of components can be quite complex, specific, and long.
- Long names are difficult to include on labels, and may not mean very much to consumers. The TGA has attempted to remedy this via the creation of shorter "label HCNs", however the level of detail in the longer, more specific HCNs, is required by the TGA laboratories (TGAL) when testing or screening products.
- Whilst procedures are now in place to quickly notify the HCN applicant, dissemination of newly approved HCNs has, to date, been restricted to individual enquiry, ELF mail-outs and the TGA News (quarterly publication). With the imminent creation of a website for the newly created Office of Complementary Medicines, this situation might

be partially remedied. The TGA could quickly update a cumulative list of all newly approved HCNs.

- The current system of allowing standardised ingredients to be expressed as non-standardised ingredients, whilst useful for sponsors, does lead to imprecise information being included in the Australian Register of Therapeutic Goods (ARTG). Whilst the TGA does not necessarily want to limit the flexibility afforded by expressing standardised ingredients as non-standardised, quantification of standardised ingredients is specific for the amount of the standardised component (or group of components) in the ingredient. The equivalent dry or fresh weight of herbal material used to make a standardised ingredient is thus usually given as a range. At present the ELF system does not allow a range to be entered in the quantity field. Sponsors are thus required to estimate the equivalent amount of dry or fresh material used to make the ingredient. This is of potential concern with regard to TGAL testing of the product, based on ARTG details.
- The TGA is unsure what HCNs actually mean to consumers. The TGA is aware that HCNs may be either marker substances with no (known) therapeutic activity, or constituents that are suspected, or known, to have a role in the therapeutic activity of the plant. Clinical trials involving herbals tend to employ ingredients that have been standardised to a particular component suspected of having therapeutic activity. Industry have stated that the use of component names is an important marketing tool, thus it may be useful for the both TGA and Industry to identify the situations in which they are used.
- Whilst the HINC holds records of the specific individual components that a group component name refers to (and the plant parts they are sourced from), there is the potential that a group of components, measured by different methods, could result in differing quantities. The same could occur for a group of components sourced from different plant parts, as there is the potential for variations in the individual components present. The TGA attempted to address this issue by including plant part in the approved HCN. However some members of Industry claimed that this was being too prescriptive.
- There is currently no means of differentiating between ingredients which have been "chemically standardised" to a particular component only, or those ingredients which have been standardised from seed to end product in an attempt to ensure consistency between all components in the plant.

Regulatory implication of the abolition of HCNs

As discussed above, HCNs are currently required to correctly express standardised herbal ingredients in the ARTG. The degree of information currently required on the ARTG reflects the needs of TGAL with regard to testing and screening of herbal products, and is also used by the TGA to compare products and to clarify safety and other issues.

The complete abolition of HCNs therefore, would mean that it would not be possible to express standardised ingredients as being standardised to a particular component. The immediate implication of this would be that the equivalent dry/fresh weight of a herbal ingredient would then be ambiguous. As the TGA considers that a change in the amount of an active ingredient creates a new product, this has obvious regulatory implications.

There is also the question of whether products should be able to claim "standardisation", when there would be no real indication of what "standardised" means.

Options for CMEC action

Option 1

Maintain the status quo.

This option would not address the current concerns of either the Complementary Healthcare Council, or the TGA.

Option 2

Omit Herbal Component Names altogether.

As highlighted in "Regulatory implication of the abolition of HCNs" above, this option would affect the expression of standardised herbal ingredients, hence the information contained in the ARTG. This could thus impede the duties of the TGAL and other sections of the TGA.

There is also the issue of what "standardised" might mean to the consumer, when not linked to a specific component. The question could be asked. "Standardised to what?"

Option 3

Allow sponsors to name herbal components as they wish.

This option could address Industry concerns regarding to speed and flexibility. Industry has not indicated how they see this model proceeding however. It is not apparent whether they mean for sponsors to name components on an individual basis as required, with the possibility of a range of names for the same substance, or whether this process would be administered by an Industry organisation such as the CHC.

This option might not meet the TGA standard of accurate, consistent naming. The basis of Australian Approved Names is to ensure that the TGA, and all stakeholders, are aware of what a particular name refers to. This allows for unambiguous and comparable substances.

Option 4

For the Industry and the TGA to work together to produce a workable mechanism that addresses both Industry and TGA concerns.

This option is to be explored at an Herbal Task Force Meeting to be held on Friday 19th February 1999. The outcome of this meeting will be forwarded to CMEC members as a late paper.

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https://www.tga.gov.au

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