Association of South East Asian Nations (ASEAN)

ANNEX X
ASEAN GENERAL PRINCIPLES FOR ESTABLISHING MAXIMUM LEVELS OF VITAMINS AND MINERALS IN HEALTH SUPPLEMENTS

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Version 4.0

DOCUMENT INFORMATION

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Version No.	History of adoption and endorsement		Reasons for revision
	ATSC adoption date	TMHSPWG endorsement date	
1	5th ATSC Meeting 29 Jul 2009		-
2	11th ATSC Meeting 27-28 Jun 2011		Inclusion of the paragraph "*The ASEAN MLs are not intended to be used as the levels of vitamins and minerals in health supplements that would bring beneficial effects to the ASEAN populations* " under Purpose & the exclusion of fluoride from the list of minerals under Scope
3	12th ATSC Meeting 19-21 Sep 2011	16TH TMHSPWH Meeting 17-18 Nov 2011	Addition of Clause 2f "*Despite the establishment of the ASEAN MLs of vitamins and minerals, Member States may consider exemption in their countries under special circumstances such as national requirements based on country exposure assessment/ consumption survey or product type classification. Such exemption with reasons should however be made known to the other Member States*" under Scope
4	15th ATSC Meeting 25-27 Jun 2012	18TH TMHSPWG Meeting 15-16 Nov 2012	Addition of Appendix 1on the established values of ASEAN maximum levels of vitamins and minerals in health supplements that includes explanatory notes on the conditions of use of vitamin K, the reasons of the non-establishment of maximum levels of Potassium and Fluoride as well as the country specific maximum levels of certain vitamins and minerals.

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PURPOSE

The main purpose of establishing maximum daily intake levels of vitamins and minerals in health supplements for ASEAN ("ASEAN ML") is to ensure manufacturers only include safe levels of vitamins and minerals in their health supplement products so that the normal use of the products under the instructions of use provided by the manufacturers will be safe for the consumers. The ASEAN MLs are not intended to be used as the levels of vitamins and minerals in health supplements that would bring beneficial effects to the ASEAN populations.

SCOPE

The following vitamins and minerals widely found in health supplements may be considered for the establishment of ASEAN ML:

Vitamins	**Minerals**
Vitamin A (Retinol)	Calcium
Vitamin D	Potassium
Vitamin E	Phosphorous
Vitamin K	Magnesium
Vitamin C	Boron
Vitamin B1	Chromium
Vitamin B2	Copper
Vitamin B6	Fluoride
Folic acid	Iodine
Vitamin B12	Iron
Biotin	Manganese
Nicotinic acid	Molybdenum
Nicotinamide	Selenium
Pantothenic acid	Zinc

Only one set of ASEAN ML should be developed for the normal healthy adult population. As far as possible, the needs of specific population groups should be factored into the setting of ASEAN ML. If this is not possible, the needs of these subgroups could be addressed by a more targeted approach through labelling or by individual dietary advice provided by qualified health professionals. ASEAN ML for children should be developed in a more targeted approach after the development of the ASEAN ML for adults.

The establishment of ASEAN ML should consist of Risk Assessment and Risk Management. The Risk Assessment component involves the derivation of upper limit (UL) of a nutrient based on the WHO Model. The Risk Management component involves managing the risk of population intake exceeding UL when deriving ASEAN ML based on the ERNA Model.

The WHO Model has limited applicability in the derivation of UL of a vitamin or mineral that has no reported adverse effects. If there is no basis for an UL because there is no evidence of adverse effects for that particular vitamin or mineral, the Highest Observed Intake (HOI), as defined in the WHO Model, should be identified.

There is no scientific basis for the use of RDA/RDIs in establishing ULs. The RDA/RDI is a measurement of nutritional adequacy and not a measurement of health risk due to excess intake. When the maximum levels are set, due account may be taken of the reference intake values of vitamins and minerals for the population as outlined in the ERNA Model. This provision should not lead to setting of maximum levels that are solely based on RDA/RDI.

Despite the establishment of the ASEAN MLs of vitamins and minerals, Members States may consider exemption in their countries under special circumstances such as national requirements based on country exposure assessment/ consumption survey or product classification type. Such exemptions with reasons should however be made known to the other Member States.

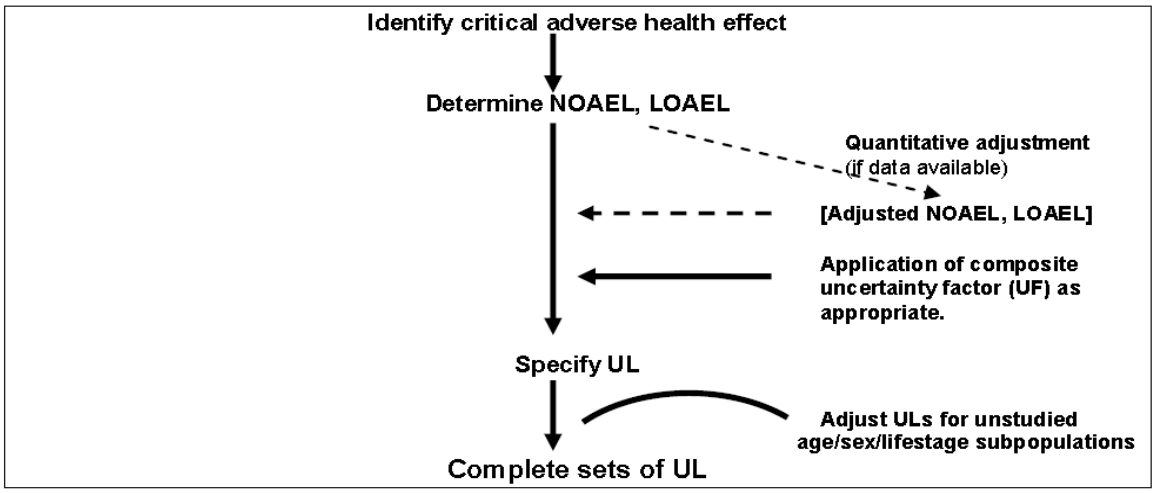
GUIDING PRINCIPLES

1. PRINCIPLES FOR ESTABLISHING UPPER LIMIT (UL) BASED ON WHO MODEL

1.1. The model for nutrient risk assessment developed by the Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment 2006[1] ("WHO Model") should be

used as the guiding principle in the development of UL. In this context, consideration of existing reports by authoritative scientific bodies i.e. EFSA, EVM and IOM (EFSA, 2006[2] ; EVM, 2003[3] ; IOM, 1997[4] ,1998[5] , 2000[6] , 2001[7]) that had incorporated some or all of the principles of the WHO Model in their nutrient risk assessments would be informative to the development of the UL.

1.2. The UL should be derived by following the steps of quantifying UL outlined in the WHO Model i.e. identifying the critical adverse effects of the nutrient, choosing the decisive scientific data upon which LOAEL or NOAEL is based, deciding on the value of UF to assign and finally calculating UL using the formula (NOAEL ÷ UF) or (LOAEL ÷ UF). The following is a schematic representation of the steps taken from Figure 4-3 in page 40 of WHO (2006).



1.3. For the purpose of accelerating the establishment of UL, the selection of parameters to be used in the derivation of the UL, namely critical adverse effects, decisive data, LOAEL or NOAEL and UF, can be based on the data already established by EFSA, EVM and IOM and if necessary, adjusted by newly available scientific data. The newly available scientific data should be obtained from widely recognized, authoritative, established references which have been published or peer reviewed.

1.4. UL should be derived from maximum supplement intake data wherever possible. UL can also be derived from maximum total dietary intake data if there are no relevant maximum supplement intake data. If food consumption data showed that the contributions of a specific vitamin or mineral from food were a significant

fraction of the UL, the food intake data should be deducted to calculate the ASEAN ML for health supplements.

1.5. The rationale for the determination of each parameter used in the derivation of UL for each vitamin and mineral should be scientifically sound and properly documented. The tabulation of comparative data from EFSA, EVM and IOM and the final set of data chosen for the derivation of UL accompanied by appropriate justification/explanation in a table format for each vitamin and mineral is deemed sufficient for this purpose.

2. PRINCIPLES FOR ESTABLISHING MAXIMUM LEVEL (ML) BASED ON ERNA MODEL

2.1. The model for nutrient risk management developed by ERNA ("ERNA Model")8 should be used as the guiding principle in the development of ASEAN ML.

2.2. Following the derivation of UL, the nutrients should be divided three groups according to the risk of population intakes exceeding UL. Group A is for nutrients that do not have reported adverse effects and there is no risk of excessive population intakes causing human health problems. Whereas Group B and C are for nutrients with reported adverse effects. Group B is for nutrients with a low risk whereas Group C is for nutrients with a potential risk of excessive population intakes causing human health problems.

2.3. PSI, which is a measurement of the safety margin between the maximum level from supplementation and population intake from food of a particular nutrient, should be used to assign nutrients to Group B or C. Nutrients with PSI of more than 1.5 (i.e. higher safety margin) are assigned to Group B and those with PSI of equal or less than 1.5 (i.e. lower safety margin) are assigned to Group C.

Adverse Effects	**Risk Categorization of Nutrients**	**PSI**	**Risk of Excessive Intakes Causing Human Health Problems**
None reported	Group A	-	None
Reported	Group B	> 1.5	Low
	Group C	<= 1.5	Potential

The following formula should be used for the calculation of PSI of nutrients with reported adverse effects.

PSI = (UL – MHI) ÷ RLV

To enable the calculation of PSI, the MHI and the RLV of these nutrients must be established. MHI should refer to the mean of highest intakes of a nutrient from foods (e.g. at 95 or 97.5 percentile) whereas RLV should refer to the labeling RDA of that nutrient which is being used as a surrogate of the desired population intake. Appropriate foreign MHI or RLV values should be considered in the absence of credible data from ASEAN countries. All MHI and RLV values should be reviewed periodically.

2.4. The following formulas may be used to establish ASEAN ML:

ASEAN ML of Group A nutrients = HOI ÷ UF – MHI

ASEAN ML of Group B nutrients = UL – MHI

ASEAN ML of Group C nutrients = UL – MHI

However, appropriate risk management measures proportionate to the relative risk associated with each risk group of nutrients should be taken when using these formulas to establish the respective ASEAN ML.

For nutrients that have no established hazards at high intakes, their maximum intake levels with sufficient evidence of safety (observed safe level) may be used to establish ASEAN ML.

Special effort must be taken in the derivation of the ASEAN ML for Group C nutrients to minimize the chance of exceeding UL. In addition, appropriate risk communication can be instituted for certain Group C nutrients on a case-by-case basis if necessary.

ASEAN MAXIMUM LEVELS

The list of established ASEAN maximum levels of vitamins and minerals appears as Appendix 1.

GLOSSARY

EFSA	European Food Safety Authority (European Union)
ERNA	European Responsible Nutrition Alliance
EVM	Expert Group on Vitamins and Minerals (United Kingdom)
FAO	Food and Agriculture Organization of the United Nations
HOI	Highest Observed Intake
IOM	Institute of Medicine, National Academies of Science (United States of America and Canada)
LOAEL	Lowest Observed Adverse Effect Level
MHI	Mean Highest Intakes (the mean of highest intakes of a nutrient from foods at 95 or 97.5 percentile)
ML	Maximum Level (a risk management value for the highest safe intake level of Vitamins and Minerals in Health Supplements in a population)
NOAEL	No Observed Adverse Effect Level
PSI	Population Safety Index
RDA	Recommended Dietary Allowance
RDI	Recommended Dietary Intake
RLV	Reference Labelling Value
UF	Uncertainty Factor
UL	Upper Limit (a risk assessment value for no adverse effects)
WHO	World Health Organization

REFERENCES

1. Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment. *A model for establishing upper levels of intake for nutrients and related substances*. Geneva: World Health Organization, 2006.

2. Scientific Committee on Food and Scientific Panel on Dietetic Products, Nutrition and Allergies. *Tolerable Upper Intake Levels for Vitamins and Minerals. Parma*: European Food Safety Authority, 2006.

3. Expert Group on Vitamins and Minerals. *Safe Upper Levels for Vitamins and Minerals*. London: Food Standards Agency, 2003.

4. Institute of Medicine. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: The National Academies Press, 1997.

5. Institute of Medicine. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. Washington, DC: The National Academies Press, 1998

6. Institute of Medicine. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: The National Academies Press, 2000.

7. Institute of Medicine. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: The National Academies Press, 2001.

8. Scientific Advisors to ERNA and EHPM. *Vitamin and mineral supplements: a risk management model*. Brussels: European Responsible Nutrition Alliance, 2004.

Appendix 1 ASEAN MAXIMUM LEVELS OF VITAMINS AND MINERALS IN HEALTH SUPPLEMENTS

Vitamin A (Retinol)	1.5 mg/day (5000 IU/day)
Vitamin D	0.025 mg/day (1000 IU/day)
Vitamin E	536 mg/day (800 IU/day)
Vitamin K	0.12 mg/day
Vitamin C	1000 mg/day
Vitamin B1	100 mg/day
Vitamin B2	40 mg/day
Vitamin B6	100 mg/day
Folic acid	0.9 mg/day
Vitamin B12	0.6 mg/day
Biotin	0.9 mg/day
Nicotinic acid	15 mg/day
Nicotinamide	450 mg/day
Pantothenic acid	200 mg/day
Calcium	1200 mg/day
Phosphorous	800 mg/day
Magnesium	350 mg/day
Boron	6.4 mg/day
Chromium	0.5 mg/day
Copper	2 mg/day
Iodine	0.15 mg/day
Iron	15 mg/day
Manganese	3.5 mg/day
Molybdenum	0.36 mg/day
Selenium	0.2 mg/day
Zinc	15 mg/day

Notes:

1. The conditions of use of Vitamin K are as follows:

Application:	For use in oral dosage form of multivitamin/mineral preparations for adults and not as a single ingredient health supplement
Vitamin K form:	Only Vitamin K1 and/or Vitamin K2
Cautionary statement:	"Consult a health care practitioner prior to use if you are on anticoagulant therapy/taking blood thinners such as warfarin"

2. The maximum levels of Potassium and Fluoride in health supplements are not established. These minerals can be used in health supplements subject to the approval of the national regulatory authority.

3. However, due to special circumstances such as national requirements based on country exposure assessment/consumption survey or product classification type, the established maximum levels of Vitamin A, Vitamin D, Vitamin E, Vitamin K, Vitamin B6, Folic acid, Nicotinamide, Calcium, Boron, Iodine, Iron, Molybdenum and Selenium are not applicable to the Member States listed below. Some national maximum levels of Member States are shown in parenthesis.

Vitamin A	: Thailand(0.8 mg/day)
Vitamin D	: Indonesia Thailand(0.005 mg/day)
Vitamin E	: Indonesia Thailand(10 mg/day)
Vitamin K	: Thailand(0.08 mg/day)
Vitamin B6	: Thailand(2 mg/day)
Folic acid	: Thailand(0.2 mg/day)
Nicotinamide	: Thailand(20 mg/day)
Calcium	: Thailand(800 mg/day)
Boron	: Thailand
Iodine	: Malaysia(0.3 mg/day) Thailand
Iron	: Indonesia Malaysia(20 mg/day*)
Molybdenum	: Thailand(0.16 mg/day)
Selenium	: Thailand(0.07 mg/day)

**For pre and antenatal use, as part of a multivitamin and mineral preparation, levels higher than the 20 mg limit established for adults may be permitted at the discretion of the DCA.*