



Association of South East Asian Nations (ASEAN)

ANNEX I

ASEAN GUIDING PRINCIPLES FOR INCLUSION INTO OR EXCLUSION FROM THE NEGATIVE LIST OF SUBSTANCES FOR HEALTH SUPPLEMENTS

Disclaimer:

This document is provided for information purpose only and subject to changes, pending the finalisation of the ASEAN Agreement on Regulatory Framework for Health Supplements. 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.

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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 June 2014	19th TMHSPWG Meeting 28-29 Jun 2013 21st TMHSPWG Meeting 27-28 June 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.



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PURPOSE

The ASEAN Guiding Principles for Inclusion into or Exclusion from the Negative List of Substances for Health Supplements lists the active substances that are prohibited from being used in or being part of the composition of Health Supplements. 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 Health Supplements 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
 - 2.1.3. CAS No
 - 2.2. Source of the substance (e.g. natural/synthetic/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)

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



3. The negative list should only include substances that are prohibited for use in a health supplement.
4. This negative list should not include:
 - 4.1. Substances in the ASEAN List of Restricted Additives and Excipients for Health Supplements.
 - 4.2. Nutrients with established ASEAN maximum levels (e.g. vitamins and minerals).
 - 4.3. Naturally occurring toxic contaminants that are within established limits (e.g. lead).
 - 4.4. 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 Health Supplements. Member States are recommended to propose relevant substances from their national regulation for inclusion into the ASEAN Negative List for Health Supplements; 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 Health Supplements should be based on scientific rationale pertaining to human safety concerns.
7. Please refer to Appendix 1 for Negative List of Substances for Health Supplements.



Appendix 1 NEGATIVE LIST OF SUBSTANCES FOR HEALTH SUPPLEMENTS

Scientific Name	Common name(s)	Harmful Animal/ Plant Part(s)	Name of Harmful Compound or Compound Class	Ban Status in HS
<i>Abrus precatorius</i> L.	Indian Licorice, Precatory bean, Jequerity, Mutual love Bean (China), Kudri Mani (Tamil), Guru Ginja (Telegu)	Seed	Abrin, which consists of abrus agglutinin, and toxic lectins abrans	Banned
<i>Aconitum</i> spp. containing aconite alkaloids	Monkshood, Aconite	Whole plant	Aconite alkaloids	Banned
<i>Adonis vernalis</i> L.	Pheasant's eye	Whole plant	Cardiac glycosides, (e.g. adonitoxin)	Banned
Animals parts containing hormones	-	Parts that may contain hormones: Pituitary gland, Thyroid gland, Parathyroid glands, Adrenal glands, Pancreas, Thymus gland, Ovary, Testes, Placenta	Growth hormone, prolactin, adrenocortico-tropic hormone, Thyroid-stimulating hormone, Follicle-stimulating hormone, luteinizing hormone, oxytocin, antidiuretic hormone, thyroid hormone, calcitonin, parathyroid hormone, mineralocorti-coids,	Banned



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			glucocorti-coids, sex hormones, insulin, glucagon, thymosin, estrogens, progesterone, testosterone	
<i>Antiaris toxicaria</i> Lesch.	Upas tree (Javanese Language- arrow poison), Bark cloth Tree	Latex, Sap	Cardiac glycoside (antiarin), Cardenolides & Alkaloids (with cardiac arresting potential)	Banned
<i>Aristolochia</i> spp.	Birthwort, Pelican flower, Sangree root, Sangrel, Serpentaria, Snakeroot, Snakeweed	Whole plant	Aristolochic acid	Banned
<i>Artemisia</i> spp. containing artemisinin	Wormwood	Leaf	Artemisinin	Banned
<i>Aspidosperma quebracho-blanco</i> Schltdl.	Quebracho	Bark	Aspido-spermine	Banned
<i>Atropa belladonna</i> L.	Deadly Nightshade	Whole plant	Scopolamine, Hyoscyamine, Atropine	Banned
<i>Azadirachta indica</i> A.Juss.	Nimba, Neem	Seeds	Azadirachtin and derivatives	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>Berberis</i> spp.-containing berberine e.g. <i>Berberis vulgaris</i> L.	Mahonia Aquifolium: Oregon Grape , Mountain Grape, Barberry. Mahonia Repens: Creeping Barberry, Creeping Mahonia, Creeping Oregon-Grape Mahonia Nervosa: Dwarf Oregon-grape, Cascade Oregon-grape, Dull Oregon-grape	Root, bark, rhizome	Berberine	Banned
<i>Brucea javanica</i> (L.) Merr.	Sumatrana amarissimus, Java brucea	Dried fruits & seed	Bruceine, Bruceantifol and Bruceoside	Banned
<i>Bufo gargarizans</i> Cantor <i>Bufo melanostictus</i> Schneider <i>Bufo vulgaris</i> Lour.	Toad, Samsu, Kodok kerok	Venom, dried secretion, whole body, egg	Cinobufagin, Resibufagenin, Bufagins, Catecholamines: Asbufothionine	Banned
<i>Calotropis gigantea</i> (L.) Dryand. <i>Calotropis procera</i> (Aiton) Dryand.	Giant milkweed Small crown flower	Whole plant	Cardiac glycosides: e.g. Calotropin	Banned
<i>Cannabis sativa</i> L. <i>Cannabis indica</i> Lam.	Marijuana	Whole plant	Cannabinoids	Banned



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<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>Cerbera manghas</i> L.	Dog bane, Pink eyed cerbera	Seed	Digitoxinglyco-side, Cerberine, Cerberoside, Thevetin	Banned
<i>Cerbera odollam</i> Gaertn.	Indian Suicide Tree, Sea Mango	Seed	Cerberin, Cerebroside, Odollin, Odolotoxin, Thevetin and Cerapain.	Banned
<i>Chelidonium majus</i> L.	Celandine, Greater Celandine, Nipplewort	Whole plant	Benzophenanthridine alkaloids: e.g. Berberine, Chelidonine, Sanguinarine, Coptisine, Chelerythrine	Banned
<i>Chondrodendron tomentosum</i> Ruiz & Pav.	Curare, Pareira, Pareira brava	Stems	Tubocurarine	Banned
<i>Cinchona</i> spp.	Quine bark	Bark	Quinoline alkaloids: e.g. quinine and derivatives	Banned
<i>Citrullus colocynthis</i> (L.) Schrud.	Bitter apple	Seed, fruit	Cucurbitacin	Banned



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<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
<i>Conium maculatum</i> L.	Hemlock	Whole plant	Coniine	Banned
<i>Croton tiglium</i> L.	Purging croton	Whole plant	Phorbol-esters, isoquinoline alkaloids (aporphine, morphinane, proaporphine type alkaloids) and crofin	Banned
<i>Datura</i> spp. containing hyoscyamine, atropine, scopolamine and apoptropine	Jimson weed, Devil's apple, Green Dragon, Zombie's Cucumber, Moon Weed, Trumpet Lily, Stinkweed	Whole plant	Hyoscyamine, Atropine, Scopolamine, Apoptropine	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



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<p><i>Dryobalanops sumatrensis</i> (J.F.Gmel.) Kosterm.</p> <p>Syn. <i>Dryobalanops aromatica</i> C.F.Gaertn.</p> <p><i>Dryobalanops lanceolata</i> Burck</p>	<p>Borneo camphor, Kapur, Malay Camphor, Sumatra camphor</p>	<p>Whole plant</p>	<p>Borneol (Borneo camphor)</p>	<p>Banned (in oral preparation)</p>
<p><i>Dryopteris filix-mas</i> (L.) Schott</p>	<p>Male Fern, aspidium, Male Shield Fern</p>	<p>Whole plant</p>	<p>Filicine, Aspidinol</p>	<p>Banned</p>
<p><i>Euphorbia antiquorum</i> L.</p> <p><i>Euphorbia trigona</i> Mill.</p>	<p>Triangular spurge</p>	<p>Whole plant</p>	<p>Phorbol esters e.g. tiglane, ingenane and daphnane types</p>	<p>Banned</p>
<p><i>Excoecaria agallocha</i> L.</p>	<p>Blinding tree</p>	<p>Whole plant</p>	<p>Excoecaria phorbol</p>	<p>Banned</p>
<p><i>Fritillaria</i> spp.</p>	<p>Fritillary bulb</p>	<p>Dried bulb</p>	<p>Steroidal and isosteroidal alkaloids: e.g. peimissine, verticine, verticinone, imperialine, isovericine, ebeiedine</p>	<p>Banned</p>
<p><i>Garcinia elliptica</i> Wall. ex Wight</p> <p><i>Garcinia hanburyi</i> Hook.f.</p>	<p>Gamboge</p>	<p>Whole plant</p>	<p>Camboagic acid, β-guttiferin, α-1-guttiferin</p>	<p>Banned</p>



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<i>Garcinia morella</i> (Gaertn.) Desr.				
<i>Gelsemium sempervirens</i> (L.) J.St.-Hil. <i>Gelsemium elegans</i> (Gardner & Chapm.) Benth.	Palaung Thay, Yellow Jessamine, Heartbreak 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
<i>Jatropha multifida</i> L.	Coral Bush, Coral Plant, Physic nut, Guatemala rhubarb	Fruit, seed	Phytotoxin (Toxalbumin - Curcin)	Banned
<i>Juniperus sabina</i> L.	Savin, Savine	Whole plant	Sabinyl acetate, Sabinene, Podophyllo-toxin and others	Banned
<i>Lantana camara</i> L.	Tembelekan (tahi ayam)	Whole plant	Lantadene and Lancamaron	Banned



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<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 chinensis</i> Lour. <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>Magnolia officinalis</i> Rehder & E.H.Wilson	Houpo, Houpohua, Lamp post, Officinal magnolia	Whole plant	Honokiol, magnolol, magnocurarine, benzylisoquinoline alkaloids: e.g. magnoflorine	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



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<i>Mitragyna speciosa</i> (Korth.) Havil.	Kratom	Whole plant	Mitragynine, 7-hydroxymitragynine	Banned
<i>Mucuna pruriens</i> (L.) DC.	Cowhage, Cowage	Seed	Dopamine, Nicotine, Physostigmine	Banned
<i>Mylabris phalerata</i> Pall. <i>Mylabris cichorii</i> Linnaeus	Blister beetle, Mylabris	Dried body	Cantharidin	Banned
<i>Nerium oleander</i> L. Syn. <i>Nerium indicum</i> Mill.	Indian oleander, Exile Tree	Whole plant	Cardenolide glycosides: e.g. stropeside, oleandrin	Banned
<i>Nicotiana tabacum</i> L.	Tobacco	Leaf	Nicotine	Banned
<i>Papaver</i> spp. containing morphine & derivatives and codeine	Opium, Poppy	Whole plant	Isoquinoline alkaloids (morphinanes): e.g. morphine, codeine, rheadine	Banned
<i>Pausinystalia johimbe</i> (K.Schum.) Pierre ex Beille	Yohimbe	Bark	Yohimbine	Banned
<i>Physostigma venenosum</i> Balf.	Calabar bean	Seed	Physostigmine	Banned



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<i>Pilocarpus microphyllus</i> Stapf ex Wardleworth <i>Pilocarpus jaborandi</i> Holmes <i>Pilocarpus pinnatifolius</i> Lem.	Jaborandi	Whole plant	Imidazole alkaloids: e.g. pilocarpine, pilocarpidine, pilosine	Banned
<i>Piper methysticum</i> G.Forst.	Kava Kava	Whole plant	Kava pyrones	Banned
<i>Plumbago zeylanica</i> L.	White leadwort	Roots	Plumbagin	Banned
<i>Plumbago indica</i> L.	Rose-coloured leadwort	Root, root bark	Plumbagin	Banned
<i>Podophyllum emodii</i> Wall. ex Hook.f. & Thomson <i>Podophyllum peltatum</i> L.	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>Punica granatum</i> L.	Pomegranate	Stem bark and root bark	Pomegranate alkaloids	Banned



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<i>Rauwolfia serpentina</i> (L.) Benth. ex Kurz Syn. <i>Ophioxylon serpentinum</i> L. <i>Rauwolfia vomitoria</i> Afzel.	Rauwolfia, Indian snakeroot, Snakeroot	Whole plant	Indole alkaloids: e.g. reserpine, serpentine, yohimbine, ajmalicine	Banned
<i>Sanguinaria canadensis</i> L.	Bloodroot, Indian Paint	Rhizome and root	Sanguinarine, Chelerythrin, Sanguirulin, Berberine, Protopine	Banned
<i>Schoenocaulon officinale</i> (Schltdl. & Cham.) A.Gray	Sabadilla	Seed	Veratrine	Banned
<i>Senecio aureus</i> L. <i>Senecio jacobaea</i> L. <i>Senecio bicolor</i> Sch.Bip. <i>Senecio nemorensis</i> L. <i>Senecio vulgaris</i> L. <i>Senecio longilobus</i> Benth. <i>Senecio scandens</i> Buch.-Ham. ex D.Don	-	Whole plant	Pyrolizidine alkaloids: e.g. senecionine, riddelliine	Banned



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<i>Solanum dulcamara</i> L. <i>Solanum americanum</i> Mill. Syn. <i>Solanum nigrum</i> L.	Bittersweet, Bittersweet Nightshade, Bitter Nightshade, Black Nightshade	Whole plant	Glycosidic steroidal alkaloids: e.g. solanidine, tomatidine	Banned
<i>Sophora tomentosa</i> L.	Sea coast Laburnum, Silver Bush	Seed	Alkaloids - Matrine, Cytisine	Banned
<i>Spigelia marilandica</i> L.	Worm grass, Pinkroot	Whole plant	Spigeline (a strychnine-like alkaloid)	Banned
<i>Stephania tetrandra</i> S.Moore	Fang ji Fen fang ji Han fang ji Stephania-root	Root	Tetrandrine	Banned
<i>Strophanthus</i> spp. containing cardenolide glycosides	Kombe Gardenia oleander, Climbing oleander	Whole plant	Cardenolide glycosides: e.g. ouabaine and aglycones: e.g. strophanthidin	Banned
<i>Strychnos nux-vomica</i> L. <i>Strychnos ignatii</i> P.J. Bergius <i>Strychnos lucida</i> R.Br. <i>Strychnos roborans</i> A.W.Hill	Nux-vomica Ignatius bean, Phayaa mue lek	Seed Fruit	Indole alkaloids (e.g. strychnine) and/or bisbenzylisoquinoline alkaloids (e.g. tubocurarine)	Banned



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<p><i>Symphytum officinale</i> L.</p> <p><i>Symphytum asperum</i> Lepech.</p> <p><i>Symphytum</i> × <i>uplandicum</i> Nyman</p> <p><i>Symphytum peregrinum</i> Ledeb.</p>	Comfrey	Whole plant	Unsaturated pyrrolizidine alkaloids	Banned
<p><i>Veratrum viride</i> Aiton</p> <p><i>Veratrum album</i> L.</p> <p><i>Veratrum mengtzeanum</i> O.Loos.</p> <p><i>Veratrum nigrum</i> L.</p> <p><i>Veratrum stenophyllum</i> Diels</p> <p><i>Veratrum maackii</i> Regel</p> <p><i>Veratrum dahuricum</i> (Turcz.) O.Loos.</p> <p><i>Veratrum grandiflorum</i> (Maxim. ex Miq.) O.Loos.</p> <p><i>Veratrum taliense</i> O.Loos.</p>	American Hellebore, Indian Poke, Indian Hellebore, False Hellebore, Green False Hellebore, White Hellebore	Whole Plant	Steroid alkaloids: e.g. protoveratrine, and alkaline esters such as jervine derivatives (furanopiperidine) e.g. cyclopamine	Banned
<p><i>Vinca minor</i> L.</p>	Lesser periwinkle	Whole plant	Indole alkaloids: Vincamine, Eburnamenine	Banned



ASEAN Guiding Principles for Inclusion into or Exclusion from the
Negative List of Substances for Health Supplements

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