



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

# ANNEX VI ASEAN GUIDING PRINCIPLES ON SAFETY SUBSTANTIATION OF TRADITIONAL MEDICINES

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*Disclaimer:*

*This document is provided for information purpose only and subject to changes, pending the finalisation of the ASEAN Agreement on Regulatory Framework for Traditional Medicines. Official references to this document can only be made once the said Agreement has been finalised.*



## DOCUMENT INFORMATION

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## INTRODUCTION

Natural resources (plants, animals or natural minerals) are widely used in the formulation of traditional medicines.

Most ingredients might be considered as safe, considering the experience or history of use of TM products. When an ingredient is well known for a specific use, the assessment may be limited to published data (including traditional references). However, under certain conditions, additional data will be required to prove the safety of the product, e.g. for a new ingredient or a new combination.

## OBJECTIVES

This document aims to provide guiding principles for safety substantiation of traditional medicines.

## GUIDING PRINCIPLES

Data to substantiate the safety of the following products shall be required

- (a) Products with new ingredient(s).
- (b) Products with ingredient(s) derived from new method(s) of purification, extraction or manufacturing.
- (c) Existing products with new combination, new dosage, new delivery system or use in special or new target population (e.g. pregnant, lactating women, children).
- (d) Existing products with safety concern. Safety concern may be newly emerging or established, and in some cases may need additional information to support safe usage in traditional medicines.

However, safety substantiation may not be necessary, for the following products, unless required by the Regulatory Authority,

- Products that do not fall under items (a), (b), (c), (d) mentioned above
- Products containing ingredient/s with lower dosage than the existing ones,



- Traditional medicines with a documented history of safe use/well established safety profile.

Safety substantiation shall be based on finished product or ingredient(s), with justification as required by the regulatory authority (e.g. rationale of combination).

The safety data that will be required to substantiate the safety of a product should be relevant, and commensurate with the nature or character of the ingredient or product in line with the intended use.

The safety information should include the following:

#### **History of use**

Ingredients with a known history of human consumption evidences (e.g. documented history of use, authoritative reference texts) may be considered for safety substantiation. In the case when the anticipated intake of this ingredient is significantly higher than the estimated historical intake, or for which the historical intake cannot be assessed, additional safety data may be required; and/or

#### **Scientific evidence on safety**

Safety data, including toxicity data, could be derived from animal and/or human studies using internationally accepted methodologies such as WHO or OECD guidelines. Acute, sub-chronic and/or chronic toxicity data may be required, however expected duration of product usage may determine the types of toxicity study. Other toxicity data such as teratogenicity, carcinogenicity, and/or mutagenicity data may be required, when necessary.

Notwithstanding the above requirements, other form(s) of scientific explanation to substantiate the safety of a product may be submitted. Furthermore, any available information on safety data from animal / human studies; reports of adverse events, safety alerts, post marketing study and epidemiological data, should be submitted.



## GLOSSARY

### **New Ingredient**

New ingredient refers to traditional medicines active ingredient/substance that has never been used in the respective ASEAN Member State.

### **New Delivery System**

New Delivery System involves a change in the method of administration and/or the dosage form of an existing traditional medicine in the respective ASEAN Member State.

### **New Combination**

A new combination product is when no product of the same active ingredients has been approved for marketing in the respective ASEAN Member State

### **New Dosage**

New Dosage refers to the quantity of active ingredients/substances administered per dose or per day that is different from the administered per dose or per day currently used for the approved product in the respective ASEAN Member State



## REFERENCES

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