



**Association of South East Asian Nations (ASEAN)**

## ANNEX II

# ASEAN GUIDING PRINCIPLES FOR THE USE OF ADDITIVES AND EXCIPIENTS IN TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS

---



## DOCUMENT INFORMATION

This version was adopted at the 15th ASEAN TRADITIONAL MEDICINES AND 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



## CONTENTS

Purpose .....	3
Guiding Principles .....	3
1. Justification for the use of additives and excipients .....	3
2. Additives and Excipients Safety .....	3
3. Specifications for the Identity and Purity of Additives and Excipients .....	4
4. Good Manufacturing Practice .....	4
5. Lists of Restricted Additives and Excipients .....	4
6. Procedures for Determination of the Use of Additives and Excipients in Traditional Medicines and Health Supplements .....	5
Glossary .....	8
References .....	9
Appendices .....	10
Appendix 1 Safety Assessment of Additives and Excipients based on Handbook of Pharmaceutical Excipients 5th edition .....	10
Appendix 2 Safety Assessment of Additives and Excipients based on Environmental Health Criteria 70 (EHC 70) .....	13
Appendix 3 The List of Restricted Additives and Excipients for Traditional Medicines and Health Supplements .....	14



## PURPOSE

1. This guideline applies to restricted and prohibited additives and excipients intended for use in traditional medicines and 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 flavoring agents<sup>1</sup>.

## GUIDING PRINCIPLES

The following criteria are guiding principles used for determination of the use of additives and excipients in traditional medicines and 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/excipient added is at or below the maximum use level and is the lowest level necessary to achieve the intended technical effect.

---

<sup>1</sup> 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<sup>2</sup>

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 a traditional medicine or health supplement product 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 traditional medicine or health supplement product 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 traditional medicines and 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 following international references can be used to substantiate the inclusion of an additive/excipient into the list of restricted additives/excipients.

---

<sup>2</sup> 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/gsaonline/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

All references are the latest editions.

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

Please refer Appendix 3 for Adopted List of Restricted Additives and Excipients.

## 6. PROCEDURES FOR DETERMINATION OF THE USE OF ADDITIVES AND EXCIPIENTS IN TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS

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

If yes, quantity/amount of additive/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/excipient is used according to the references

If yes, the quantity of the additive/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



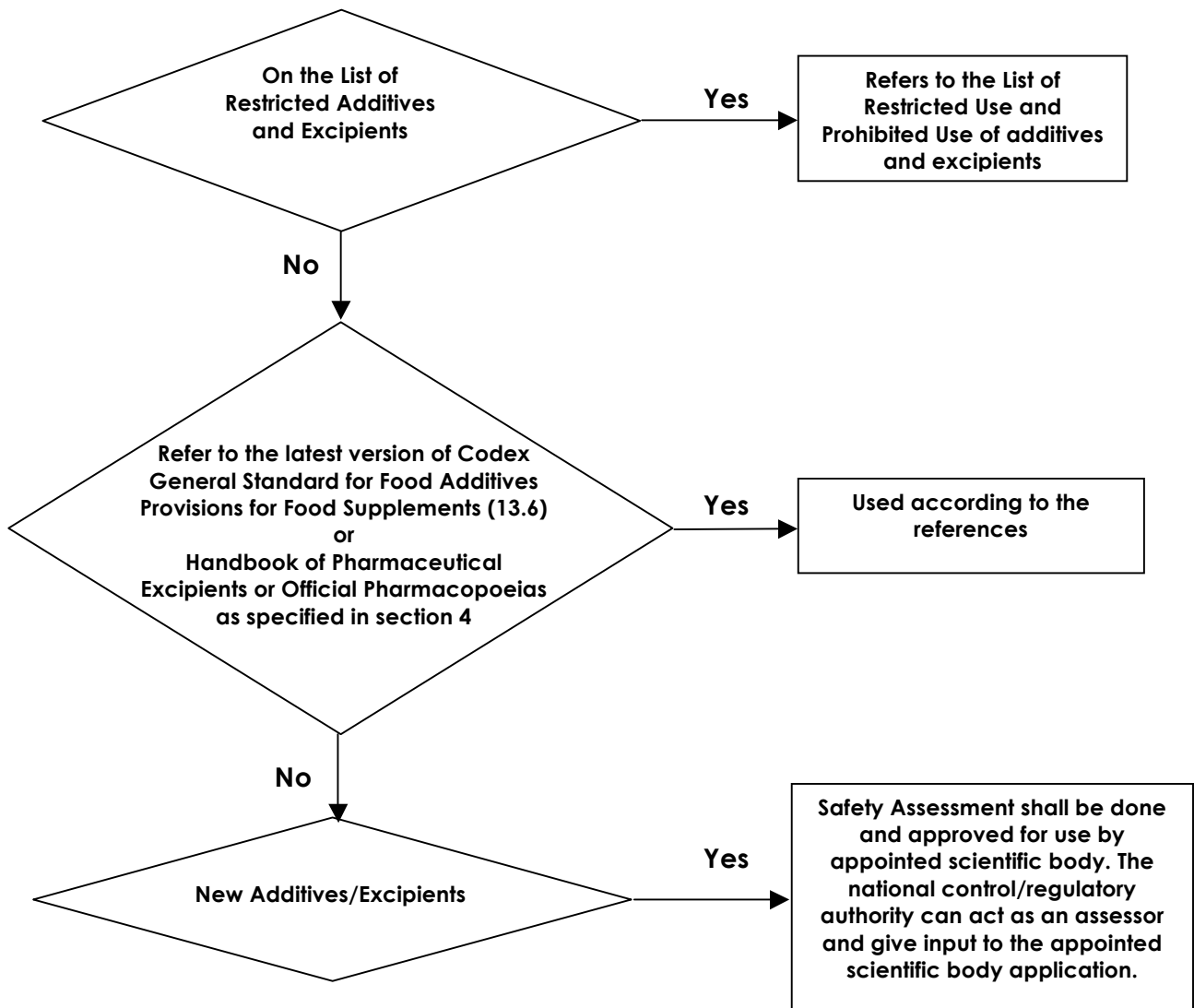
**Step 3** – The new additive/excipient is not allowed to be used in traditional medicines and health supplements unless the safety assessment of that additive/excipient has been evaluated and approved for use by the national control/regulatory authority.

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 1), Environmental Health Criteria (EHC70\*) – Principles for the Safety Assessment of Food Additives and Contaminants in Food (Appendix 2) or other suitable literature/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 Traditional Medicines and 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 traditional medicine and health supplement products 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: coloring agents, preservatives, adjuvants, stabilizers, thickeners, emulsifiers, pH adjusters, etc.

**Maximum Use Level** of an additive/excipient is the highest concentration of the additive/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 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. Pharmacopoeial 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 2 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
- 2.4. Use of human studies in safety evaluation



- 2.4.1. Epidemiological studies
- 2.4.2. Food intolerance\*
- 2.5. Setting the Acceptable Daily Intake (ADI)\*
  - 2.5.1. Determination of the no-observed-effect level (NOEL)
  - 2.5.2. Use of the safety factor
  - 2.5.3. Toxicological versus physiological responses
  - 2.5.4. Group ADIs
  - 2.5.5. Special situations
  - 2.5.6. Comparing the ADI with potential exposure



## Appendix 3 THE LIST OF RESTRICTED ADDITIVES AND EXCIPIENTS FOR TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS

This list is adopted at the 19th ACCSQ Traditional Medicines and Health Supplements Scientific Committee Meeting on 24-27 June 2013, Bagan, Myanmar and endorsed at the 19th ACCSQ Traditional Medicines and Health Supplements Product Working Group Meeting on 28-29 June 2013, Bagan, Myanmar.

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
<b>Coloring agent</b>						
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 34 <sup>th</sup> 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 34 <sup>th</sup> CAC (2012)	
3	Caramel III – Ammonia process	150c	- Ammonia caramel	20,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> 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 34 <sup>th</sup>	





APPENDIX 3 Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
					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 34 <sup>th</sup> CAC (2012)	
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 34 <sup>th</sup> CAC (2012)	
7	Carotenal, beta-apo- 8'	160e	- CI. Food Orange 6	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	beta-Carotenes (B. trispora)	160a(iii)	- CI. Food Orange 5	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	beta-Carotenes (synthetic)	160a(i)	- CI. Food Orange 5	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> 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 34 <sup>th</sup> CAC (2012)	



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
<b>APPENDIX 3</b>						
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 34 <sup>th</sup> 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 34 <sup>th</sup> CAC (2012)	Surface treatment
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 34 <sup>th</sup> CAC (2012)	
10	Grape Skin Extract	163(ii)	- ENO - Enociania	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> 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 34 <sup>th</sup> 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 34 <sup>th</sup> CAC (2012)	Surface treatment
	Iron oxide, red	172(ii)	- C.I. Pigment Red 101 - C.I. Pigment Red 102	7,500	Codex GSFA Provisions	Surface treatment



Item	APPENDIX 3 Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
			- CI (1975) No. 77491		updated up to 34 <sup>th</sup> CAC (2012)	
	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 34 <sup>th</sup> 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 34 <sup>th</sup> CAC (2012)	
	Riboflavin from <i>Bacillus subtilis</i>	101 (iii)	-	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
14	Riboflavin 5' – phosphate sodium	101 (ii)	- Vitamin B2 Ester Monosodium Salt	300	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> 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 34 <sup>th</sup> 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 34 <sup>th</sup> CAC (2012)	



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
<b>Sweetener</b>						
1	Acesulfame Potassium	950	- Acesulfame K	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> 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 ester	5500	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	Not to exceed the maximum use level for 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 34 <sup>th</sup> CAC (2012)	As Cyclamic acid
	Calcium cyclamate	952 (ii)	-	1250	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As Cyclamic acid
	Sodium cyclamate	952 (iv)	-	1250	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As Cyclamic acid



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
<b>APPENDIX 3</b>						
4	Neotame	961	-	90	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
5	Saccharin	954 (i)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	Calcium saccharin	954 (ii)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	Potassium saccharin	954 (iii)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	Sodium saccharin	954 (iv)	-	1200	Codex GSFA Provisions for Food Category 13.6 updated up to 33 <sup>rd</sup> CAC (2012)	
6	Sucralose (Trichloro-galactosucrose)	955	- 4,1',6'-trichlorogalacto sucrose	2400	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
7	Steviol glycosides	960	-	2500	Codex GSFA Provisions for Food Category 13.6	- As steviol equivalents. - For use in chewable



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
					updated up to 34 <sup>th</sup> CAC (2012)	supplements only.
<b>Preparatives 3</b>						
1	Methyl paraben	218 / 99-76-3	- E218 - 4-hydroxybenzoic acid methyl ester - methyl p-hydroxy-benzoate - <i>Nipagin M</i> - <i>Uniphen P-23</i>	150 - 200 (Oral solutions and suspensions) 200 - 3000 (Topical prep.)	Handbook of Pharmaceutical Excipients 5 <sup>th</sup> Editions, 2006 p 466-470	
2	Benzoic acid	210	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As benzoic acid.
	Sodium benzoate	211	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As benzoic acid.
	Potassium benzoate	212	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As benzoic acid.
	Calcium benzoate	213	-	2000	Codex GSFA Provisions for Food Category 13.6	As benzoic acid.



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
					updated up to 34 <sup>th</sup> CAC (2012)	
<b>APPENDIX 3</b>	Propylol	52-51-7	<ul style="list-style-type: none"> <li>- 2-Bromo-2-nitro-1,3-propanediol</li> <li>- □-bromo- □-nitrotrimethyleneglycol</li> <li>- <i>Myacide</i>.</li> </ul>	100 – 1000 (w/v)	Handbook of Pharmaceutical Excipients 6 <sup>th</sup> Editions, 2009 p 70-72	Topical use
4	Benzyl alcohol	100-51-6	<ul style="list-style-type: none"> <li>- Alcohol benzylicus</li> <li>- Benzenemethanol</li> <li>- Phenylcarbinol</li> <li>- Phenylmethanol</li> <li>- alpha-Hydroxytoluene</li> <li>- alpha-toluenol</li> </ul>	20000 (v/v)	Handbook of Pharmaceutical Excipients 6 <sup>th</sup> Editions, 2009 p 64-66	
5	Cetrimide	8044-71-1	<ul style="list-style-type: none"> <li>- <i>Bromat</i></li> <li>- <i>Cetab</i></li> <li>- <i>Cetavlon</i></li> <li>- <i>Cetraol</i></li> <li>- <i>Lissolamine V</i></li> <li>- <i>Micol</i></li> <li>- <i>Morpan CHSA</i></li> <li>- <i>Morphans</i></li> <li>- <i>Quammonium</i></li> <li>- <i>Sucitide</i></li> <li>- <i>Centrimidum</i></li> </ul>	50 (w/v)	Handbook of Pharmaceutical Excipients 6 <sup>th</sup> Editions, 2009 p 152-154	Topical Use
6	Propionic acid	79-09-4	<ul style="list-style-type: none"> <li>- E280</li> <li>- Carboxyethane</li> <li>- Ethanecarboxylic acid</li> </ul>	3000 - 10000	Handbook of Pharmaceutical Excipients 6 <sup>th</sup> Editions,	



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note	
<b>APPENDIX 3</b>			<ul style="list-style-type: none"> <li>- ethylformic acid</li> <li>- Metacetic acid</li> <li>- methylacetic acid</li> <li>- Propanoic acid</li> <li>- Pseudoacetic acid</li> </ul>		2009 p 586-587		
	7	Sorbic acid	200	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As sorbic acid.
		Sodium sorbate	201	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As sorbic acid.
		Potassium sorbate	202	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As sorbic acid.
	Calcium sorbate	203	-	2000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As sorbic acid.	
<b>Antioxidants</b>							
1	Alpha-Tocopherol	10191-41-0	<ul style="list-style-type: none"> <li>- <i>Copherol F1300</i></li> <li>- (±)-3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-</li> </ul>	10 - 500 (used in oil or fat-based)	Handbook of Pharmaceutical Excipients 6th Editions,		





Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note	
<b>APPENDIX 3</b>			trimethyltridecyl)-2H-1-benzopyran-6-ol - E307 - synthetic alpha tocopherol - all-rac- $\alpha$ -tocopherol - dl- $\alpha$ -tocopherol - 5,7,8-trimethyltolcol - RRR- $\alpha$ -Tocopherolum	formulations) (v/v)	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 - Vitamin C - Acidum ascorbicum	100 - 1000 (used in aqueous formulations ) (w/v)	Handbook of Pharmaceutical Excipients 6 <sup>th</sup> Editions, 2009 p 43-46	
	3	Ascorbyl palmitate	304	- Vitamin C palmitate	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As ascorbyl stearate.
		Ascorbyl stearate	305	- Vitamin C stearate	500	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	As ascorbyl stearate.
4	Butylated hydroxyanisole	320	- BHA	400	Codex GSFA Provisions for Food Category 13.6	- Fat or oil basis. - Singly or in combination:	



Guiding Principles for the Use of Additives and Excipients in Traditional Medicines and Health Supplements

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
					updated up to 34 <sup>th</sup> CAC (2012)	butylated hydroxyanisole (BHA, INS 320), butylated hydroxytoluene (BHT, INS 321) and propyl gallate (INS 310).
<b>APPENDIX 3</b> 5	Butylated hydroxytoluene	321	- BHT	400	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> 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 34 <sup>th</sup> 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).
7	Calcium disodium ethylenediaminetetra acetate	385	- Calcium disodium edetate - Calcium disodium EDTA	150	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> 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	150	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	- As anhydrous calcium disodium ethylenediaminetetra acetate.



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
			(Ethylene-Dinitrilo) - Tetraacetate - Disodium Edetate - Disodium EDTA - Disodium Ethylenediaminetetraacetate			
<b>APPENDIX 3</b> <b>Excipients (Anticaking, Emulsifier, Glazing agent, Stabilizer, Solvent, etc.)</b>						
1	Castor oil	1503	Ricinus oil	1000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
2	Carnauba wax	903	-	5000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	Surface treatment.
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	20,000- 100,000	Handbook of Pharmaceutical Excipients 6 <sup>th</sup> Editions, 2009 p 155-156	Coating agent Emulsifier



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
<b>APPENDIX 3</b>			<ul style="list-style-type: none"> <li>- Kessco CA</li> <li>- Lanette 16</li> <li>- Lipocol C</li> <li>- palmityl</li> <li>- Alcohol</li> <li>- Rita CA</li> <li>- Tego Alkanol 16.</li> <li>- Alcohol cetylicus</li> <li>- HallStar CO-1695</li> <li>- Nacol 16-95</li> <li>- Speziol C16 Pharma</li> <li>- Vegarol 1695</li> </ul>			
	4	Diacetyltartaric and fatty acid esters of glycerol	472e	<ul style="list-style-type: none"> <li>- DATEM</li> <li>- Diacetyltartaric acid esters of mono- and diglycerides</li> <li>- Mixed acetic and tartaric acid esters of mono and diglycerides of fatty acids; INS No. 472f</li> <li>- Mixed Glycerol Esters of Diacetyltartaric Acid and Fatty Acids from Food Fats</li> <li>- Tartaric, acetic and fatty acid esters of glycerol, mixed</li> </ul>	5000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)
5	Magnesium Stearate	557-04-0	<ul style="list-style-type: none"> <li>- Magnesium octadecanoate</li> <li>- octadecanoic acid</li> <li>- magnesium salt</li> </ul>	2500 - 50000	Handbook of Pharmaceutical Excipients 6 <sup>th</sup> Editions,	Lubricant



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
<b>APPENDIX 3</b>			<ul style="list-style-type: none"> <li>- stearic acid</li> <li>- magnesium salt.</li> <li>- Dibasic magnesium stearate</li> <li>- Magnesium distearate</li> <li>- Magnesii stearas</li> <li>- Synpro 90</li> </ul>		2009 p 404-407	
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 34 <sup>th</sup> CAC (2012)	As phosphorus.
7	Polydimethylsiloxane	900a	<ul style="list-style-type: none"> <li>- Dimethylpolysiloxane</li> <li>- Dimethylsilicone fluid</li> <li>- Dimethylsilicone oil</li> <li>- Poly(dimethylsiloxane)</li> </ul>	50	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
8	Polyethylene glycol	1521	<ul style="list-style-type: none"> <li>- Macrogol</li> <li>- PEG</li> </ul>	70,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
9	Polyoxyethylene (20) sorbitan monolaurate	432	- Polysorbate 20	25,000	Codex GSFA Provisions	



Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
<b>APPENDIX 3</b>					updated up to 34 <sup>th</sup> CAC (2012)	
	Polyoxyethylene (20) sorbitan monooleate	433	- Polysorbate 80	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	Polyoxyethylene (20) sorbitan monopalmitate	434	- Polysorbate 40	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	Polyoxyethylene (20) sorbitan monostearate	435	- Polysorbate 60	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
	Polyoxyethylene (20) sorbitan tristearate	436	- Polysorbate 65	25,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	
10	Polyvinyl alcohol	1203	- PVOH - Vinyl alcohol polymer	45,000	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	Coating agent, Stabilizer
11	Potassium citrate	6100-05-6 / 866-84-2	- Citrate of potash - Citric acid potassium salt - E332 - Tripotassium citrate	3,000-20,000	Handbook of Pharmaceutical Excipients 6th Editions, 2009	Alkalizing agent Buffering agent Sequestering agent.



Guiding Principles for the Use of Additives and Excipients in Traditional Medicines and Health Supplements

Item	Common name	INS No./ CAS No.	Synonym(s)	Limit (mg/kg product)	Reference (Scientific rational and/or technical reference)	Note
			monohydrate - Kalii citras		p 574-576	
12	Sucroglycerides	474	-	2500	Codex GSFA Provisions for Food Category 13.6 updated up to 34 <sup>th</sup> CAC (2012)	