Herbal Medicines Compendium

U.S. Pharmacopeial Convention

Herbal Medicines Compendium
General Notices
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The *General Notices* for the United States Pharmacopeial Convention's (USP) *Herbal Medicines Compendium* (*HMC)* presents the basic assumptions, definitions, and default conditions for the interpretation, application, and use of monographs provided in the *HMC*. Where the requirements of an individual monograph differ from these *General Notices* or any referenced or otherwise applicable general chapter, the monograph requirements apply and supersede the requirements of the *General Notices* or the general chapter, whether or not the monograph explicitly states the difference.

1. TITLE AND REVISION

The full title of this publication is the *Herbal Medicines Compendium* (*HMC*). Where the term "*HMC*" is used without further qualification, it refers only to authorized text posted at http://hmc.usp.org The text as presented is immediately and continuously effective and applicable, unless revised or otherwise specified.

2. SCOPE AND PURPOSE

HMC includes standards for herbal articles used in traditional medicines. Herbal articles, for the purpose of *HMC*, are herbal ingredients in their entire form as well as their processed forms (e.g., powders, extracts, fractions, not including isolated pure compounds). The *HMC* does not include animal-origin, synthetic chemical, or biotechnology-derived medicines.

The scope of herbal articles eligible for inclusion in the *HMC* is limited to articles that (1) are approved by a national authority for use as ingredients of herbal medicines, or are included in a national pharmacopeia; and (2) are deemed appropriate for inclusion in the *HMC* by a USP Expert Committee. USP's standard-development and admission decisions regarding an herbal article are performed for the sole purpose of determining quality criteria for the compendium and should not be relied upon as any finding about the intrinsic safety or effectiveness of the herbal article. USP does not endorse the safety of an herbal article in the *HMC* and does not provide dosage or other therapeutic information.

The purpose of *HMC* is to help assure that herbal articles that qualify for inclusion in *HMC* conform to the represented identity and are of good quality by providing up-to-date, relevant monograph standards including their specified USP Reference Standards. Taken together, these *HMC* standards are available to any interested party including manufacturers, suppliers, purchasers, and national pharmacopeias and regulatory authorities to demonstrate conformity of an herbal article to *HMC* standards through testing.

The *HMC*, including monographs, *General Notices*, and applicable general chapters is freely available at http://hmc.usp.org and may be further adopted or adapted without charge. A history of prior revisions to *HMC* monographs is provided in the "Related Monographs" sections of the website. USP reference materials for the *HMC* will be offered through the USP catalog.

3. THE *HMC* MONOGRAPH

Monographs in the *HMC* are authorized by a USP Expert Committee and are therefore deemed suitable for use. Authorized *HMC* monographs consist of introductory information followed by a specification that consists of tests, procedures, and acceptance criteria as well as additional requirements as needed. As there can be more than one procedure for a test in the *HMC* monograph, manufacturers should specify a single procedure in their certificate of analysis or equivalent document so that the analyst understands how to test the herbal article (see section 7. Demonstrating and Indicating Conformance). Manufacturers are encouraged to submit their alternative procedures with validation for evaluation by a USP Expert Committee for possible inclusion in *HMC* (see section 10.30 Alternative and Harmonized Methods and Procedures).

4. GENERAL CHAPTERS

A monograph in the *HMC* may incorporate by reference one or more general chapters. General chapters referenced in *HMC* monographs may include general chapters from the *United States Pharmacopeia–National Formulary* (*USP-NF*). General chapters specific to the *HMC* may also be developed and referenced. When a general chapter is referenced within a monograph, the number of the general chapter appears in angle brackets adjacent to the chapter name (e.g., <621> *Chromatography*). When a general chapter is referenced in a monograph, acceptance criteria may be presented after a colon or may be presented in the general chapter. Some general chapters may serve as introductory overviews of a test or of analytical techniques. They may reference other general chapters that contain techniques, details of the procedures, and, at times, acceptance criteria.

5. AUTHORIZED STATUS

HMC standards are authorized by the USP Council of Experts following the current effective version of the Rules and Procedures of the Council of Experts. An *HMC* monograph may rely on general chapters and other general text in the *USP–NF* as well as the *HMC General Notices* and general chapters. When referenced in an *HMC* monograph, this text is also considered authorized. USP reference materials cited in an *HMC* monograph also are authorized by a USP Expert Committee.

6. LEGAL RECOGNITION

If an *HMC* monograph or other related standard is adopted or adapted for use by an interested stakeholder (e.g. a manufacturer, or a national or regulatory

authority establishing a role for *HMC* in law, regulation etc.), it may become subject to enforcement depending on applicable national requirements.

7. DEMONSTRATING AND INDICATING CONFORMANCE

An herbal article is considered to be in conformance with an *HMC* monograph when (1) the name and identity conform to those provided in the *HMC* monograph, (2) the herbal article complies with the procedures in the *HMC*, and (3) is analyzed using USP Reference Standards specified in the *HMC* monograph. A manufacturer or supplier may label the herbal article "Herbal Medicines Compendium" or "HMC" if the article demonstrates conformance to *HMC* monograph requirements at any time during the shelf life provided a retest date or equivalent is indicated. If there are multiple procedures in a monograph then the certificate of analysis or equivalent document must indicate the particular procedure used. The designation "Herbal Medicines Compendium" or "HMC" does not constitute an endorsement by USP and/or represent assurance by USP that the herbal article is known to comply with all applicable requirements. When the designation "Herbal Medicines Compendium" or "HMC" is used on the label of an article to indicate conformance with *HMC* standards, the designation shall appear in conjunction with the authorized title of the article. The designation is not to be enclosed in any symbol such as a circle or a square. An article may only be designated "Herbal Medicines Compendium" or "HMC" with regard to the current applicable version of *HMC* standard or a directly adopted version; articles may not be designated "Herbal Medicines Compendium" or "HMC" with regard to standards adapted from *HMC*.

8. ACCEPTANCE CRITERIA

Acceptance criteria are numerical limits, ranges, or other suitable measures for acceptance of the results of analytical procedures. The acceptance criteria indicated in an *HMC* monograph allow for analytical error, for unavoidable variations in manufacturing, and for deterioration to an extent considered acceptable under practical conditions. Producing an article to stricter criteria than those specified in the monograph does not constitute the basis for a claim that the article "exceeds" the compendial requirements.

9. MONOGRAPH COMPONENTS

9.10. Added Substances

Added substances are presumed to be unsuitable for inclusion in an authorized article and therefore prohibited, if: (1) they exceed the minimum quantity required for providing their intended effect; (2) their presence affects the bioavailability, therapeutic efficacy, or safety of the article; or (3) they interfere with the assays and tests prescribed for determining compliance with *HMC* standards.

The air in a container of an article may, where appropriate, be evacuated or be replaced by carbon dioxide, helium, argon, or nitrogen, or by a mixture of these gases.

9.10.10. Added Substances, Excipients, and Ingredients in Authorized Herbal Articles

Suitable substances and excipients such as antimicrobial agents, pharmaceutical bases, carriers, flavors, preservatives, stabilizers, and vehicles may be added to an authorized herbal article to enhance its stability, usefulness, or to facilitate its preparation, unless otherwise specified in the individual monograph.

Authorized herbal articles may contain only the specific added substances that are permitted by the individual monograph, where feasible. Where such addition is permitted, the label shall indicate the name(s) and amount(s) of any added substance(s).

9.20. Nomenclature

HMC monograph title includes the Latin binomial, without the authority, followed by the plant part(s) and, where applicable, the type of processed form(s) subject of the monograph. The name of the plant part or processed form is expressed in English. If more than one species is represented in a monograph then the Genus name is used followed by the word "species" (or its abbreviation spp.), the plant part(s), and, where applicable, the type of processed form(s). A descriptor, such as geographical origin, may be included in cases where is there is a need to differentiate related monographs. The complete Latin binomial including the authority information is cited in the definition section of the monograph.

9.30. Identity

A section titled *Identification* is provided to establish the identity of articles as they are purported to be (e.g., those taken from labeled containers), and to establish whether they are the articles named in *HMC*. The *Identification* test for an herbal article may consist of one or more procedures. When a compendial test for identity is undertaken, all requirements of every specified procedure in the *Identification* test must be met to establish identity.

9.40. Assay

Assay tests are included for the determination of the composition of the article and conformance to the authorized *HMC* standard.

9.50. Contaminants and Foreign Substances

Tests for the presence of contaminants and foreign substances are provided to limit such substances to amounts that are unobjectionable under conditions in which the article is customarily employed. Procedures and acceptance criteria suitable for detecting and controlling contaminants that may result from a change in the processing methods or that may be introduced from external sources should be employed, where the presence of the contaminant is inconsistent with applicable GMPs.

9.60. Residual Solvents in *HMC* Articles

All *HMC* articles are subject to relevant control of residual solvents, even when no test is specified in the individual monograph. If solvents are used during production, they must be of suitable quality. In addition, the toxicity and residual level of each

solvent shall be taken into consideration, and the solvents limited according to the principles defined and the requirements specified in General Chapter <467> *Residual Solvents*, using the general methods presented therein or other suitable methods.

9.70. Reference Materials

Any reference materials included as a component of a monograph are authentic specimens that have been approved as suitable for use as comparison standards in *HMC* tests. Any "USP" Reference Standards referred to in a monograph means reference materials available from USP as indicated in its catalogue. Where a procedure calls for the use of a compendial article rather than for a USP Reference Standard as a standard of reference, an article meeting all of the compendial monograph requirements for that article shall be used. If any *HMC* monographs require the use of a new USP Reference Standard that is not currently available, that portion of the monograph containing the requirement shall not be required for compliance.

Unless otherwise directed in the procedure in the individual monograph or in a general chapter, USP Reference Materials are to be used in accordance with the applicable, available instructions on the label.

10. TESTING PRACTICES AND PROCEDURES

10.10. Safe Laboratory Practices

In performing compendial procedures, safe laboratory practices shall be followed, including precautionary measures, protective equipment, and work practices consistent with the chemicals and procedures used. Before undertaking any procedure described in *HMC*, the analyst should be aware of the hazards associated with the chemicals and the techniques and means of protecting against them. The *HMC* is not designed to describe such hazards or protective measures.

10.20. Automated Procedures

Automated and manual procedures employing the same chemistry are considered equivalent.

10.30. Alternative and Harmonized Methods and Procedures

Alternative methods and/or procedures may be used if they provide advantages in terms of accuracy, sensitivity, precision, selectivity, or adaptability to automation or computerized data reduction, or in other special circumstances. Such alternative procedures and methods shall be validated as described in the General Chapter <1225> *Validation of Compendial Procedures* and must be shown to give equivalent or better results. Only those results obtained by the methods and procedures given in the compendium are conclusive.

Alternative procedures may be submitted for evaluation by a USP Expert Committee as a potential replacement or addition to the monograph procedures (see section 3. The *HMC* Monograph).

Certain general chapters contain a statement that the text in question is harmonized with the corresponding text of the *European Pharmacopoeia* and/or the *Japanese Pharmacopoeia* and that these texts are interchangeable. Therefore, if an herbal article is found to comply with a requirement using an interchangeable method or procedure from one of these pharmacopeias, it should comply with the requirements of the *HMC*. When a difference appears, or in the event of dispute, only the result obtained by the method and/or procedure given in the *HMC* is conclusive.

10.40. Dried, Anhydrous, or Solvent-Free Basis

All calculations in the compendia assume an "as-is" basis unless otherwise specified.

Test procedures may be performed on the undried substance and the results calculated on the dried or anhydrous basis, provided a test for *Loss on Drying* or *Water Determination,* respectively, is given in the monograph. Where the presence of moisture or other volatile material may interfere with the procedure, previous drying of the substance is specified in the individual monograph and is obligatory.

The term "solvent-free" signifies that the calculation shall be corrected for the presence of known solvents as determined using the methods described in General Chapter <467> *Residual Solvents* unless a test for limit of organic solvents is provided in the monograph.

The term "previously dried" without qualification signifies that the substance shall be dried as directed under General Chapter <731> *Loss on Drying* or General Chapter <921> Water *Determination* (gravimetric determination).

Where drying in vacuum over a desiccant is directed, a vacuum desiccator, a vacuum drying pistol, or other suitable vacuum drying apparatus shall be used.

10.40.10. Dried To Constant Weight

"Dried to constant weight" means that drying shall be continued until two consecutive weighings, the second of which is taken after an additional drying period appropriate to the nature and quantity of the residue, do not differ by more than 0.50 mg/g of substance taken.

10.50. Preparation of Solutions

10.50.10. Filtration

Where a procedure gives direction to "filter" without further qualification, the liquid shall be passed through suitable filter paper or equivalent device until the filtrate is clear. Due to the possibility of filter effects, the initial volumes of a filtrate may be discarded.

10.50.20. Solutions

Unless otherwise specified, all solutions shall be prepared with *Purified Water, HMC*. Solutions for quantitative measures shall be prepared using accurately weighed or accurately measured analytes (see section 12.10, *About*).

An expression such as “(1 in 10)” means that 1 part by volume of a liquid shall be diluted with, or 1 part *by weight* of a solid shall be dissolved in, a sufficient quantity of the diluent or solvent to make the volume of the finished solution 10 parts by volume. An expression such as “(20:5:2)” means that the respective numbers of parts, by volume, of the designated liquids shall be mixed, unless otherwise indicated.

10.50.20.1. Adjustments to Solutions

When a specified concentration is called for in a procedure, a solution of other normality or molarity may be used; provided that allowance is made for the difference in concentration and that the change does not increase the error of measurement.

Unless otherwise indicated, analyte concentrations shall be prepared to within 10% of the indicated value. In the special case in which a procedure is adapted to the working range of an instrument, solution concentrations may differ from the indicated value by more than 10%, with appropriate changes in associated calculations. Any changes shall fall within the validated range of the instrument.

When adjustment of pH is indicated with either an acid or base and the concentration is not indicated, appropriate concentrations of that acid or base may be used.

10.60. Units Necessary to Complete a Test

Unless otherwise specified, a sufficient number of units to ensure a suitable analytical result shall be taken.

10.70. Reagents

The proper conduct of the compendial procedures and the reliability of the results depend, in part, upon the quality of the reagents used in the performance of the procedures. Unless otherwise specified, reagents conforming to the specifications set forth in the current edition of *Reagent Chemicals* published by the American Chemical Society (ACS) shall be used. Where such ACS reagent specifications are not available or where the required purity differs, compendial specifications for reagents of acceptable quality are provided (see the *Reagents, Indicators, and Solutions* section of *HMC*). Reagents not covered by any of these specifications should be of a grade suitable to the proper performance of the method of assay or test involved.

10.80. Equipment

Unless otherwise specified, a specification for a definite size or type of container or apparatus in a procedure is given solely as a recommendation. Other dimensions or types may be used if they are suitable for the intended use.

10.80.10. Apparatus for Measurement

Where volumetric flasks or other exact measuring, weighing, or sorting devices are specified, this or other equipment of at least equivalent accuracy shall be employed.

10.80.10.1. Pipet

Where a pipet is specified, a suitable buret may be substituted. Where a “to contain” pipet is specified, a suitable volumetric flask may be substituted.

10.80.10.2. Light Protection

Where low-actinic or light-resistant containers are specified, either containers specially treated to protect contents from light or clear containers that have been rendered opaque by application of a suitable coating or wrapping may be used.

10.80.20. Instrumental Apparatus

An instrument may be substituted for the specified instrument if the substitute uses the same fundamental principles of operation and is of equivalent or greater sensitivity and accuracy. These characteristics shall be qualified as appropriate. Where a particular brand or source of a material, instrument, or piece of equipment, or the name and address of a manufacturer or distributor, is mentioned (ordinarily in a footnote), this identification is furnished solely for informational purposes as a matter of convenience, without implication of approval, endorsement, or certification.

10.80.20.1. Chromatographic Tubes and Columns

The term “diameter” refers to internal diameter (ID).

10.80.20.2. Tubing

The term “diameter” refers to outside diameter (OD).

10.80.20.3. Steam Bath

Where use of a steam bath is directed, use actively flowing steam or another regulated heat source controlled at an equivalent temperature.

10.80.20.4. Water Bath

A water bath requires vigorously boiling water unless otherwise specified.

11. TEST RESULTS

11.10. Interpretation of Requirements

Analytical results observed in the laboratory (or calculated from experimental measurements) are compared with stated acceptance criteria to determine whether the article conforms to compendial requirements.

The reportable value, which often is a summary value for several individual determinations, is compared with the acceptance criteria. The reportable value is the end result of a completed measurement procedure, as documented.

Where acceptance criteria are expressed numerically herein through specification of an upper and/or lower limit, permitted values include the specified values themselves, but no values outside the limit(s). Acceptance criteria are considered significant to the last digit shown.

11.10.10. Nominal Concentrations in Equations

Where a “nominal concentration” is specified, calculate the concentration based on the label claim. In *Assay* procedures, water correction is typically stated in the *Definition* and on the label of the USP Reference Material. For other procedures, correction for assayed content, potency, or both is made prior to using the concentration in the equation provided in the monograph.

11.20. Equivalence Statements in Titrimetric Procedures

The directions for titrimetric procedures conclude with a statement of the weight of the analyte that is equivalent to each mL of the standardized titrant. In such an equivalence statement, the number of significant figures in the concentration of the titrant should be understood to correspond to the number of significant figures in the weight of the analyte. Corrections to calculations based on the blank determination are to be made for all titrimetric assays where appropriate (see General Chapter <541> *Titrimetry*).

11.30. Rounding Rules

The observed or calculated values shall be rounded off to the number of decimal places that is in agreement with the limit expression. Numbers should not be rounded until the final calculations for the reportable value have been completed. Intermediate calculations (e.g., slope for linearity) may be rounded for reporting purposes, but the original (not rounded) value should be used for any additional required calculations. Acceptance criteria are fixed numbers and are not rounded.

When rounding is required, consider only one digit in the decimal place to the right of the last place in the limit expression. If this digit is smaller than 5, it is eliminated and the preceding digit is unchanged. If this digit is equal to or greater than 5, it is eliminated and the preceding digit is increased by 1.

Illustration of Rounding Numerical Values for Comparison with Requirements

Compendial Requirement	Unrounded Value	Rounded Result	Conforms
Assay limit ≥ 98.0%	97.96%	98.0%	Yes
	97.92%	97.9%	No
	97.95%	98.0%	Yes
Assay limit ≤ 101.5%	101.55%	101.6%	No
	101.46%	101.5%	Yes
	101.45%	101.5%	Yes
Limit test ≤ 0.02%	0.025%	0.03%	No
	0.015%	0.02%	Yes
	0.027%	0.03%	No
Limit test ≤ 3 ppm	3.5 ppm	4 ppm	No
	3.4 ppm	3 ppm	Yes
	2.5 ppm	3 ppm	Yes

12. TERMS AND DEFINITIONS

12.10. About

"About" indicates a quantity within 10%.

If the measurement is stated to be "accurately measured" or "accurately weighed," follow the statements in the general chapters General Chapter <31> *Volumetric Apparatus* and General Chapter <41> *Weights and Balances*, respectively.

12.20. Alcohol Content

Percentages of alcohol, such as those under the heading *Alcohol Determination,* refer to percentage by volume of C_2H_5OH at 15.56°. Where a formula, test, or *Assay* calls for alcohol, ethyl alcohol, or ethanol, the *HMC* monograph article *Alcohol* shall be used. Where reference is made to "C_2H_5OH", absolute (100%) ethanol is intended. Where a procedure calls for dehydrated alcohol, alcohol absolute, or anhydrous alcohol, the *HMC* monograph article *Dehydrated Alcohol* shall be used.

12.30. Atomic Weights

Atomic weights used in computing molecular weights and the factors in the assays and elsewhere are those established by the International Union of Pure and Applied Chemistry (IUPAC) Commission on Atomic Weights and Isotopic Abundances.

12.40. Blank Determinations

Where it is directed that "any necessary correction" be made by a blank determination, the determination shall be conducted using the same quantities of the same reagents treated in the same manner as the solution or mixture containing the portion of the substance under assay or test, but with the substance itself omitted.

12.50. Concomitantly

"Concomitantly" denotes that the determinations or measurements are to be performed in immediate succession.

12.60. Desiccator

The instruction "in a desiccator" indicates use of a tightly closed container of suitable size and design that maintains an atmosphere of low moisture content by means of a suitable desiccant such as anhydrous calcium chloride, magnesium perchlorate, phosphorus pentoxide, or silica gel. See also section 12.180, *Vacuum Desiccator*.

12.70. Logarithms

Logarithms are to the base 10.

12.80. Microbial Strain

A microbial strain cited and identified by its American Type Culture Collection (ATCC) catalog number shall be used directly or, if subcultured, shall be used not more than five passages removed from the original strain.

12.90. NLT/NMT

"NLT" means "not less than". "NMT" means "not more than".

12.100. Percent

"Percent" used without qualification means:

- For mixtures of solids and semisolids, percent weight in weight;
- For solutions or suspensions of solids in liquids, percent weight in volume;
- For solutions of liquids in liquids, percent volume in volume;
- For solutions of gases in liquids, percent weight in volume.

For example, a 1% solution is prepared by dissolving 1 g of a solid or semisolid, or 1 mL of a liquid, in sufficient solvent to make 100 mL of the solution.

12.110. Percentage Concentrations

Percentage concentrations are expressed as follows:

- "Percent weight in weight" (w/w) is defined as the number of g of a solute in 100 g of solution.
- "Percent weight in volume" (w/v) is defined as number of g of a solute in 100 mL of solution.
- "Percent volume in volume" (v/v) is defined as the number of mL of a solute in 100 mL of solution.

12.120. Pressure

Pressure is determined by use of a suitable manometer or barometer calibrated in terms of the pressure exerted by a column of mercury of the stated height.

12.130. Specific Gravity

Specific gravity is the weight of a substance in air at 25° divided by the weight of an equal volume of water at the same temperature.

12.140. Temperatures

Temperatures are expressed in centigrade (Celsius) degrees, and all measurements are made at 25° unless otherwise indicated. Where moderate heat is specified, any temperature not higher than 45° (113° F) is indicated.

12.150. Time

Unless otherwise specified, rounding rules, as described in section 11.30, *Rounding Rules*, apply to any time specified.

12.160. Transfer

"Transfer" indicates a quantitative manipulation.

12.170. Vacuum

"Vacuum" denotes exposure to a pressure of less than 20 mm of mercury (2.67 kPa), unless otherwise indicated.

12.180. Vacuum Desiccator

"Vacuum desiccator" indicates a desiccator that maintains a low-moisture atmosphere at a reduced pressure of not more than 20 mm of mercury (2.67 kPa) or at the pressure designated in the individual monograph.

12.190. Water

12.190.10. Water as an Ingredient in an Article

As an ingredient in an article, water meets the requirements of the appropriate water monograph in *HMC*.

12.190.20. Water in the Manufacture of Herbal Article

When used in the manufacture of an herbal article, water may meet the requirements for drinking water as set forth in the regulations of the U.S. Environmental Protection Agency (potable water).

12.190.30. Water in a Monograph Procedure

When water is called for in a monograph procedure, the *HMC* monograph article *Purified Water* shall be used unless otherwise specified. Definitions for *High-Purity Water* and *Carbon Dioxide-Free* Water are provided in General Chapter <660> General Chapter <660> *Containers—Glass*. Definitions of other types of water are provided in General Chapter <1231> *Water for Pharmaceutical Purposes*.

12.200. Weights and Measures

In general, weights and measures are expressed in the International System of Units (SI) as established and revised by the *Conférence Générale des Poids et Mesures (CGPM)*. For compendial purposes, the term "weight" is considered to be synonymous with "mass."

Molality is designated by the symbol "m" preceded by a number that represents the number of moles of the designated solute contained in 1 kg of the designated solvent.

Molarity is designated by the symbol “M” preceded by a number that represents the number of moles of the designated solute contained in an amount of the designated solvent that is sufficient to prepare 1 L of solution.

Symbols commonly employed for SI metric units and other units are as follows:

Unit Symbols as Used Within *HMC*

Units	Symbol	Notes
Length		
meter	m	
decimeter	dm	
centimeter	cm	
millimeter	mm	
micrometer	µm	Previously referred to as a micron
nanometer	nm	Previously the symbol mµ (for millimicron) was used
Ångström	Å	Equal to 0.1 nm
Mass		
kilogram	kg	
gram	g	
milligram	mg	
microgram	µg	The symbol µg is used in *HMC* to represent micrograms, but micrograms may be represented as “mcg” for labeling and prescribing purposes.
nanogram	ng	
picogram	pg	
femtogram	fg	
dalton	Da	Also referred to as the unified atomic mass unit and is equal to 1/12 times the mass of the free carbon 12 atom.
Time		
second	s	
minute	min	
hour	h	
Volume		
liter	L	1 L is equal to 1 dm or 1000 cm^3 (cubic centimeters)
deciliter	dL	
milliliter	mL	1 mL is equal to 1 cm^3, sometimes referred to as cc
microliter	µL	
Temperature		
Kelvin	K	
Celsius	°	
Fahrenheit	°F	
Amount of Substance		
mole	mol	Historically referred to as gram-molecular weight or gram-atomic weight
millimole	mmol	

Unit Symbols as Used Within *HMC*

Units	Symbol	Notes
equivalent	Eq	Also referred as gram-equivalent weight. It is used in the calculation of substance concentration in Normality units. This unit is no longer preferred for use in analytical chemistry or metrology.
milliequivalent	mEq	
osmole	Osmol	Osmotic pressure of a solution, related to substance concentration.
milliosmole	mOsmol	
Pressure		
pascal	Pa	
kilopascal	kPa	
pounds per square inch	psi	
millimeter of mercury	mmHg	Equal to 133.322 Pa
bar	bar	1 bar equals 0.1 MPa
Electrical units		
ampere	A	
volt	V	
millivolt	mV	
hertz	Hz	Unit of frequency
kilohertz	kHz	
megahertz	MHz	
electron volt	eV	
kiloelectron volt	keV	
megaelectron volt	meV	
Radiation		
becquerel	Bq	SI unit of activity for radionuclides
kilobecquerel	kBq	
megabecquerel	MBq	
gigabecquerel	GBq	
Curie	Ci	Non-SI unit of activity for radionuclides
millicurie	mCi	
microcurie	µCi	
nanocurie	nCi	
gray	Gy	Absorbed dose
milligray	mGy	
sievert	Sv	dose equivalent
Other		
acceleration due to gravity	g_n	Used to express rate of centrifugation
revolutions per minute	rpm	Used to express rate of centrifugation

Selected SI Prefixes

Name	Symbol	Factor
giga	G	10^9 or 1,000,000,000
mega	M	10^6 or 1,000,000
kilo	k	10^3 or 1,000
deci	d	10^{-1} or 0.1
centi	c	10^{-2} or 0.01
milli	m	10^{-3} or 0.001
micro	µ	10^{-6} or 0.000,001
nano	n	10^{-9}
pico	p	10^{-12}
femto	f	10^{-15}

13. PRESERVATION, PACKAGING, STORAGE, AND LABELING

13.10. Storage Under Nonspecific Conditions

If no specific directions or limitations are provided in the *Packaging and Storage* section of an individual *HMC* monograph or in the labeling of an article recognized in *HMC,* the conditions of storage shall include storage at controlled room temperature, protection from moisture, and, where necessary, protection from light. Such articles shall be protected from moisture, freezing, and excessive heat, and, where necessary, from light during shipping and distribution.

13.20. Containers

The container is that which holds the article and is or may be in direct contact with the article. The immediate container is that which is in direct contact with the article at all times. The closure is a part of the container.

Before being filled, the container should be clean. Special precautions and cleaning procedures may be necessary to ensure that each container is clean and that extraneous matter is not introduced into or onto the article.

The container does not interact physically or chemically with the article placed in it so as to alter the composition, quality, or purity of the article beyond the monograph requirements.

13.20.10. Light-Resistant Container

A light-resistant container (see *Light Transmission Test* under General Chapter <671> Containers—Performance Testing) protects the contents from the effects of light by virtue of the specific properties of the material of which it is composed, including any coating applied to it. Alternatively, a clear and colorless or a translucent container may be made light-resistant by means of an opaque covering, in which case the label of the container bears a statement that the opaque covering is needed until the contents are to be used. Where it is directed to “protect from light” in an individual monograph, preservation in a light-resistant container is intended.

Where an article is required to be packaged in a light-resistant container, and if the container is made light-resistant by means of an opaque covering, a single-use, unit-

dose container or mnemonic pack for dispensing may not be removed from the outer opaque covering before dispensing.

13.20.20. Well-Closed Container

A well-closed container protects the contents from extraneous solids and from loss of the article under the ordinary or customary conditions of handling, shipment, storage, and distribution.

13.20.30. Tight Container

A tight container protects the contents from contamination by extraneous liquids, solids, or vapors; from loss of the article; and from efflorescence, deliquescence, or evaporation under the ordinary or customary conditions of handling, shipment, storage, and distribution; and is capable of tight reclosure.

[NOTE—Where packaging and storage in a *tight container* or a *well-closed container* is specified in the individual monograph, the container used for an article when dispensed on prescription meets the requirements under General Chapter <671> Containers—Performance Testing]

13.30. Storage Temperature and Humidity

Specific directions are stated in some monographs with respect to the temperatures and humidity at which articles shall be stored and distributed (including the shipment of articles to the consumer) when stability data indicate that storage and distribution at a lower or a higher temperature and a higher humidity produce undesirable results. Such directions apply except where the label on an article states a different storage temperature on the basis of stability studies. Where no specific storage directions or limitations are provided in the individual monograph, but the label of an article states a storage temperature that is based on stability studies, such labeled storage directions apply. The conditions are defined by the following terms.

13.30.10. Freezer

"Freezer" indicates a place in which the temperature is maintained thermostatically between -25° and -10° (-13° and 14°F).

13.30.20. Cold

Any temperature not exceeding 8° (46°F) is "cold." A "refrigerator" is a cold place in which the temperature is maintained thermostatically between 2° and 8° (36° and 46°F).

13.30.30. Cool

Any temperature between 8° and 15° (46° and 59°F) is"cool." An article for which storage in a *cool place* is directed may, alternatively, be stored and distributed in a *refrigerator,* unless otherwise specified by the individual monograph.

13.30.40. Controlled Cold Temperature

"Controlled cold temperature" is defined as temperature maintained thermostatically between 2° and 8° (36° and 46° F), that allows for excursions in temperature between 0° and 15° (32° and 59° F) that may be experienced during storage, shipping, and distribution such that the allowable calculated mean kinetic temperature is not more than 8° (46° F). Transient spikes up to 25° (77° F) may be permitted if the manufacturer so instructs and provided that such spikes do not exceed 24 hours unless supported by stability data or the manufacturer instructs otherwise.

13.30.50. Room Temperature

"Room temperature" indicates the temperature prevailing in a working area.

13.30.60. Controlled Room Temperature

"Controlled room temperature" indicates a temperature maintained thermostatically that encompasses the usual and customary working environment of 20° to 25° (68° to 77°F); that results in a mean kinetic temperature calculated to be not more than 25°; and that allows for excursions between 15° and 30° (59° and 86°F) that are experienced in pharmacies,
hospitals, and warehouses. Provided the mean kinetic temperature remains in the allowed range, transient spikes up to 40° are permitted as long as they do not exceed 24 hours. Spikes above 40° may be permitted if the manufacturer so instructs. Articles may be labeled for storage at "controlled room temperature" or at "up to 25°", or other wording based on the same mean kinetic temperature. The mean kinetic temperature is a calculated value that may be used as an isothermal storage temperature that simulates the non-isothermal effects of storage temperature variations.

An article for which storage at *controlled room temperature* is directed may, alternatively, be stored and distributed in a *cool place,* unless otherwise specified in the individual monograph or on the label.

13.30.70. Warm

Any temperature between 30° and 40° (86° and 104°F) is "warm."

13.30.80. Excessive Heat

"Excessive heat" means any temperature above 40° (104°F).

13.30.90. Protection From Freezing

Where, in addition to the risk of breakage of the container, freezing subjects an article to loss of potency, or to destructive alteration of its characteristics, the container label bears an appropriate instruction to protect the article from freezing.

13.30.100. Dry Place

The term “dry place” denotes a place that does not exceed 40% average relative humidity at *Controlled Room Temperature* or the equivalent water vapor pressure at other temperatures. The determination may be made by direct measurement at the place or may be based on reported climatic conditions. Determination is based on not less than 12 equally spaced measurements that encompass either a season, a year, or, where recorded data demonstrate, the storage period of the article. There may be values of up to 45% relative humidity provided that the average value is 40% relative humidity.

Storage in a container validated to protect the article from moisture vapor, including storage in bulk, is considered storage in a dry place.

13.40. Labeling

The term “labeling” designates all labels and other written, printed, or graphic matter upon an immediate container of an article or upon, or in, any package or wrapper in which the article is enclosed, except any outer shipping container. The term “label” designates that part of the labeling upon the immediate container.

A shipping container containing a single article, unless such container is also essentially the immediate container or the outside of the consumer package, is labeled with a minimum of the article identification, lot number, and conditions for storage and distribution.

In addition to the labeling standards contained in this compendium, an herbal article is subject to compliance with such labeling requirements as may be promulgated by governmental bodies.