

BOTANICAL ABSTRACT/DISCUSSION FRAMEWORK

SENTENCES for ABSTRACT

Because formulations may contain more than one botanical ingredient in a formulation, caution was urged to avoid reaching [levels or thresholds] of toxicological concern for constituents. Industry should use the procedures needed to limit impurities.

Keep in mind the 150 word limit of the Abstract.

GUIDANCE for DISCUSSION

THE HEAVY METAL/PESTICIDE BOILER PLATE

The Expert Panel expressed concern about pesticide residues and heavy metals that may be present in botanical ingredients. They stressed that the cosmetics industry should continue to use procedures necessary to limit these impurities in ingredients before blending the ingredients into cosmetic formulations.

THE AFLATOXIN BOILER PLATE {IF APPLICABLE}

Aflatoxins have been detected in [*plant (part) where aflatoxins were found*]. The Panel believes that aflatoxins will not be present at levels of toxicological concern in [*botanical ingredient group*]; the Panel adopted the USDA designation of ≤ 15 ppb as corresponding to “negative” aflatoxin content.

CONSTITUENT FRAMEWORK

The basic framework for the constituent Discussion has three parts:

- 1) **Opening Paragraph.** An overview of the general issue that multiple botanical ingredients in a single formulation or in multiple formulations used simultaneously or sequentially can contribute, cumulatively, to total exposures to constituents of concern in the formulation (e.g., pulegone). *{This paragraph is boiler plate/static}*
- 2) **Description of Constituents [Constructed by the Writer].** One or more paragraphs describing the constituent(s) of concern for the botanical ingredient(s); include potential adverse health endpoints, amounts in the plant/extract, previous CIR report conclusions, limits or other restrictions specified by the Panel or regulatory agencies or other organizations, as appropriate. *{This/These paragraph(s) are written to support the choice of the third paragraph}*
- 3) **Wrap Up Paragraph.** Three paragraphs to choose from that provide a framework for discussion language, as appropriate.

Opening Paragraph

A cosmetic formulation may contain multiple botanical ingredients, each of which can contribute to the total concentration of constituents of concern in the formulation. This may include the combined use of multiple ingredients derived from a single plant species or plant group. Cumulative exposure may also occur when more than one product containing one or more constituents of concern are used simultaneously (e.g., multiple make up products) or sequentially (e.g., shampoo and conditioner).

Then Use One of the Following:

- 1) If no concentration limit has been specified for the constituent(s) of concern, and the threshold of toxicological concern (TTC) approach was not applied:**

{Example Discussion Paragraph}

The Panel noted that a constituent of these ingredients is hypericin. Hypericin has been shown to be a photosensitizer in visible light and to be potentially teratogenic based on the results of a study using rat embryos. Hypericin was reported to be present in samples of various parts of the plant at 5 – 18,000 ppm. Another constituent is quercetin. Quercetin may be genotoxic, and is reported to be in *H. perforatum* plant parts at 1000 – 20000 ppm. However, the maximum concentration of use of *H. perforatum* extracts in cosmetics was reported to be 0.07%. This indicates that exposures to hypericin, quercetin and other minor constituents of these ingredients in cosmetics would be clearly below levels of toxicological concern.

Followed by:

{Framework}

The Panel noted that the use of other botanical ingredients that may contain [*constituent(s)*], in combination with [*botanical name*] ingredients in a single formulation, could result in exposures that exceed levels of toxicological concern. Other constituents that may be of concern are potential sensitizers that may be present. Thus, cosmetic products containing one or more botanical ingredient(s) should be formulated to ensure that total exposures to such constituents remain below levels of toxicological concern when the products are used as intended, whether these products typically are used singly, simultaneously, or sequentially. The Panel recognized that every extract would likely be somewhat different and that the characterization of the composition of the plant-derived ingredients addressed in this safety assessment is broad. Nonetheless, the available composition data represent what would be found commonly in ingredients prepared in the manner described. The conclusion regarding safety, therefore, is valid only for ingredients prepared in a manner that produces a chemical profile similar to that described in this report. Extracts not prepared in a manner that produces similar chemical profiles could be considered safe only if they have similar safety test profiles.

- 2) If no concentration limit has been specified for the constituent(s) of concern, and the TTC approach was applied:**

{Example Discussion Paragraphs}

Other safety test data of individual constituents of calendula (e.g., lutein), did not suggest any adverse effects. There are no dermal reproductive or developmental toxicity data on calendula extracts, but data on coriander oil, high in linalool and other terpenes, demonstrated that adverse effects occurred only at maternally toxic doses.

Previous CIR safety assessments of fatty acids, plant sterols, paraffin, p-hydroxybenzoic acid, salicylic acid, and tocopherol, all of which are constituents of calendula extracts, supported that these constituents would be safe at the levels found in calendula extracts and at the use concentrations of these extracts. In previous CIR safety assessments of other constituents of calendula extracts, including pyrogallol, pyrocatechol, and t-butylhydroquinone, adverse effects were

identified. These concerns were considered relevant to this safety assessment because, for example, tannins comprise 6% - 10% of material derived from calendula. Analysis of calendula extracts, however, demonstrated that catechol, pyrogallol, coumarins (esculetin, scopoletin, and umbelliferon), and α -tocopherolquinone were not present at detectable concentrations. Given the low use concentrations of the extracts, and concentrations of constituents in these extracts, which represent only a small percentage of the total ingredient (below the level of detection in some cases), the Panel concluded that these extracts, as described, did not present a concern as used in cosmetics.

Followed by:

{Framework}

The Panel also noted that the use of other botanical ingredients that may contain [*constituent(s)*], in combination with [*botanical name*] ingredients in a single formulation, could result in exposures that exceed the threshold of toxicological concern. Other constituents that may be of concern are potential sensitizers that may be present. Thus, cosmetic products containing one or more botanical ingredient(s) should be formulated to ensure that total exposures to such constituents remain below the threshold of toxicological concern, whether these products typically are used singly, simultaneously, or sequentially. The Panel recognized that every extract would likely be somewhat different and that the characterization of the composition of the plant-derived ingredients addressed in this safety assessment is broad. Nonetheless, the available composition data represent what would be found commonly in ingredients prepared in the manner described. The conclusion regarding safety, therefore, is valid only for ingredients prepared in a manner that produces a chemical profile similar to that described in this report. Extracts not prepared in a manner that produces similar chemical profiles, could be considered safe only if they have similar safety test profiles.

3) If there is a limit on the constituent(s) of concern:

{Example Discussion Paragraph}

Because pulegone is toxic, the Panel limited it to $\leq 1\%$ in cosmetic grade peppermint (*mentha piperita*) oil, peppermint (*mentha piperita*) extract, peppermint (*mentha piperita*) leaves, and peppermint (*mentha piperita*) water. The Panel was confident that this concentration was achievable both by controlling the time of harvest and through the patented technique described in this report. Recent data reported that peppermint (*mentha piperita*) oil is used at $\leq 3\%$ in rinse-off formulations and $\leq 0.2\%$ in leave-on formulations. This concentration of use data, coupled with the Panel's $\leq 1\%$ restriction on pulegone, suggested to the Panel that pulegone toxicity would not occur with cosmetic use.

Or:

{Example Discussion Paragraph}

Pulegone is listed as a constituent of *P. quinquefolius*. The Panel recalled that pulegone toxicity was a concern for peppermint oil used as a cosmetic ingredient, for which the Panel adopted a concentration limit of $\leq 1\%$ pulegone. Because of the low use concentrations of ginseng-derived ingredients, the Panel was confident that a toxic concentration of pulegone could not be reached in cosmetics. For example, recent data indicate that *P. quinquefolius*-derived ingredients were used at a maximum of 0.002%.

Followed by:

{Framework}

The Panel noted that the use of other botanical ingredients that may contain [*constituent(s)*], in combination with [*botanical name*] ingredients in a single formulation, or in formulations that are used at the same time or in close time proximity, could result in exposures that exceed levels of toxicological concern. Other constituents that may be of concern are potential sensitizers that may be present. Thus, cosmetic products containing one or more botanical ingredient(s)

should be formulated to ensure concentrations of [constituent(s)] do not exceed the limit set by the Panel [*or other source (FDA, USDA, etc.) if appropriate*], and that total exposures to such constituents remain below the levels of toxicological concern, whether these products typically are used simultaneously or sequentially. In setting the concentration limits for such constituents, the Panel takes into consideration the total exposure from the use of multiple products containing the same constituents.

The Panel recognized that every extract would likely be somewhat different and that the characterization of the composition of the plant-derived ingredients addressed in this safety assessment is broad. Nonetheless, the available composition data represent what would be found commonly in ingredients prepared in the manner described. The conclusion regarding safety, therefore, is valid only for ingredients prepared in a manner that produces a chemical profile similar to that described in this report. Extracts not prepared in a manner that produces similar chemical profiles, could be considered safe only if they have similar safety test profiles.