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GUIDELINES ON PHYSICAL TEST PARAMETERS FOR DOSAGE FORMS OF HEALTH SUPPLEMENTS AND TRADITIONAL MEDICINES

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1. Introduction

- 1.1 Dealers of Health Supplements (HS) and Traditional Medicines (TM) are required to ensure that their products are safe and conform to the applicable safety and quality standards.
- 1.2 The objective of these guidelines is to provide guidance on the physical test parameters for the different dosage forms in the finished products to ensure they consistently meet the required standards throughout the product life cycle.

2. Physical Test Parameters

- 2.1 A dosage form is defined as the physical form of a dose of a product which is intended for oral or topical administration. Each dosage form contains a single or mixed combination of the active components and other substances, e.g., additives or excipients, in a formulation (see Appendix 1).
- 2.2 The key functions of dosage forms are to:
 - a. Protect the product contents from degradation or deterioration, such as oxidation, hydrolysis, or reduction.
 - b. Provide safe and convenient delivery of the product contents.
 - c. Improve taste or conceal odour of the product contents.
- 2.3 Essential test parameters are as follows:
 - 2.3.1 **Disintegration** determines the rate and extent of the product contents to disintegrate within the prescribed time when placed in a liquid medium under stipulated test conditions. Complete disintegration is defined as that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the test apparatus or adhering to the lower surface of the disk (if used) is a soft mass having no palpably firm core.
 - 2.3.2 **Dissolution** is a test to measure the rate and extent of the release of the intended substance(s) from the product to form a solution under controlled conditions, i.e. if the compound(s) for a botanical is dissolved within the time frame and under specified conditions.

- 2.3.3 **Hardness** is a type of in-process control which routinely measures the mechanical integrity of the dosage form, i.e., the force that cause breakage(s). Interpretation of the hardness of the dosage form must consider the mean value and consistency of the test results for multiple dosage units. The resultant range of values provides valuable information on the consistency of the manufacturing process.
- 2.3.4 **Friability** measures the resistance of the dosage form to chipping and surface abrasion during manufacturing, handling, and transportation. Chipping and abrasion can each have a significant impact upon the success of subsequent manufacturing operations such as coating and packaging and impact the consumer's expectation of the final dosage form.
- 2.3.5 **pH** of liquid oral products (i.e., aqueous formulations) is susceptible to changes from exposure to atmospheric carbon dioxide (CO₂), which can affect the flavour and stability of the contents of the finished products.
- 2.3.6 **Uniformity of Dosage Units** measures how evenly distributed the active substances are distributed in the product, which can also be demonstrated by the content uniformity or mass variation.
- **Content uniformity** is based on the assay of the contents of active substances in a number of dosage units to determine whether the individual contents are within the set limits.
 - **Mass variation / Weight Variation / Filling variation** is applicable for solids (including powders, granules, etc) that are packaged in single-unit containers or capsules, tablets, or liquid contents enclosed in unit-dose containers or soft capsules.

- 2.4 The following test parameters for the different dosage forms should be conducted and the test results to be documented in the reports:

DOSAGE FORMS		RECOMMENDED TEST PARAMETERS
ORAL / INTERNAL USE	CAPSULES	1. Disintegration or Dissolution 2. Uniformity of dosage units
	TABLETS	1. Disintegration or Dissolution* 2. Hardness or friability 3. Uniformity of dosage units
	PILLS	1. Disintegration or Dissolution 2. Uniformity of dosage units
	POWDER	1. Particle size variation 2. Uniformity of dosage units
	GRANULES	1. Disintegration or Dissolution 2. Particle size variation 3. Uniformity of dosage units (single-unit containers)
	GELS / PASTILLES / GUMMIES	1. Disintegration or Dissolution 2. Uniformity of dosage units
	TEABAGS	1. Uniformity of dosage units
	LIQUIDS	1. Uniformity of dosage units 2. pH (for aqueous-based products) 3. Ethanol and/or methanol (if applicable) 4. Preservatives (if applicable) 5. Sucrose content (if applicable)
TOPICAL / EXTERNAL USE	CREAMS, GELS, LOTIONS, OINTMENTS PASTES, PLASTERS PATCHES	1. Uniformity of dosage units

* Not applicable to chewable tablets

- 2.5 The appropriate testing methods and permissible limits are found in the established international pharmacopeias, e.g., British Pharmacopeia (BP), Chinese Pharmacopeia (ChP), European Pharmacopeia (EP), Japanese Pharmacopeia (JP) and United States Pharmacopeia (USP).
- 2.6 The products should meet the acceptance criteria stated in recognised pharmacopoeias. Should these standards be unavailable, the acceptance criteria and test methods for the test parameters may be determined by the manufacturer/product owner. The acceptance criteria and the test method used should be included in the test reports.

- 2.7 Other acceptable references for test methods are:
- American Herbal Pharmacopoeia (AHP)
 - Association of Official Analytical Chemist International: Official Methods of Analysis
 - Microbiological: Food & Drug Administration Bacteriological Analytical Manual
 - WHO – Quality Control Methods for Herbal Materials
 - Standard of ASEAN Herbal Medicines (SAHM) Volume I & II
 - International Organization for Standardization (ISO)
 - ICS 67 – Food Technology
 - ICS 67.050 – General methods of tests and analysis for food products
 - Food Chemical Codex (FCC)
 - Office of Dietary Supplement, National Institute of Health. US: Dietary Supplement Analytical Methods/Reference Materials (AMRM) Program
<http://ods.od.nih.gov/Research/AMRMProgramWebsite.aspx>
 - TLC Atlas of Chinese Crude Drugs in Pharmacopoeia of The People's Republic of China Vol. 1
- 2.8 Accredited or in-house methods validated according to the principles defined by ICH or ASEAN Guidelines on validation of analytical procedures are also acceptable.

3. References

- 3.1 British Pharmacopeia
- 3.2 Chinese Pharmacopeia
- 3.3 European Pharmacopeia
- 3.4 Japanese Pharmacopeia
- 3.5 United States Pharmacopeia
- 3.6 Natural Medicines Comprehensive Database
- 3.7 Martindale: The Complete Drug Reference
- 3.8 Micromedex Solutions, 2017 Truven Health Analytics Inc
- 3.9 Physicians' Desk Reference (PDR) for Herbal Medicines
- 3.10 ASEAN Guidelines on Good Manufacturing Practice for Traditional Medicines
- 3.11 ASEAN Guidelines on Good Manufacturing Practice for Health Supplements

Appendix 1 - Common Dosage Forms

Oral Preparations

- a) Capsules** Solids, liquids or paste-like contents that consist of one or more active substances with or without excipients, e.g., solvents, diluents, lubricants and disintegrating agents filled in shells of various shapes and capacities.
- Examples of capsules:
Hard shell capsules, softgel capsules, and modified release capsules
- b) Granules** Preparations consisting of solid, dry aggregate of powder particles.
- Examples of granules:
Coated granules, effervescent granules, extended-release granules, and delayed-release granules
- c) Powders** Oral powders preparations consisting of solid, loose, dry particles of varying degrees of fineness.
- d) Pills** Spherical or quasi-spherical solid preparations which are made of raw materials and suitable excipient materials.
- e) Tablets** Solid preparations consisting of compressed uniform volumes of particles.
- Examples of tablets:
Caplets, chewable tablets, coated and uncoated tablets, effervescent tablets, lozenges
- f) Liquids (Oral)** Presented as solutions, suspensions, emulsions or tinctures. A solution refers to a clear liquid preparation made by dissolving the raw materials in a suitable solvent, while an oral suspension refers to a liquid preparation made by dispersing poorly soluble solid raw materials in a liquid medium. An oral emulsion is an oil-in-water liquid preparation made of two immiscible liquids for oral administration. The product contents may contain excipients such as dispersing, suspending, thickening, and emulsifying agents. Tinctures are liquid preparations obtained by extracting or dissolving raw materials with suitable solvents such as ethanol and glycerol.

- g) Teas** Refers to crushed pieces, powder or granules of herbal materials contained in a bag for decoction, with or without appropriate excipients that are intended for preparation as solutions before use.
- h) Gels/ Pastilles / Gummies** Solid or semi-solid dosage form consisting of gelling agent(s), sugars, water, sweeteners, and flavouring agents to enhance consumer acceptance and mask the taste of the ingredients.

Topical Preparations

- a) Creams** Semi-solid preparations formed by dissolving or dispersing the active substances uniformly in an emulsion type matrix. There are two main types of creams, i.e., lipophilic creams usually contain water-in-oil emulsifying agents such as wool alcohols, sorbitan esters and monoglycerides, whereas hydrophilic creams contain oil-in-water emulsifying agents, e.g., sodium or trolamine soaps, sulphated fatty alcohols, polysorbates, etc.
- b) Gels** Thick liquid or semi-solid preparations using a gel matrix. A gel matrix is a single-phase dispersion system, which is divided into water and oil. The hydrophilic gels (hydrogels) are generally composed of water, glycerine or propylene glycol and cellulose derivatives, gelatin or starch, whereas the lipophilic gels are preparations whose bases usually consist of liquid paraffin with polyethylene or fatty oils gelled with colloidal silica or aluminium or zinc soaps.
- c) Liquids (topical)** Liquid preparations consisting of raw materials with suitable solvents to be applied on the skin.
- d) Ointments** Uniform semi-solid external preparations consisting of raw materials with an oily or water-soluble base. Typical bases used for the formulation are hard, liquid and light liquid paraffin, vegetable oils, animal fats, synthetic glycerides, waxes and liquid polyalkylsiloxanes.
- e) Pastes** Semi-solid preparations of stiff consistency composed of a large number of solid powders of raw materials uniformly dispersed in a suitable matrix intended for cutaneous application.

**f) Patches /
Plasters**

Semi-solid substance for external preparation that is applied on a support material. May consist of an adhesive layer that may contain active substances.

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