



Association of South East Asian Nations (ASEAN)

ANNEX I

ASEAN GUIDING PRINCIPLES FOR INCLUSION INTO OR EXCLUSION FROM THE NEGATIVE LIST OF SUBSTANCES FOR TRADITIONAL MEDICINES

Disclaimer:

This document is provided for information purpose only and subject to changes, pending the finalisation of the ASEAN Agreement on Regulatory Framework for Traditional Medicines. Official references to this document can only be made once the said Agreement has been finalised.



DOCUMENT INFORMATION

This version was adopted at the 28th ASEAN TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS SCIENTIFIC COMMITTEE MEETING (ATSC) 14 October 2015, Makati City, Philippines and endorsed at the 24th ACCSQ TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS PRODUCT WORKING GROUP (TMHSPWG) MEETING 15-16 October 2015, Makati City, Philippines.

Version No.	History of adoption and endorsement		Reasons for revision
	Adoption date	Endorsement date	
1	9th ATSC Meeting 22-23 Nov 2010	14th TMHSPWG Meeting 24-25 Nov 2010	-
2	13th ATSC Meeting 14-15 Nov 2011	16th TMHSPWG Meeting 17-18 Nov 2011	Editorial changes. The word "legislations" to be replaced with "regulations" in entire document to address the concerns that may arise from legal complexities.
3	18th ATSC Meeting 11-13 Mar 2013 23rd ATSC Meeting 23-24 Jun 2014	19th TMHSPWG Meeting 28-29 Jun 2013 21st TMHSPWG Meeting 27-28 Jun 2014	Editorial changes. To delete Clause 3 from the Guiding Principles, and to create separate negative list for TM and HS. Updated the adopted list of substances.
4	28 th ATSC Meeting 14 Oct 2015	24 th TMHSPWG Meeting 15-16 Oct 2015	To separate Guiding Principles for TM and HS, and to revise Appendix 1 for TM and HS. Updated the adopted list of substances.
5	29 th ATSC Meeting 1 Jun 2016	25 th TMHSPWG Meeting 2-3 Jun 2016	To remove "Nicotiana tabacum L." from Appendix 1.



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Purpose

The ASEAN Guiding Principles for Inclusion into or Exclusion from the Negative List of Substances for Traditional Medicines lists the active substances that are prohibited from being used in or being part of the composition of Traditional Medicines. This list is prepared from the following guidelines established to govern the acceptance of active substances to the list based on scientific justification.

GUIDING PRINCIPLES

1. A substance must carry a scientifically demonstrated/proven safety concern that its inclusion into a Traditional Medicine will be harmful to human health¹.
2. A substance that qualifies for inclusion into the list should carry the following details but not limited to:
 - 2.1. Identity of the substance
 - 2.1.1. Taxonomy classification e.g. scientific name by genus and species
 - 2.1.2. Common name
 - 2.2. Source of the substance (e.g. natural/certain part or whole plant /animal)
 - 2.3. Rationale for inclusion (e.g. toxic² effect of the substance e.g. acute, sub-acute, chronic, specific toxicity)
 - 2.4. References (e.g. formulary, monograph/scientific report)
3. The negative list should only include substances that are prohibited for use in a traditional medicine .

¹ "Harmful to human health" is defined as any experience affecting the population resulting in any of the following outcomes: death, a life-threatening adverse experience, inpatient hospitalisation or prolongation of existing hospitalisation, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalisation may be considered harmful when, based on appropriate medical judgment, they may jeopardise the individual and may require medical or surgical intervention to prevent one of the outcomes previously listed.

²It is important to differentiate between potential side effects and toxic effects



4. This negative list should not include:
 - 4.1. Substances in the ASEAN List of Restricted Additives and Excipients for Traditional Medicines.
 - 4.2. Naturally occurring toxic contaminants that are within established limits (e.g. lead).
 - 4.3. Substances which are prohibited under existing wildlife protection laws of all Member States.
5. Prohibited substances in the national regulations of ASEAN Member States, where applicable, are prohibited in Traditional Medicines. Member States are recommended to propose relevant substances from their national regulation for inclusion into the ASEAN Negative List for Traditional Medicines; as long as their inclusion meets the criteria set in this guideline.
6. Proposal for inclusion or exclusion of substances into the ASEAN Negative List for Traditional Medicines should be based on scientific rationale pertaining to human safety concerns.
7. Please refer to Appendix 1 for Negative List of Substances for Traditional Medicines.



APPENDIX

Appendix 1 NEGATIVE LIST OF SUBSTANCES FOR TRADITIONAL MEDICINES

Scientific Name	Common name(s)	Harmful Animal/ Plant Part(s)	Name of Harmful Compound or Compound Class	Ban Status in TM
<i>Adonis vernalis</i> L.	Pheasant's eye	Whole plant	Cardiac glycosides, (e.g. adonitoxin)	Banned
<i>Aristolochia</i> spp.	Birthwort, Pelican flower, Sangree root, Sangrel, Serpentaria, Snakeroot, Snakeweed	Whole plant	Aristolochic acid	Banned
<i>Aspidosperma quebracho-blanco</i> Schltld.	Quebracho	Bark	Aspidospermine	Banned
<i>Atropa belladonna</i> L.	Deadly Nightshade	Whole plant	Scopolamine, Hyoscyamine, Atropine	Banned
<i>Barnardia japonica</i> (Thunb.) Schult. & Schult.f. Syn. <i>Scilla sinensis</i> (Lour.) Merr.	-	Bulb	Cardiac glycosides	Banned



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<i>Calotropis gigantea</i> (L.) Dryand. <i>Calotropis procera</i> (Aiton) Dryand.	Giant milkweed Small crownflower	Latex	Cardiac glycosides: e.g. Calotropin	Banned
<i>Cannabis sativa</i> L. <i>Cannabis indica</i> Lam.	Marijuana	Whole plant	Cannabinoids	Banned
<i>Catharanthus roseus</i> (L.) G.Don Syn. <i>Vinca rosea</i> L.	Rosy Periwinkle, Madagascar Periwinkle, Old Maid	Whole plant	Vinca alkaloids	Banned
<i>Chondrodendron tomentosum</i> Ruiz & Pav.	Curare, Pareira, Pareira brava	Stems	Tubocurarine	Banned
<i>Citrullus colocynthis</i> (L.) Schrad.	Bitter apple	Seed, fruit	Cucurbitacin	Banned
<i>Claviceps purpurea</i> (Fr.) Tul.	Ergot	Sclerotium	Ergot alkaloids (including Ergotamine and Ergometrine)	Banned
<i>Colchicum autumnale</i> L.	Meadow saffron	Seed	Cochicine	Banned



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<i>Conium maculatum</i> L.	Hemlock	Whole plant	Coniine	Banned
<i>Delphinium staphisagria</i> L.	Stavesacre	Seeds	Delphinine, Staphisine	Banned
<i>Digitalis</i> spp. containing cardenolides	-	Whole plant	Cardenolides e.g. digoxin	Banned
<i>Drimia maritima</i> (L.) Stearn Syn. <i>Urginea maritima</i> (L.) Baker	Sea squill, Red squill, Sea onion, Squill	Bulb	Cardiac glycosides	Banned
<i>Excoecaria agallocha</i> L.	Blinding tree	Latex	Excoecaria phorbol	Banned
<i>Gelsemium sempervirens</i> (L.) J.St.-Hil. <i>Gelsemium elegans</i> (Gardner & Chapm.) Benth.	Palaung Thay, Yellow Jessamine, Hearthbreak grass	Root, leaf and rhizome	Gelsemium Indole alkaloids (e.g. Gelsemine & Gelseminine)	Banned
<i>Gluta usitata</i> (Wall.) Ding Hou Syn. <i>Melanorrhoea usitata</i> Wall.	Vanish tree	Latex	Urushic acid, Urushiol, Cardanol, Cardol, Anacardic acid	Banned
<i>Hyoscyamus muticus</i> L. <i>Hyoscyamus niger</i> L.	Henbane, Henblain, Jusquaime	Whole plant	Tropane alkaloids: e.g. atropine, hyoscyamine, hyoscine	Banned



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<i>Juniperus sabina</i> L.	Savin, Savine	Extracted Essential oil (i.e. Savin Oil)	Sabinyol acetate, Sabinene, Podophyllo-toxin and others	Banned
<i>Larrea tridentata</i> (Sessé & Moc. ex DC.) Coville <i>Larrea mexicana</i> Moric.	Chaparral	Whole plant	Lignans: Nordihydroguaiaretic acid (NDGA)	Banned
<i>Lobelia nicotianifolia</i> Roth ex Schult. <i>Lobelia inflata</i> L. <i>Lobelia tupa</i> L.	Indian Tobacco	Whole plant	Piperidine alkaloids: e.g. Lobeline	Banned
<i>Lytta vesicatoria</i> Linn.	Spanish fly	Whole body	Cantharidin	Banned
<i>Melaleuca alternifolia</i> (Maiden & Betche) Cheel	Tea tree	Leaf and terminal branch (Tea Tree Oil)	Tea tree oil: terpinen-4-ol, alpha- terpinene, 1,8-cineol, p-cymene, alpha-terpineol, alpha-pinene, terpinolenes	Banned in TM (oral)
<i>Mitragyna speciosa</i> (Korth.) Havil.	Kratom	Whole plant	Mitragynine, 7-hydroxymitragynine	Banned
<i>Papaver</i> spp. containing morphine & derivatives and codeine	Opium, Poppy	Whole plant	Isoquinoline alkaloids (morphinanes): e.g. morphine, codeine, rhouadine	Banned



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<p><i>Pilocarpus microphyllus</i> Stapf ex Wardleworth</p> <p><i>Pilocarpus jaborandi</i> Holmes</p> <p><i>Pilocarpus pennatifolius</i> Lem.</p>	Jaborandi	Bark, leaf	Imidazole alkaloids: e.g. pilocarpine	Banned
<i>Piper methysticum</i> G.Forst.	Kava Kava	Whole plant	Kava pyrones	Banned
<p><i>Podophyllum emodi</i> Wall. ex Hook.f. & Thomson</p> <p><i>Podophyllum peltatum</i> L.</p>	American mayapple, Mandrake	Root, leaf	Resin podophyllin composed of cyclolignans, e.g. podophyllotoxin, alpha and beta peltatins and their derivatives	Banned
<i>Psilocybe cubensis</i> (Earle) Singer	Gold caps, Shrooms, Magic Mushrooms, Sacred Mushrooms	Whole plant	Psilocybine, Psilocin	Banned
<i>Schoenocaulon officinale</i> (Schltdl. & Cham.) A.Gray	Sabadilla	Seed	Veratrine	Banned
<p><i>Senecio aureus</i> L.</p> <p><i>Senecio jacobaea</i> L.</p> <p><i>Senecio bicolor</i> Sch.Bip.</p> <p><i>Senecio nemorensis</i> L.</p>	-	Whole plant	Pyrrolizidine alkaloids: e.g. senecionine, riddelliine	Banned



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<p><i>Senecio vulgaris</i> L.</p> <p><i>Senecio longilobus</i> Benth.</p> <p><i>Senecio scandens</i> Buch.-Ham. ex D.Don</p>				
<p><i>Solanum dulcamara</i> L.</p> <p><i>Solanum americanum</i> Mill.</p> <p>Syn. <i>Solanum nigrum</i> L.</p>	<p>Bittersweet, Bittersweet Nightshade, Bitter Nightshade</p> <p>Black Nightshade</p>	Leaf, flowering tops	Glycosidic steroidal alkaloids: e.g. solanidine, tomatidine	Banned
<i>Spigelia marilandica</i> L.	Worm grass, Pinkroot	Whole plant	Spigeline (a strychnine-like alkaloid)	Banned
<i>Strophanthus</i> spp. containing cardenolide glycosides	<p>Kombe</p> <p>Gardenia oleander, Climbing oleander</p>	Whole plant	Cardenolide glycosides: e.g. ouabaine and aglycones: e.g. strophanthidin	Banned
<p><i>Veratrum viride</i> Aiton</p> <p><i>Veratrum album</i> L.</p> <p><i>Veratrum mengtzeanum</i> O.Loes.</p> <p><i>Veratrum nigrum</i> L.</p> <p><i>Veratrum stenophyllum</i> Diels</p>	<p>American Hellebore, Indian Poke, Indian Hellebore, False Hellebore, Green False Hellebore, White Hellebore</p>	Whole Plant	Veratrum alkaloids including Veratramine, Cyclopamine, Cycloposine, Jervine, and Muldamine	Banned



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<i>Veratrum maackii</i> Regel <i>Veratrum dahuricum</i> (Turcz.) O.Loes. <i>Veratrum grandiflorum</i> (Maxim. ex Miq.) O.Loes. <i>Veratrum taliense</i> O.Loes.				
<i>Vinca minor</i> L.	Lesser periwinkle	Whole plant	Indole alkaloids: Vincamine, eburnamenine	Banned

[Information on the observed and predicted harmful effect and supporting references are available as a compendium of the negative list.]