Association of South East Asian Nations (ASEAN)

ANNEX II
ASEAN GUIDING PRINCIPLES FOR THE USE OF ADDITIVES AND EXCIPIENTS IN 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.

Version 3.0

DOCUMENT INFORMATION

This version was adopted at the 15th ASEAN HEALTH SUPPLEMENTS SCIENTIFIC COMMITTEE MEETING (ATSC) 25-27 June 2012, Singapore and endorsed at the 17th ACCSQ TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS PRODUCT WORKING GROUP (TMHSPWG) MEETING 29-30 June 2012, Singapore.

Version No.	History of adoption and endorsement		Reasons for revision
	ATSC adoption date	TMHSPWG endorsement date	
1	9th ATSC Meeting 22 -23 Nov 2010	14th ACCSQ TMHS PWG Meeting 24-25 Nov 2010	-
2	15th ATSC Meeting 25-27 Jun 2012 19th ATSC Meeting 24-27 Jun 2013	17th ACCSQ TMHS PWG Meeting 29-30 Jun 2012 19th ACCSQ TMHS PWG Meeting 28-29 Jun 2013	Amend the use of the term "national control authority" to "national control/regulatory authority". Update the list of adopted additives and excipients
3	27th ATSC Meeting 1-3 Jun 2015	23rd ACCSQ TMHS PWG Meeting 4-5 Jun 2015	To limit the scope of document to Health Supplements

CONTENTS

PURPOSE

1. This guideline applies to restricted and prohibited additives and excipients intended for use in health supplements in order to assist ASEAN member states in the application of agreed requirements, to protect the consumers, and to facilitate fair trade.
2. This guideline does not include flavouring agents[1].

GUIDING PRINCIPLES

The following criteria are guiding principles used for determination of the use of additives and excipients in health supplements.

1. JUSTIFICATION FOR THE USE OF ADDITIVES AND EXCIPIENTS

The use of additives and excipients is justified only when such use has an advantage, does not present an appreciable health risk to consumers, does not mislead the consumer, and serves one or more of the technological functions set out by Codex and/or international references and the needs set out from (A) through (C) below, and only where these objectives cannot be achieved by other means that are economically and technologically practicable:

A. to preserve the quality of the product.
B. to enhance the keeping quality or stability of a product or to improve its organoleptic properties, provided that this does not change the nature, substance or quality of the product so as to deceive the consumer;
C. to provide aids in the manufacture, processing, preparation, treatment, packing, transport or storage of product, provided that the additive is not used to disguise the effects of the use of faulty raw materials or of undesirable (including unhygienic) practices or techniques during the course of any of these activities.

2. ADDITIVES AND EXCIPIENTS SAFETY

All additives and excipients must not pose hazards or unacceptable risks to consumers' health. The quantity of an additive or excipient added is at or below the maximum use level and is the lowest level necessary to achieve the intended technical effect.

[1] There is no restriction/prohibition on the use of any substance as flavouring agents for as long as their use can be supported by international references.

3. SPECIFICATIONS FOR THE IDENTITY AND PURITY OF ADDITIVES AND EXCIPIENTS

Additives and excipients should be of appropriate food or pharmaceutical grade quality and should at all times conform with the applicable Specifications of Identity and Purity recommended by the Codex Alimentarius Commission or the official pharmacopoeias or, in the absence of such specifications, with appropriate specifications developed by responsible national or international bodies. In terms of safety, food or pharmaceutical grade quality is achieved by conformance of additives and excipients to their specifications as a whole.

4. GOOD MANUFACTURING PRACTICE[2]

All additives and excipients used under conditions of Good Manufacturing Practice should include the following:

A. the quantity of the additive or excipient added to health supplements shall be limited to the lowest possible level necessary to accomplish its desired effect;
B. the quantity of the additive or excipient that becomes a component of a health supplement as a result of its use in the manufacturing, processing or packaging of such a product and which is not intended to accomplish any physical, or other technical effect in the product itself, is reduced to the extent reasonably possible; and,
C. The additive or excipient is of appropriate food or pharmaceutical grade quality and is prepared and handled in the same way as a food or pharmaceutical ingredient.

5. LISTS OF RESTRICTED ADDITIVES AND EXCIPIENTS

The list of restricted additives and excipients used in health supplements goes together with their maximum use levels. The maximum use level of zero means that additive or excipient is prohibited for use. The adopted List of Restricted Additives and Excipients appears in Appendix 1.

The latest edition of the following international references can be used to substantiate the inclusion of an additive or excipient into the list of restricted additives and excipients.

[2] The term Good Manufacturing Practice should not be interpreted as GMP standards for pharmaceutical products. It should be interpreted as good manufacturing practice for the use of additives/excipients. For additional information, see the Codex Alimentarius Commission Procedural Manual. Relations between Commodity Committees and General Committees- Food Additives and Contaminants.

1. Codex General Standard for Food Additives (GSFA) Online Database (http://www.codexalimentarius.net/gsfaonline/index.html?lang=en)
2. Handbook of Pharmaceutical Excipients
3. All Official Pharmacopoeias
   3.1. National Pharmacopoeia of each country
   3.2. British Pharmacopoeia (BP)
   3.3. The United States Pharmacopoeia/National Formulary (USP/NF)
   3.4. European Pharmacopoeia (Ph.Eur)
   3.5. The Pharmacopoeia of China
   3.6. Japanese Pharmacopoeia (JP)
   3.7. The Pharmacopoeia of India

The list as well as the maximum use levels may be subjected to change upon periodic review of updated international references. Scientific data submitted from ASEAN member states can be provided for consideration in order to amend the list.

6. Procedures for Determination of the Use of Additives and Excipients in Health Supplements

Step 1 - Verify whether an additive or excipient used in health supplements is in the list of restricted additives and excipients.

If yes, quantity/amount of additive or excipient used is below/at the maximum level of the additive/ excipient as determined in the list.

If no, go to step 2

Step 2 - Verify whether the additive or excipient is used according to the references

If yes, the quantity of the additive or excipient added shall be limited to the lowest possible level by technological justification necessary to accomplish its desired effect.

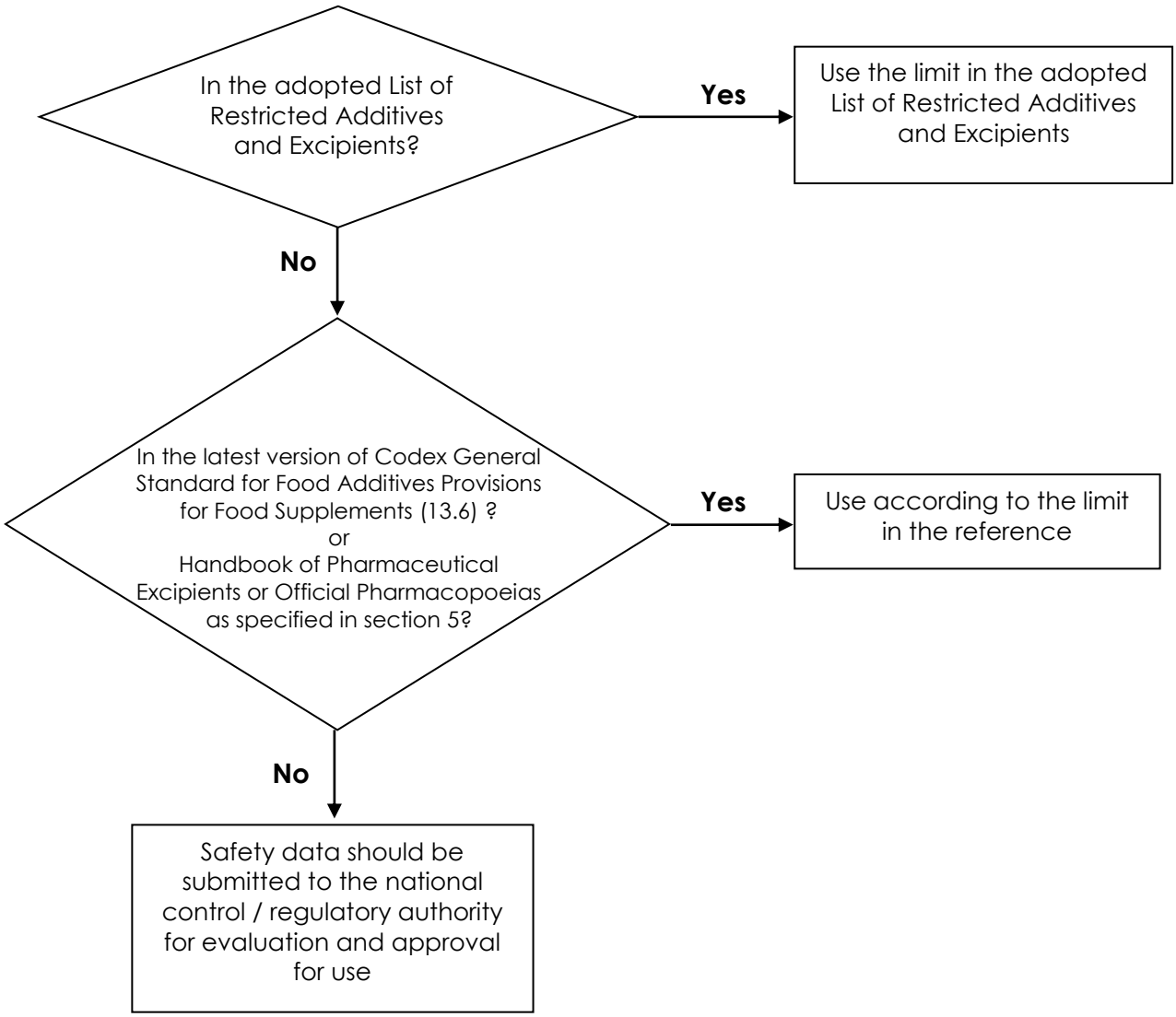
If no, go to step 3

Step 3 – The new additive or excipient is not allowed to be used in health supplements unless the safety assessment of that additive or excipient has been evaluated and approved for use by the national control or regulatory authority.

During the safety assessment of new additives and excipients, reference can be made to international publications such as Handbook of Pharmaceutical Excipients 5th edition (Appendix 2), Environmental Health Criteria (EHC70*) – Principles for the Safety Assessment of Food Additives and Contaminants in Food (Appendix 3) or other suitable literature or guidelines.

* EHC 70 is the publication concerned with reviewing the basis for decision-making by the Joint Expert Committee on Food Additives (JECFA) of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO).

Diagram 1: Procedures for Determination of the Use of Additives and Excipients in Health Supplements



GLOSSARY

Codex - The Codex Alimentarius Commission was created in 1963 by FAO and WHO to develop food standards, guidelines and related texts such as codes of practice under the Joint FAO/WHO Food Standards Programme. The main purposes of this Programme are protecting health of the consumers and ensuring fair trade practices in the food trade, and promoting coordination of all food standards work undertaken by international governmental and non-governmental organizations.

Additives and Excipients mean any substances not normally consumed by themselves and not normally used as typical ingredients or active substances, the intentional addition of which to health supplements for a technological purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such products results, or may be reasonably expected to result (directly or indirectly), in them or their by-products becoming the components of or otherwise affecting the characteristics of the products. Such substances may include: colouring agents, preservatives, adjuvants, stabilizers, thickeners, emulsifiers, pH adjusters, etc.

Maximum Use Level of an additive or excipient is the highest concentration of the additive or excipient determined to be functionally effective and agreed to be safe by the Codex Alimentarius Commission or the official pharmacopoeias.

REFERENCES

1. Codex Alimentarius International Food Standards. *Codex General Standard for Food Additives (GSFA) Online Database*. http://www.codexalimentarius.org/standards/gsfa/en/ (Accessed 2 Jan 2012).

2. Codex Alimentarius International Food Standards. *Codex General Standard for Food Additives*. http://www.codexalimentarius.org/standards/list-of-standards/en/ (Accessed 2 Jan 2010).

3. International Programme on Chemical Safety. *Principles for the Safety Assessment of Food Additives and Contaminants in Food.* http://www.inchem.org/documents/ehc/ehc/ehc70.htm (Accessed 2 Jan 2009).

4. Raymond C R, Paul J S, Cook, Walter G C, Marian E F. *Handbook of Pharmaceutical Excipients, 7th edition*. London: Pharmaceutical Press, 2012.

5. Raymond C R, Paul J S, Marian E Q. *Handbook of Pharmaceutical Excipients, 6th edition*. London: The Pharmaceutical Press and the American Pharmacists Association, 2009.

6. Raymond C R, Paul J S, Sian C O. *Handbook of Pharmaceutical Excipients, 5th edition*. London: The Pharmaceutical Press and the American Pharmacists Association, 2006.

APPENDICES

Appendix 1 THE LIST OF RESTRICTED ADDITIVES AND EXCIPIENTS FOR HEALTH SUPPLEMENTS

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
Coloring agent						
1	Allura Red AC	129	- CI (1975) No.16035 - CI Food Red 17 - FD&C Red No.40	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
2	Brilliant Blue FCF	133	- CI (1975) No. 42900 - CI Food Blue 2 - FD&C Blue No.1	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
3	Caramel III – Ammonia process	150c	- Ammonia caramel	20,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
4	Caramel IV - Sulphite Ammonia Process	150d	- Sulfite ammonia caramel	20,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
5	Carmines	120	- Carmine - CI (1975) No. 75470 - CI Natural Red 4 - Cochineal carmine	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
6	Carotenes, beta (vegetable)	160a(ii)	- Carotenes-natural - CI Food Orange 5 - Mixed carotenes - Natural beta-carotene	600	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
7	Carotenal, beta-apo-8'	160e	- CI. Food Orange 6	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	beta-Carotenes (B. trispora)	160a(iii)	- CI. Food Orange 5	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	beta-Carotenes (synthetic)	160a(i)	- CI. Food Orange 5	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Carotenoic acid, ethyl ester, beta-apo-8'-	160f	- CI. Food Orange 7 (Ethyl Ester)	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
8	Chlorophylls, Copper Complexes	141(i)	- C.I. (1975) No. 75810 - CI Natural Green 3 - Copper chlorophyll - Copper phaeophytin	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Surface treatment
	Chlorophyllin copper complexes, potassium and sodium salts	141(ii)	- C.I. (1975) No. 75810 - Potassium copper chlorophyllin - Sodium copper chlorophyllin	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Surface treatment

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
9	Fast Green FCF	143	- C.I. Food Green 3 - CI (1975) No. 42053 - FD&C Green No. 3	600	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
10	Grape Skin Extract	163(ii)	- ENO - Enociania	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Expressed as anthocyanin
11	Indigotine (Indigo carmine)	132	- C.I. Food Blue 1 - CI (1975) No. 73015 - FD&C Blue No. 2 - Indigo Carmine	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
12	Iron oxide, black	172(i)	- C.I. Pigment Black 11 - CI (1975) No. 77499	7,500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Surface treatment
	Iron oxide, red	172(ii)	- C.I. Pigment Red 101 - C.I. Pigment Red 102 - CI (1975) No. 77491	7,500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Surface treatment
	Iron oxide, yellow	172(iii)	- C.I. Pigment Yellow 42 - C.I. Pigment Yellow 43 - CI (1975) No. 77492	7,500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Surface treatment
13	Ponceau 4R (Cochineal Red A)	124	- CI Food Red 7 - Cochineal Red A - New Coccine	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
					CAC (2012)	
14	Riboflavin from *Bacillus subtilis*	101(iii)	-	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Riboflavin 5' – phosphate sodium	101(ii)	- Vitamin B2 Ester Monosodium Salt	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Riboflavin, synthetic	101(i)	- Riboflavin 5'-phosphate ester monosodium salt - Vitamin B2 phosphate ester monosodium salt	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
15	Sunset Yellow FCF	110	- CI (1975) No. 15985 - CI Food Yellow 3 - Crelborange S - FD&C Yellow No. 6	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
Sweetener						
1	Acesulfame Potassium	950	- Acesulfame K	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Not to exceed the maximum use level for acesulfame potassium (INS 950) singly or in combination with aspartame-acesulfame salt (INS 962)
2	Aspartame	951	- APM - Aspartyl phenylalanine methyl	5500	Codex GSFA Provisions for Food Category 13.6	Not to exceed the maximum use level for

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
			ester		updated up to 34th CAC (2012)	aspartame (INS 951) singly or in combination with aspartame-acesulfame salt (INS 962)
3	Cyclamic acid	952 (i)	- Cyclohexylsulfamic acid	1250	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As Cyclamic acid
	Calcium cyclamate	952 (ii)	-	1250	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As Cyclamic acid
	Sodium cyclamate	952 (iv)	-	1250	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As Cyclamic acid
4	Neotame	961	-	90	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
5	Saccharin	954 (i)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Calcium saccharin	954 (ii)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 34th	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
					CAC (2012)	
	Potassium saccharin	954 (iii)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Sodium saccharin	954 (iv)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 33rd CAC (2012)	
6	Sucralose (Trichloro-galactosucrose)	955	- 4,1',6'-trichlorogalacto sucrose	2400	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
7	Steviol glycosides	960	-	2500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	- As steviol equivalents. - For use in chewable supplements only.
Preservatives						
1	Methyl paraben	218 / 99-76-3	- E218 - 4-hydroxybenzoic acid methyl ester - methyl p-hydroxy-benzoate - *Nipagin M* - *Uniphen P-23*	150 - 2000 (Oral solutions and suspensions) 200 - 3000 (Topical prep.)	Handbook of Pharmaceutical Excipients 5th Editions, 2006 p 466-470	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
2	Benzoic acid	210	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As benzoic acid.
	Sodium benzoate	211	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As benzoic acid.
	Potassium benzoate	212	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As benzoic acid.
	Calcium benzoate	213	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As benzoic acid.
3	Bronopol	52-51-7	- 2-Bromo-2-nitro-1,3-propanediol - β-bromo- β-nitrotrimethyleneglycol - *Myacide*.	100 – 1000)w/v)	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 70-72	Topical use
4	Benzyl alcohol	100-51-6	- Alcohol benzylicus - Benzenemethanol - Phenylcarbinol - Phenylmethanol - alpha-Hydroxytoluene - alpha-toluenol	20000 (v/v)	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 64-66	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
5	Cetrimide	8044-71-1	- *Bromat* - *Cetab* - *Cetavlon* - *Cetraol* - *Lissolamine V* - *Micol* - *Morpan CHSA* - *Morphans* - *Quammonium* - *Sucitide* - Centrimidum	50 (w/v)	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 152-154	Topical Use
6	Propionic acid	79-09-4	- E280 - Carboxyethane - Ethanecarboxylic acid - ethylformic acid - Metacetonic acid - methylacetic acid - Propanoic acid - Pseudoacetic acid	3000 - 10000	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 586-587	
7	Sorbic acid	200	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As sorbic acid.
	Sodium sorbate	201	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As sorbic acid.

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
	Potassium sorbate	202	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As sorbic acid.
	Calcium sorbate	203	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As sorbic acid.
Antioxidants						
1	Alpha-Tocopherol	10191-41-0	- *Copherol F1300* - (±)-3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-benzopyran-6-ol - E307 - synthetic alpha tocopherol - all-*rac*-*a*-atocopherol - *dl*-*a* -tocopherol - 5,7,8-trimethyltocol - RRR- *a* -Tocopherolum	10 - 500 (used in oil or fat-based formulations) (v/v)	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 31-33	
2	Ascorbic acid	50-81-7	- C-97 - cevitamic acid - 2,3-didehydro-L-*threo*-hexono-1,4-lactone; - E300 - 3-oxo-L-gulofuranolactone, enol form	100 - 1000 (used in aqueous formulations) (w/v)	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 43-46	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
			- Vitamin C - Acidum ascorbicum			
3	Ascorbyl palmitate	304	- Vitamin C palmitate	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As ascorbyl stearate.
	Ascorbyl stearate	305	- Vitamin C stearate	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As ascorbyl stearate.
4	Butylated hydoxyanisole	320	- BHA	400	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	- Fat or oil basis. - Singly or in combination: butylated hydroxyanisole (BHA, INS 320), butylated hydroxytoluene (BHT, INS 321) and propyl gallate (INS 310).
5	Butylated hydoxytoluene	321	- BHT	400	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	- Fat or oil basis. - Singly or in combination: butylated hydroxyanisole (BHA, INS 320), butylated hydroxytoluene (BHT, INS 321) and propyl gallate (INS 310).
6	Propyl gallate	310	- Propyl Gallate	400	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	- Fat or oil basis. - Singly or in combination: butylated hydroxyanisole (BHA, INS 320), butylated hydroxytoluene (BHT, INS 321) and propyl gallate (INS 310).

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
7	Calcium disodium ethylenediaminetetra acetate	385	- Calcium disodium edetate - Calcium disodium EDTA	150	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	- As anhydrous calcium disodium ethylenediaminetetra acetate.
	Disodium ethylenediaminetetra acetate	386	- Calcium Disodium (Ethylene-Dinitrilo)-Tetraacetate - Calcium Disodium Edetate - Calcium Disodium EDTA - Calcium Disodium Ethylenediaminetetraacetate - Disodium Dihydrogen (Ethylene-Dinitrilo) - Tetraacetate - Disodium Edetate - Disodium EDTA - Disodium Ethylenediaminetetraacetate	150	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	- As anhydrous calcium disodium ethylenediaminetetra acetate.
Excipients (Anticaking, Emulsifier, Glazing agent, Stabilizer, Solvent, etc.)						
1	Castor oil	1503	Ricinus oil	1000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
2	Carnauba wax	903	-	5000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Surface treatment.

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
3	Cetyl alcohol	36653-82-4	- *Avol* - *Cachalot* - *Crodacol C70* - *Crodacol C90* - *Crodacol C95* - Ethal - Ethol - 1-hexadecanol - *n*-hexadecyl alcohol - *Hyfatol 16-95* - *Hyfatol 16-98* - *Kessco CA* - *Lanette 16* - *Lipocol C* - palmityl - Alcohol - *Rita CA* - *Tego Alkanol 16.* - Alcohol cetylicus - HallStar CO-1695 - Nacol 16-95 - Speziol C16 Pharma - Vegarol 1695	20,000-100,000	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 155-156	Coating agent Emulsifier
4	Diacetyltartaric and fatty acid esters of glycerol	472e	- DATEM - Diacetyltartaric acid esters of mono- and diglycerides - Mixed acetic and tartaric acid esters of mono and diglycerides of fatty acids; INS	5000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
			No. 472f - Mixed Glycerol Esters of Diacetyltartaric Acid and Fatty Acids from Food Fats - Tartaric, acetic and fatty acid esters of glycerol, mixed			
5	Magnesium Stearate	557-04-0	- Magnesium octadecanoate - octadecanoic acid - magnesium salt - stearic acid - magnesium salt. - Dibasic magnesium stearate - Magnesium distearate - Magnesii stearas - Synpro 90	2500 - 50000	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 404-407	Lubricant
6	Phosphates	338; 339(i)-(iii); 340(i)-(iii); 341(i)-(iii); 342(i),(ii); 343(i)-(iii); 450(i)-(iii), (v)-(vii); 451(i), (ii); 452(i)-(v); 542	-	2200	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	As phosphorus.
7	Polydimethylsiloxane	900a	- Dimethylpolysiloxane - Dimethylsilicone fluid	50	Codex GSFA Provisions for Food Category 13.6	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
			- Dimethylsilicone oil - Poly(dimethylsiloxane)		updated up to 34th CAC (2012)	
8	Polyethylene glycol	1521	- Macrogol - PEG	70,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
9	Polyoxyethylene (20) sorbitan monolaurate	432	- Polysorbate 20	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Polyoxyethylene (20) sorbitan monooleate	433	- Polysorbate 80	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Polyoxyethylene (20) sorbitan monopalmitate	434	- Polysorbate 40	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Polyoxyethylene (20) sorbitan monostearate	435	- Polysorbate 60	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	
	Polyoxyethylene (20) sorbitan tristearate	436	- Polysorbate 65	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
10	Polyvinyl alcohol	1203	- PVOH - Vinyl alcohol polymer	45,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	Coating agent, Stabilizer
11	Potassium citrate	6100-05-6 / 866-84-2	- Citrate of potash - Citric acid potassium salt - E332 - Tripotassium citrate monohydrate - Kalii citras	3,000-20,000	Handbook of Pharmaceutical Excipients 6th Editions, 2009 p 574-576	Alkalizing agent Buffering agent Sequestering agent.
12	Sucroglycerides	474	-	2500	Codex GSFA Provisions for Food Category 13.6 updated up to 34th CAC (2012)	

Appendix 2 SAFETY ASSESSMENT OF ADDITIVES AND EXCIPIENTS BASED ON HANDBOOK OF PHARMACEUTICAL EXCIPIENTS 5TH EDITION

Specifications of Pharmaceutical Excipients

1. Nonproprietary names

Excipient names used in the current British Pharmacopoeia, European Pharmacopoeia, Japanese Pharmacopoeia, and the United States Pharmacopoeia/ National Formulary (USP/NF)

2. Synonyms

3. Chemical name and CAS registry number

The unique Chemical Abstract Services number for an excipient along with the chemical name.

4. Empirical formula and molecular weight

5. Structural formula

6. Functional category

The lists of functions that an excipient is generally thought to perform.

7. Applications in pharmaceutical formulation of technology

The various applications of excipient.

8. Description

The details of physical appearance of the excipient.

9. Pharmocopoeial specifications

The compendial standards for the excipient is obtained from the British Pharmacopoeia (BP), European Pharmacopoeia (Ph.Eur), Japanese Pharmacopoeia (JP) and the United States Pharmacopoeia/ National Formulary (USP/NF)

10. Typical properties

11. Stability and storage conditions

The conditions under which the bulk material as received from the supplier should be stored and storage and stability of the dosage forms that contain the excipient.

12. Incompatibilities

Incompatibilities for the excipients either with other excipients or with active ingredients, if an incompatibility is not listed it does not mean it does not occur but simply that it has not been reported or is not well known. Every formulation should be tested for incompatibilities prior to use in a commercial product.

13. Method of manufacture

The common methods of manufacture and additional processes are used to give the excipient its physical characteristics. In some cases the possibility of impurities will be indicated in the method of manufacture.

14. Safety

The types of formulations in which the excipient has been used and presents relevant data concerning possible hazards, adverse reactions that have reported, and relevant animal toxicity data are also shown.

15. Handling precautions

The possible hazards associated with handling the excipient and makes recommendations for suitable containment and protection methods. A familiarity with current good laboratory practice (GLP) and current good manufacturing practice (GMP) and standard chemical handling procedures is assumed.

16. Regulatory status

The accepted uses in foods and licensed pharmaceuticals where known. However, the status of excipients varies from one nation to another and appropriate regulatory bodies should be consulted for guidance.

17. Related substances

18. Comments

Include additional information and observations relevant to the excipient. Where appropriate, the different grades of the excipient available are discussed. Comments are the option of the listed author (s) unless referenced or indicated otherwise.

19. Specific references

A list of references cited within the monograph.

20. General references (if any)

The references which have general information about this type of excipients or the types of dosage forms made these excipients.

21. Authors

The current authors of the monograph.

22. Date of revision

The date on which changes were last made to the text of the monograph.

Appendix 3 SAFETY ASSESSMENT OF ADDITIVES AND EXCIPIENTS BASED ON ENVIRONMENTAL HEALTH CRITERIA 70 (EHC 70)

Principles for the Safety Assessment of Food Additives and Contaminants in Food

1. CHEMICAL COMPOSITION AND THE DEVELOPMENT OF SPECIFICATIONS

1.1. Identity and purity

1.2. Reactions and fate of food additives and contaminants in food

1.3. Specifications

2. TEST PROCEDURES AND EVALUATION

2.1. End-points in experimental toxicity studies

2.1.1. Effects with functional manifestations

2.1.2. Non-neoplastic lesions with morphological manifestations

2.1.3. Neoplasms

2.1.4. Reproduction/developmental toxicity

2.1.5. In vitro studies

2.2. The use of metabolic and pharmacokinetic studies in safety assessment

2.2.1. Identifying relevant animal species.

2.2.2. Determining the mechanisms of toxicity

2.2.3. Metabolism into normal body constituents

2.2.4. Influence of the gut microflora in safety assessment

2.2.4.1. Effects of the gut microflora on the chemical

2.2.4.2. Effects of the chemical on the gut microflora

2.3. Influence of age, nutritional status, and health status on the design and interpretation of studies

2.3.1. Age

2.3.1.1. History

2.3.1.2. Usefulness of studies involving in utero exposure

2.3.1.3. Complications of aging

2.3.2. Nutritional status

2.3.3. Health status

2.3.4. Study design