Association of South East Asian Nations (ASEAN)

ANNEX III

ASEAN GUIDELINES ON LIMITS OF CONTAMINANTS 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.

Version 2.0

DOCUMENT INFORMATION

This version is adopted at the 27th ACCSQ TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS SCIENTIFIC COMMITTEE MEETING (ATSC) 1-2 June 2015, Kuala Lumpur, Malaysia and endorsed at the 23rd ACCSQ TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS PRODUCT WORKING GROUP (TMHSPWG) MEETING 4-5 June 2015, Kuala Lumpur, Malaysia.

Version No.	History of adoption and endorsement		Reasons for revision
	ATSC adoption date	TMHSPWG endorsement date	
1	18th ATSC Meeting 11– 14 March 2013	19th TMHSPWG Meeting 28-29 June 2013	-
2	27th ATSC Meeting 1-2 June 2015	23rd TMHSPWG Meeting 4-5 June 2015	• To include a table of "History of Changes" under "Document Information" • To replace "litre" to "L" and "ml" to "mL" • To amend the first paragraph under "Section 3.Pesticide Residues" • To remove "Task Force's " for examples of International guidelines/standards on pesticide residue

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Introduction

The ASEAN Guidelines on Limits of Contaminants for Health Supplements (HS) is developed by taking into consideration the safety and quality requirements of HS.

Other limits of contaminants may be reviewed and included into the guideline as deemed necessary.

In determining the limits of microbial contamination, the following was taken into consideration:

- The nature of the product whether it is a pure compound, an extract, raw material or its combination.
- The route of administration.
- The method of preparation, e.g boiling.

Objective

The objective of these guidelines is to provide specifications on the limits of heavy metals and microbial contaminants of the various dosage forms to ensure their quality and safety. These guidelines also provide guidance notes on the control of pesticides in HS.

ASEAN Limits of Contaminants for HS

1. Limit on heavy metals:

Maximum limit for heavy metals:

1.1. Lead: NMT 10.0 mg/kg or 10.0 mg/L (10.0ppm)

1.2. Arsenic: NMT 5.0 mg/kg or 5.0 mg/L (5.0ppm)*

1.3. Mercury: NMT 0.5 mg/kg or 0.5 mg/L (0.5ppm)

1.4. Cadmium: NMT 0.3 mg/kg or 0.3 mg/L (0.3ppm)

Note: *Due to special circumstances such as national regulatory requirement, the limits of arsenic in the Philippines is 0.3 mg/kg or 0.3 mg/L (0.3 ppm)

2. Limit for Microbial Contaminations

The limit used is based on British Pharmacopoeia (2013). Hence, the specifications may change as required according to the compendium requirements from time to time.

The list is not necessarily exhaustive and for a given preparation, it may be necessary to test for other micro-organisms depending on the nature of the starting materials and in the manufacturing process.

Test for Microbial Contamination

Table I Microbiological Quality of Health Supplement (not applicable to products containing viable microorganisms as active ingredients)

Route of Administration	Acceptable criteria for microbiological quality		
	TAMC (CFU/g or CFU/ mL)	TYMC (CFU/g or CFU/ mL)	Specified Microorganisms
For Oral Use			
A. Health supplement products containing material of plant origin, with or without excipients, intended for the preparation of infusions and decoctions using boiling water (for example herbal teas, with or without added flavourings)	NMT 5×10^7	NMT 5×10^5	- NMT 10^3 CFU of *Escherichia coli* in 1g or 1mL - Absence of *Salmonella* in 25g or 25mL
B. Health supplement products containing materials of plant origin, with or without excipients, where the method of processing (for example, extraction) or pre-treatment reduces the levels of organisms to below those stated for this	NMT 5×10^4	NMT 5×10^2	- NMT 10^2 CFU of bile-tolerant gram-negative bacteria in 1g or 1mL - Absence of *Escherichia coli* in 1g or 1mL

category			- Absence of *Salmonella* in 25g or 25mL
C. Health supplement products containing materials of plant origin, with or without excipients, where it can be demonstrated that the method of processing (for example, extraction with low strength ethanol or water that is not boiling or low temperature concentration) or, of pre-treatment, would not reduce the level of organisms sufficiently to reach the criteria required under B	NMT 5×10^5	NMT 5×10^4	- NMT 10^4 CFU of bile-tolerant gram-negative bacteria in 1g or 1mL - Absence of *Escherichia coli* in 1g or 1mL - Absence of *Salmonella* in 25g or 25mL
D. Health supplement products containing materials of natural (animal, plant or mineral) origin for which antimicrobial pre-treatment is not feasible and for which the competent authority accepts TAMC of the raw material exceeding 10^3 CFU/gram or CFU/mL	NMT 2×10^4	NMT 2×10^2	- NMT 10^2 CFU of bile-tolerant gram-negative bacteria in 1g or 1mL - Absence of *Salmonella* in 10g or 10mL - Absence of *Escherichia coli* in 1g or 1mL - Absence of *Staphylococcus aureus* in 1g or 1mL
E. Aqueous preparations which does not fall under category A, B, C or D	NMT 2×10^2	NMT 2×10	- Absence of *Escherichia coli* in 1g or 1mL

F. Non-aqueous preparations which does not fall under category A, B, C or D	NMT 2 x 10^3	NMT 2 x 10^2	- Absence of *Escherichia coli* in 1g or 1mL

Not all member states will allow all the route of administration mentioned above

The limits for microbial contamination for Health Supplements with routes of administration not specified above shall be determined by the regulatory authority of each Member State.

3. Pesticide Residues

The safety and quality of plant materials and finished products containing materials of plant origin have become a major concern for health authorities, pharmaceutical industries and the public. Undesirable and/or undeclared substances have been present or have been purported to be present in plant materials or products containing materials of plant origin in many parts of the world. These substances have included pesticides, radioactive particles, microbes including pathogens, mycotoxins and heavy metals.

The control on pesticides will not be on finished products as:

- the risk is very low due to the small unit size and also the dilution effect from other non-pesticide containing ingredients and excipients.
- pesticides are internationally regulated and there are global harmonizations on regulations currently in process.
- currently no other economic bloc has regulations on pesticide residues in health supplements

The onus is on the suppliers of raw materials and manufacturers of HS products to ensure that the raw materials supplied and used comply with the law.

The control of pesticide residues in raw materials should be covered under Good Agriculture Practice (GAP).

Emphasis is on the raw material supply and reliance is thus placed on horizontal legislation rather than vertical legislation.

Recommendations

Pesticide Residue limits should remain under review and if conditions change in the future, for example, from post marketing surveillance data, a new assessment for the need of the limits for the finished product can be conducted, taking into consideration international guidelines/standards.[1]

Steps to be taken by each member country on pesticide control:

1. To promote closer cooperation and liaison between Ministry of Health and the ministries responsible for control of pesticides and GAP in agricultural products (in most countries it will be the Ministry of Agriculture).

2. To reinforce, during GMP training on the need for manufacturers to be responsible and not to accept raw materials that do not comply with applicable pesticide residue limits.

GLOSSARY

NMT Not More Than

TAMC Total Aerobic Microbial Count

TYMC Total Combined Yeasts/Moulds Count

CFU Colony Forming Unit

[1] Below are examples of International guidelines/standards on pesticide residues for reference:

A. WHO has suggested that the limits for pesticide residues to be established following the recommendations of the Food and Agriculture Organization of United Nations and WHO for food and animal feed. Analytical methodology for the assessment of specific pesticides residues for medicinal plant materials are described in the WHO guidelines on QC methods for medicinal plants.

B. EMEA guideline on specifications; test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products (CPMP/QWP/2820/00 Rev 1). The guideline states that where possible, the limit of pesticide residues should be controlled at the herbal substance and/or herbal preparations (e.g. extraction) level.

C. BP has established limits for pesticide residues in herbal drug (i.e. whole, fragmented, or cut plants parts of plants, algae, fungi or lichen, in an unprocessed state, usually in dried form but sometimes fresh). USP also has established analytical methods and limits for pesticide residues in articles of botanical origin.