HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

JULY 2023

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

Guidelines Version 3

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1. Introduction

1.1. Dealers of health supplements (HS) and traditional medicines (TM), medicated oils, balms (MOB) and medicated plasters 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 products (i.e., aqueous formulations) is susceptible to changes from exposure to atmospheric carbon dioxide (CO2), which can affect the flavour, if applicable and stability of the contents of the finished products.

2.3.6. **Uniformity of Dosage Units** measures how evenly 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 content 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.

2.3.7. **Delivery rate** (for aerosols) is the amount of the product delivered in gram/second.

2.3.8. **Delivered amount** (for aerosols) is the total amount of product in a container.

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

DOSAGE FORMS		RECOMMENDED TEST PARAMETERS
ORAL / INTERNAL USE	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)
TOPICAL / EXTERNAL USE	CREAMS, GELS, LOTIONS, OINTMENTS PASTES, PLASTERS PATCHES	1. Uniformity of dosage units
	AEROSOLS, SPRAYS	1. Uniformity of dosage units (for metered dose) 2. Delivery rate (for non-metered dose) 3. Delivered amount (for non-metered dose)
	NASAL STICKS	1. Uniformity of dosage units

* Not applicable to chewable tablets; ** Not applicable for coated tablets. For non-coated tablets, hardness or friability may be included as part of in-process control testing.

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.

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 https://ods.od.nih.gov/Research/AMRMProgramWebsite.aspx
- TLC Atlas of Chinese Crude Drugs in Pharmacopeia 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. Physical Test Parameter Reports for Dosage Forms

3.1 Testing of physical parameters should be conducted on finished products. Product specification sheet or certificate of analysis on raw materials or intermediates may not be used to replace testing on finished products.

3.2 The test report should minimally contain the following information:

a) Date of report
b) Brand name (if applicable) and product name
c) Dosage form
d) Batch number
e) Physical test parameter(s), test result(s) and set specification(s)
f) Name and signature of analyst or person responsible

4. References

4.1 British Pharmacopeia

4.2 Chinese Pharmacopeia

4.3 European Pharmacopeia

4.4 Japanese Pharmacopeia

4.5 United States Pharmacopeia

4.6 Natural Medicines Comprehensive Database

4.7 Martindale: The Complete Drug Reference

4.8 Micromedex Solutions, 2017 Truven Health Analytics Inc

4.9 Physicians' Desk Reference (PDR) for Herbal Medicines

4.10 ASEAN Guidelines on Good Manufacturing Practice for Traditional Medicines

4.11 ASEAN Guidelines on Good Manufacturing Practice for Health Supplements

Appendix 1 - Common Dosage Forms

Oral Preparations for Internal Use

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 for External Use

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.
g) Aerosols, Sprays	Aerosols are liquid or solid preparations packaged under pressure and intended to produce a fine mist of particles or droplets. Sprays are non-pressurised liquid preparations that are intended for application as a mist to the intended area. An aerosol or spray may be metered or non-metered. In a metered dose aerosol or spray, a metering valve delivers an accurate volume of the product from the container.
h) Nasal Sticks	Solid preparations intended for inhalation by insertion into the nasal cavity.

Revision History

Version	Date of publication	Summary of changes*
1	March 2022	New document
2	July 2022	• Amended the test parameter 'Filling variation' to 'Uniformity of dosage units'. • Revised Appendix 1 to provide clarity on common dosage forms.
3	July 2023	• Included medicated oils, balms and medicated plasters. • Included new dosage forms aerosols, sprays and nasal sticks and their corresponding test parameters.

*Editorial changes are not reflected

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