ASEAN Cosmetic Scientific Body

Botanical Safety Assessment Guidance Document

[Version 2014-01]

An ASEAN guidance document for evaluating the safety of botanical

An ASEAN Guidance document for evaluating the safety of botanical raw materials used in cosmetics

CONTENTS

BOTANICAL SAFETY ASSESSMENT GUIDANCE DOCUMENT

1. INTRODUCTION

There is a growing trend of using botanical raw materials in personal care products globally. A major percentage of these botanical raw materials used in the ASEAN region are those used in traditional medicine or from the many exotic plants of the rich ASEAN flora, which may be part of local folklore, food to many local ASEAN people, or derived from niche flora available worldwide.

This document offers guidance to safety assessors evaluating the safety of these botanical raw materials in cosmetic products, considering the preparation of the botanical, concentration of use, possibility of harmful substances in the plant, traditional or non-traditional botanical ingredients.

This is a guidance document for safety assessment of botanical raw materials.

2. SCOPE

This guidance document contains a set of recommendations in terms of the type/ extent of data / information that should be collected to review each botanical raw material for use in cosmetics.

'Botanical raw materials' means any part or parts of a plant / herb / shrub / tree, or extracts thereof (includes plant juices, oils, etc.). Algae, Fungi and preparations or extracts thereof also included under the scope

Isolated/highly purified single chemical entities, from botanicals, is not in the scope of this document.

3. BASIS

The guidance in this document is based on the principles of Hazard identification and Risk Assessment (WHO)[1,2].

This guidance is developed based on scientific published, peer-reviewed references

4. BOTANICAL RAW MATERIAL CHARACTERIZATION

This includes collecting data on several parameters as listed below. These data, given below in the table, is a guide to help understand the profile of the botanical raw material. It is left to an expert safety assessor to judge the most relevant mix of these data for making an appropriate risk assessment.

Table. Botanical Raw Materials Characterization

Parameter	Description
Source of botanical raw material*	Botanical name of plant source (preferably Scientific name and / or local name) ;
	Part(s) of plant used ;
Physical Characterization*	General description of the organoleptic of the botanical raw materials (powder, liquid, colour, odour, etc.)
History of Traditional Use	Reference to any traditional use
Method of Preparation*	Ratio plant / solvent, Solubility of the preparation, Residual solvent(s), if used.
	Process of extraction / concentration / fractionation, if any
	Comparison to any known traditional method
	Aqueous or Solvent (specify solvent), if extracted
Chemical Characterization (if applicable)	Testing and analyses of at least 2 batches to confirm consistency
Contamination	Analysis - (e.g.: microbiological, mycotoxins, pesticides, heavy metals, residual proteins, if applicable.) Residual pesticide levels may be substantiated using one of the following: - Total Organochlorines, Organophosphates, Carbamates and Pyrethroids levels

	- EU Pharmacopeia – analysis of pesticides listed (preferred) - OR, Use of solvents or purification methods that would exclude the presence of pesticides
	Botanical raw materials are naturally prone to microbial and heavy metal contamination. Heavy metal and Microbial contamination will be determined based on ACD guideline on finished product

*) Mandatory

The above information should be obtained from the following recognized references, but not limited to:

- Authoritative text (from ASEAN countries/ TCM (Traditional Chinese Medicine) / Ayurveda / Any other)
- Pharmacopoeia
- Official monographs such as WHO monographs, national monographs, Merck Index, Martindale.
- Peer reviewed research articles published in reputable scientific journals or websites, e.g. MEDLINE, EMBASE, TOXLINE, ISI.
- Text books or Research reports published by academic institutes or governmental agencies

5. EXPOSURE ASSESSMENT

The following data on product use should be considered for assessment:

- Type of product (leave-on/rinse-off/ whole body/face only/ oral care/ hair etc.)
- Quantity of use and /or max level of use
- Target population (regions/ adults / children etc.)
- Method of application

6. TOXICOLOGY TESTING

If the characterization data is incomplete and/or does not provide an adequate profile for the risk assessment of the botanical raw material, then actual testing may be needed. For the traditional one, local tolerance assessment may be sufficient instead of toxicological testing. Any testing should consider product usage, route of exposure and normal level of use.

A list of testing is suggested for botanical raw materials:

- Genotoxicity (non-mammalian & mammalian system) – the mutagenic and genotoxic potentials should be assessed according to existing test guidances. *in vitro* testing methods should preferentially be used e.g. (i) *in vitro* bacterial mutation assay (Ames test); (ii) *in vitro* micronucleus assay.

- UV absorption – If it absorbs in the UV range then one would need photo-toxicity tests – photosensitization/ phototoxicity. These end-points need to be assessed using validated and accepted protocols.

- Skin Sensitization – available *in vitro* testing methods (must consider validation status). There is also the fully validated and OECD accepted Local Lymph Node Assay (LLNA), which, though a considerably refined test, is still an animal test.

- Irritation – available *in vitro* testing methods (must consider validation status).

- Systemic toxicity– If the use-level and the data gaps are significant, then systemic toxicity data may become necessary.

7. RISK ASSESSMENT APPROACHES

The following approaches have been provided as examples of how the above hazard data —as described in sections 4 – 6 can be used for the risk assessment of raw material in the finished product. It is not necessary to use all of the approaches. These could be considered as risk assessment options and choices can be made as a case-to-case basis.

a. History of Safe Use[1]

The principles for applying the history of safe use concept are relevant to traditional cosmetic botanical ingredient[1]. It allows the recognition of presumption of safety without further testing, based on long term history of use with no reported adverse effect and with no significant increased exposure.

This risk assessment is based on expert judgement if the associated traditional use data for the botanical raw material in question can actually be used to assure safety in the cosmetic use-context requested.

b. The Comparative Approach[2]

This is especially useful when botanical raw materials from other populations or regions need to be used in populations or regions never exposed to that raw material.

Once the characterization data is available, this can be then compared with known botanical raw materials of the region or population and assess safety based on a comparison and match of the chemical entities involved.

c. TTC Approaches for Safety Assessment[2c,3,4,5,6,7]

The TTC approach is a risk assessment tool based on establishing relevant exposure threshold values for cosmetic raw materials. It is expected that below these threshold values there would not be any significant risk to human health. Hence a critical starting point for applying this tool is an accurate assessment of the exposure of the concerned botanical raw material from the cosmetic product. Various committees such as WHO/IPCS or EU/SCCS have reviewed and published opinions on the use and relevance of this approach as well[4].

The TTC concept is also being considered for skin sensitization and inhalation hazards[6,7].

d. Local Tolerance Assessment

Local Tolerance Assessment of finished product is conducted when complete safety data on traditional botanical raw materials is not available, in order

- Sensitization –the product containing the botanical raw material can be evaluated via human testing e.g. HRIPT

- Irritation –the product containing the botanical raw material can be evaluated via human testing, e.g. human covered patch testing.

8. MAKING A DECISION

The careful compilation and review of the characterization data will help to understand the potential hazards of the botanical raw material. This needs to be followed by risk assessment, which will help the safety assessor make a final decision on the safety of the botanical raw material. These steps can be summarised in the following points:

- Carefully review the characterization data to understand the botanical raw material profile;

- If the characterization data is incomplete, more toxicity testing could be considered, however toxicity testing may not be needed for traditional botanical raw material;

- If the botanical raw material has adequate information on the safe use as a commonly and widely used food ingredient, then clinical safety data may be enough for using it in cosmetics.

Please refer to **Appendix 1 - DECISION CHART FOR SAFETY ASSESSMENT OF BOTANICAL RAW MATERIALS** ***for a summary of the decision making process.***

9. REFERENCES:

1. History of safe use as applied to the safety assessment of novel foods and foods derived from genetically modified organisms. *Constable, et al (2007) Food and Chemical Toxicology 45, 2513–2525*

2. Safety aspects of genetically modified foods of plant origins. Report of a Joint FAO/WHO expert consultation on foods derived from biotechnology. *WHO, Geneva, Switzerland, 29 May – 2 June, (2000).*

    a. The safety assessment of novel foods. *Jones, et al, (1996), Food and Chemical Toxicology, 34, 931-940*

    b. Guidance for the safety assessment of botanicals and botanical preparations for use in food and food supplements. *Schilter, et al (2003), Food and Chemical Toxicology, 41, 1625-1649*

    c. Safety of botanical ingredients in personal care products/cosmetics. *Eric, et al (2011), Food and Chemical Toxicology, 49, 324-341*

3. Application of the threshold of toxicological concern to the safety evaluation of cosmetic ingredients. *Kroes, et al, (2007), Food and Chemical Toxicology 45, 2533–2562*

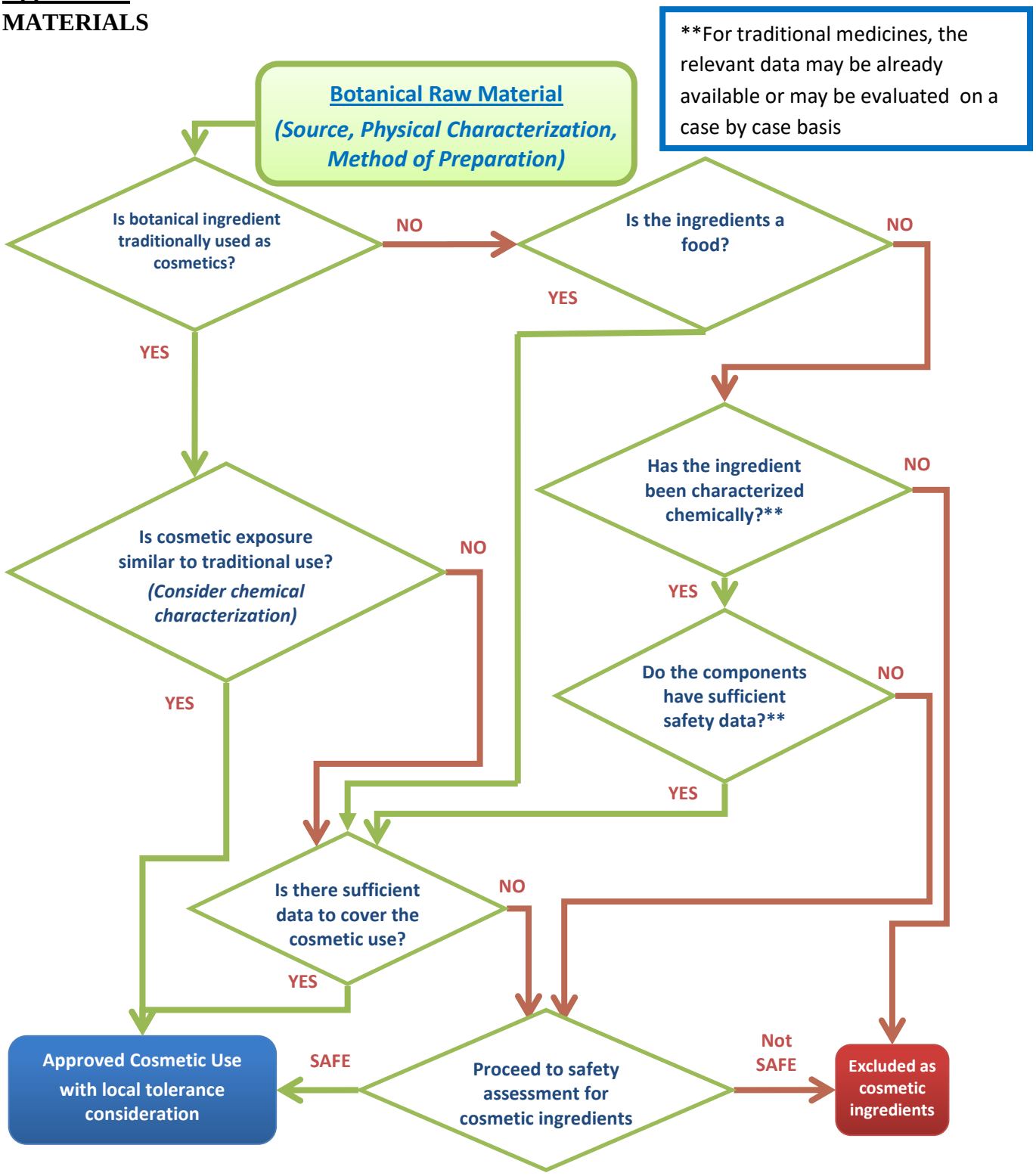
4. SCCS/SCHER/SCENIHROpinion on use of the Threshold of Toxicological Concern (TTC) Approach for Human Safety Assessment of Chemical Substances with focus on Cosmetics and Consumer Products, *European Commission Scientific Committees, (2012), SCCP/1171/08*

5. Threshold of Toxicological Concern (ttc), *A tool for assessing Substances of unknown Toxicity present at low levels in the diet.* ILSI Europe concise monograph series, ILSI Press 2005

6. Refinement of the Dermal Sensitisation Threshold (DST) approach using a larger dataset and incorporating mechanistic chemistry domains. Safford et al (2011), Regul Toxicol Pharmacol. 2011 Jul;60(2):218-24

7. The application of the toxicological threshold of concern (TTC) to inhalation exposure for aerosol ingredients in consumer products, *Carthew et al (2009), Food and Chemical Toxicology, 47 / 6,1287-1295*

Appendix 1: DECISION CHART FOR SAFETY ASSESSMENT OF BOTANICAL RAW MATERIALS



Appendix 2: GLOSSARY

ACD: *ASEAN Cosmetic Directive*

Adverse effect: *an undesired harmful effect*

Alternative methods: *All those procedures which can replace/reduce/refine the need for animal experiments*

Assessment: *Evaluation or appraisal of an analysis of facts and the inference of possible consequences concerning a particular object and not a test.*

Ayurveda: *Indian traditional medicine*

Dose: *Total amount of test substance or product administered.*

Exposure: *Amount of a test substance or product that reaches a target organism, system, or population in a specific frequency for a defined duration.*

Fractionation: *Separation process in which a certain quantity of a mixture (gas, solid, liquid, suspension or isotope) is divided during a phase transition, up in a number of smaller quantities (fractions) in which the composition varies according to a gradient*

Hazard: *Inherent property of an agent or situation having the potential to cause adverse effects when an organism, system, or population is exposed to that agent.*

HPLC: *High-performance liquid chromatography*

HRIPT: *Human Repeat Insult Patch Testing*

IPCS: *International Programme on Chemical Safety*

In vitro test methods: *Using organs, tissue sections and tissue cultures, isolated cells and their cultures, cell lines and subcellular fractions*

LLNA: *The local lymph node assay is a well-established method for assessing skin sensitization; it involves the use of mice and provides an alternative to tests requiring guinea pigs.*

Local tolerance assessment: *Clinical safety assessment of products and test substances at the site of first contact (e.g. skin, eye, mucous membrane)*

OECD: *Organisation for Economic Co-operation and Development*

Risk: *The probability of an adverse effect caused under specified circumstances by exposure to substances*

Risk assessment: *The process of making a decision recommendation on whether existing risks are tolerable and present risk control measures are adequate.*

Safety: *Practical certainty that adverse effects will not result from exposure to an agent under defined circumstances*

SCCS: *Scientific Committee on Consumer Safety in the European Union*

Systemic toxicity: *A toxicological effect that affects a target organ(s) except local effects as explained in local tolerance.*

Threshold: *Dose or exposure concentration of an agent below which a stated effect is not observed or expected to occur*

TLC: *Thin layer chromatography*

TTC: *Threshold of Toxicological Concern*

UV: *Ultraviolet light*

WHO: *World Health Organisation*