Technical Alert

Important updates on ingredients/substances/raw materials

1) CMA Version 4 Release of Allergens/Substances questionnaire
2) New Substances – New CMA working group
3) Comparable Overseas (Assessment) Bodies (draft list)
4) NEW SUBSTANCE evaluations – CMA working group for applicants, to discuss policy/technical developments and issues
5) Other ingredient updates.

1) CMA Version 4 Release of Allergens/Substances questionnaire

We are pleased to release the *NEW* Version 4 of the "Allergens and other Substances of Concern" raw material questionnaire for industry, with a number of improvements, including:

- The columns have been considerably simplified and the key removed, allowing more accuracy and flexibility in filling out the form under the "TGO 92" labelling expectations.
- Flavours, fragrances, and colours have now been added ("Other substances"), with reference to the current TGA Advertising guidance on the term "natural".
- The notes to the substances have been further examined and amended for clarity and consistency with guidelines.
- Links have been updated and "future-proofed" where possible to minimise the need for future minor updates.

Access to the new Version 4 document is available to all industry members via the CMA webpage.

Please note that the addition of other items to the document, such as animal products, GMO, or non-legislated substances of concerns have not been supported by supplier members, where that information is either available on other standard supplied documents, or is voluntary information that can be requested on an individual basis.

2) New Substances - CMA working group

Complementary Medicines Australia regularly attend TGA industry meetings to discuss issues and developments in the regulation of complementary medicines. Targeted consultations or developments can occur through this forum.

In response to recent developments through this work, Complementary Medicines Australia are convening a new specific working group for members who are closely involved in NEW SUBSTANCE applications due to a number of issues coming up through this forum and also through member enquiries. We invite members who are actively involved in new substance applications to join – including raw material supplies, sponsors, and consultants – to discuss key policy issues, developments, and future options. Please send interest/enquiries to Lucy.Lang@cmaustralia.org.au

Current agenda items arising are:

- ***Competing new substance applications with exclusivity provision***: The process for releasing information about new substances under TGA evaluation has only recently been formed. There are ongoing concerns arising from both the TGA and industry members on the recently introduced process, in the event of possibly competing applications, which require further examination and discussion.

- ***PROPOSED mandatory preliminary assessment requirements***: To align with other TGA processes and ensure rapid processing of applications, the TGA are proposing to create mandatory preliminary assessment information for new substances.
- ***Any other ongoing developments or issues***; such as Comparable Overseas Bodies (see below), compositional guidelines, PIs and any other issues arising.

3) Comparable Overseas (Assessment) Bodies

A preview of the Comparable Overseas (or Assessment) Bodies or "COBs" is now available through CMA, including the updated draft guidelines. The drafted list includes bodies such as FSANZ, EFSA, FDA, Health Canada, and more.

Evaluation reports from comparable overseas regulators or bodies (COBs) may be used to assess either the safety, quality, or efficacy of a product or substance for registered complementary medicines, assessed listed medicines and substances for use in listed medicines.

A preview of the current draft with the list of COBs are included in Table 1 of the DRAFT COB document (member login to CMA website required). Please note this is only for interest, until the TGA officially proceed to publication and incorporation of COBs into the application processes. Whether a COB may assess each category of safety, quality, or efficacy may change on a regular basis depending upon changes occurring with those COBs.

4) Proprietary Ingredients – Issue and REMINDER to check requirements

Both the TGA and industry members are reporting ongoing issues with proprietary ingredients (either active, or excipient ingredients). Key issues are:

- Accuracy of conversion of the quantity of ingredient or restricted components/ingredients.
- Restrictions in the Permissible Ingredients Determination / TGO 92 / Poisons Standard.

Conflicting views

Industry members are rightly expressing concerns that there are issues with the correctness of the proprietary ingredient in the system, that some ingredients are outdated as to regulatory requirements and restrictions; further that the ELF validation rules are often not capable of identifying an issue and preventing an ineligible medicine from being listed. This can cause serious impacts on sponsor costs and resources, if a listed medicine is in production and is then found to have compliance issues that the sponsor may not have been aware of. Sponsors retain the legal responsibility if issues occur due to the certifications made at the time of listing.

Conversely, the TGA have expressed that the Proprietary Ingredient system is not a TGA “cost-recovered” activity, is done manually, and is largely reliant on correct information and ingredient conversions being provided to both the TGA (full information) and separately to the sponsors/manufacturers (partial information). The TGA have provided feedback that sometimes information is being provided to each party in a way that doesn’t match, and therefore causes compliance issues and additional work for the TGA, and can be issues that are very lengthy to resolve, if at all. The TGA have indicated that ensuring correct and accurate information is present on the ARTG and labels is the sponsors responsibility, even in the case of proprietary ingredients, where complete information is not available to the sponsor. The TGA have flagged that they therefore have ongoing concerns and may be re-examining the future operation of the proprietary ingredient system.

Reminder

CMA will continue advocating for IT system and TGA process improvements to help protect industry members and improve arrangements to alleviate pressure on sponsors as much as possible. However under existing arrangements, to preserve the integrity of the proprietary ingredient system and prevent inadvertent compliance issues for sponsors, Proprietary Ingredient Suppliers and Sponsors (and where relevant Consultants and Manufacturers) could benefit from reviewing existing PIs to ensure currency of information - accuracy of content and compliance with regulatory requirements such as the Permissible Ingredients Determination.

For example, PI suppliers and sponsors need to ensure (or communicate to ensure) that both the sponsor/manufacturer records and TGA records are consistent and correct for the following:

- ☐ That ingredients have correct conversion equations applied and accurate quantities determined. For example, vitamin conversions, and mineral salt equivalencies (currently we understand that for salts including mineral salts, the TGA use stoichiometric calculation of cations/anions). Accurate quantities are particularly necessary for restricted ingredients or components that have attached warning statements or quantity limits, as a calculation difference can result in supply interruption for a missing warning statement.
- ☐ Hydration levels of salts are correctly included and represented as the correct AAN, and other hydration issues, such as moisture, are correctly controlled for within the specifications for the finished product.
- ☐ Herbal species, names, plant parts, equivalencies, and other details are correct.
- ☐ That there are not any solvents or excipients used that are not permissible in listed medicines, or are not permissible for that specific ingredient.
- ☐ That any ingredients, or components of an ingredient, that is included in either the 26BB Permissible Ingredients Determination or related regulatory documents such as the TGO 92 labelling order (substances of concerns) or the Poisons Standard, are adequately disclosed and available to sponsors such that they can meet all of the regulatory requirements (such as quantity restrictions and warning statements).

5) Other ingredient updates.

Permissible Ingredients Determination – possible changes being discussed by TGA

The TGA have noted that the Permissible Ingredients Determination requires manually reproducing requirements from documents such as the TGO 92 labelling order and the Poisons Standard, but it does not replace those documents for compliance obligations. This creates other regulatory issues. For example, to be absolutely assured of compliance in product development, documents such as the Poisons Standard need to be double-checked by sponsors and consultants. Therefore it was suggested that this should be removed to ensure accuracy and prevent doubling of requirements.

CMA notes that the removal of the central source of information would be significantly inconvenient, that the Poisons Standard is difficult to meaningfully access and understand, which may increase inadvertent non-compliance and reduce Government goals to improve safety controls.

As this issue is central to regulatory controls, and is under active TGA consideration, CMA is seeking feedback from members on the above issue, such as ideas, suggestions or views, and this will also be discussed at regulatory committees.

Members are encouraged to forward any identified issues to technical@cmaustralia.org.au for attention by the Committee Secretariat.

ENDS