GENERAL NOTICES AND REQUIREMENTS

The General Notices and Requirements section (the General Notices) presents the basic assumptions, definitions, and default conditions for the interpretation and application of the United States Pharmacopeia (USP) and the National Formulary (NF).

Requirements stated in these General Notices apply to all articles recognized in the USP and NF (the “compendia”) and to all general chapters unless specifically stated otherwise. Where the requirements of an individual monograph differ from the General Notices or a 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 (consisting of four volumes and including its Supplements), is The Pharmacopeia of the United States of America, Thirty-Eighth Revision and the National Formulary, Thirty-Third Edition. These titles may be abbreviated to USP 38, to NF 33, and to USP 38–NF 33. The United States Pharmacopeia, Thirty-Eighth Revision, and the National Formulary, Thirty-Third Edition, supersede all earlier revisions. Where the terms “USP,” “NF,” or “USP–NF” are used without further qualification during the period in which these compendia are official, they refer only to USP 38, NF 33, and any Supplement(s) thereto. The same titles, with no further distinction, apply equally to print or electronic presentation of these contents. Although USP and NF are published under one cover and share these General Notices, they are separate compendia.

This revision is official beginning April 1, 2015, unless otherwise indicated in specific text. Supplements to USP and NF are published periodically. Interim Revision Announcements are revisions to USP and NF that are published on the USP website. Interim Revision Announcements contain official revisions and their effective dates. Announcements of the availability of new USP Reference Standards and announcements of tests or procedures that are held in abeyance pending availability of required USP Reference Standards are also available on the “New Official Text” tab of USP’s website.

Revision Bulletins are revisions to official text or postponements that require expedited publication. They are published on the USP website and generally are official immediately unless otherwise specified in the Revision Bulletin. Errata are corrections to items erroneously published that have not received the approval of the Council of Experts and that do not reflect the official requirements.

2. OFFICIAL STATUS AND LEGAL RECOGNITION

2.10. Official Text

Official text is text contained in USP and NF, including monographs, general chapters, and these General Notices. Revisions to official text are provided in Supplements, Interim Revision Announcements, and Revision Bulletins. General chapters numbered from 1000 to 1999 are considered interpretive and are intended to provide information on, give definition to, or describe a particular subject. They contain no mandatory requirements applicable to any official article unless specifically referenced in General Notices, a monograph, or a general chapter numbered below 1000. General chapters numbered above 2000 apply only to articles that are intended for use as dietary ingredients and dietary supplements.

2.20. Official Articles

An official article is an article that is recognized in USP or NF. An article is deemed to be recognized and included in a compendium when a monograph for the article is published in the compendium and an official date is generally or specifically assigned to the monograph.

The title specified in a monograph is the official title for such article. Other names considered to be synonyms of the official titles may not be used as substitutes for official titles.

Official articles include both official substances and official products. An official substance is a drug substance, excipient, dietary ingredient, other ingredient, or component of a finished device for which the monograph title includes no indication of the nature of the finished form.

An official product is a drug product, dietary supplement, compounded preparation, or finished device for which a monograph is provided.

2.30. Legal Recognition

The USP and NF are recognized in the laws and regulations of many countries throughout the world. Regulatory authorities may enforce the standards presented in the USP and NF, but because recognition of the USP and NF may vary by country, users should understand applicable laws and regulations. In the United States under the Federal Food, Drug, and Cosmetic Act (FDCA), both USP and NF are recognized as official compendia. A drug with a name recognized in USP–NF must comply with compendial identity standards or be deemed adulterated, misbranded, or both. See, e.g., FDCA § 501(b) and 502(e)(3)(b); also FDA regulations, 21 CFR § 299.5(a&b). To avoid being deemed adulterated, such drugs must also comply with compendial standards for strength, quality, and purity, unless labeled to show all respects in which the drug differs. See, e.g., FDCA § 501(b) and 21 CFR § 299.5(c). In addition, to avoid being deemed misbranded, drugs recognized in USP–NF must also be packaged and labeled in compliance with compendial standards. See FDCA § 502(g).

A dietary supplement represented as conforming to specifications in USP will be deemed a misbranded food if it fails to so conform. See FDCA § 403(s)(2)(D).

Enforcement of USP standards is the responsibility of FDA and other government authorities in the U.S. and elsewhere. USP has no role in enforcement.

3. CONFORMANCE TO STANDARDS

3.10. Applicability of Standards

Standards for an article recognized in the compendia (USP–NF) are expressed in the article’s monograph, applicable general chapters, and General Notices. Unless specifically exempted elsewhere in a compendium, the identity, strength, quality, and purity of an article are determined by the official tests, procedures, and acceptance criteria, whether incorporated in the monograph itself, in the General Notices, or in the applicable general chapters. Early adoption of revised standards is allowed. Where revised
standards for an existing article have been published as final approved “official text” (as approved in section 2.10) but are not yet official (six months after publication, unless otherwise specified; see “official date,” section 2.20); compliance with the revised standard shall not preclude a finding or indication of conformance with compendial standards, unless USP specifies otherwise by prohibiting early adoption in a particular standard.

The standards in the relevant monograph, general chapters, and General Notices apply equally to any article from production to expiration. The manufacturer’s specifications, and good manufacturing practices generally (including, e.g., Quality by Design initiatives), are developed and followed to ensure that the article will comply with compendial standards until its expiration date, when stored as directed. Thus, any official article is expected to meet the compendial standards if tested, and any official article actually tested as directed in the relevant monograph must meet such standards to demonstrate compliance.

At times, compendial standards take on the character of statistical procedures, with multiple units involved and perhaps a sequential procedural design to allow the user to determine that the tested article meets or does not meet the standard. The similarity to statistical procedures may seem to suggest an intent to make inference to some larger group of units, but in all cases, statements about whether the compendial standard is met apply only to the units tested. Repeats, replicates, statistical rejection of outliers, or extrapolations of results to larger populations, as well as the necessity and appropriate frequency of batch testing, are neither specified nor prescribed by the compendia. Frequency of testing and sampling are left to the preferences or direction of those performing compliance testing, and other users of USP-NF, including manufacturers, buyers, or regulatory authorities.

Official products are prepared according to recognized principles of good manufacturing practice and from ingredients that meet USP or NF standards, where standards for such ingredients exist (for dietary supplements, see section 3.10.10). Official substances are prepared according to recognized principles of good manufacturing practice and from ingredients complying with specifications designed to ensure that the resultant substances meet the requirements of the compendial monographs.

3.10.10. Applicability of Standards to Drug Products, Drug Substances, and Excipients

The applicable USP or NF standard applies to any article marketed in the United States that (1) is recognized in the compendium and (2) is intended or labeled for use as a drug or as an ingredient in a drug. Such articles (drug products, drug substances, and excipients) include both human drugs (whether dispensed by prescription, “over the counter,” or otherwise), as well as animal drugs. The applicable standard applies to such articles whether or not the added designation “USP” or “NF” is used. The standards apply equally to articles bearing the official titles or names derived by transposition of the definitive words of official titles or transposition in the order of the names of two or more active ingredients in official titles, or where there is use of synonyms with the intention or effect of suggesting a significant degree of identity with the official title or name.

3.10.20. Applicability of Standards to Medical Devices, Dietary Supplements, and Their Components and Ingredients

An article recognized in USP or NF shall comply with the compendial standards if the article is a medical device, component intended for a medical device, dietary supplement, dietary ingredient, or other ingredient that is intended for incorporation into a dietary supplement, and is labeled as conforming to the USP or NF.

Generally, dietary supplements are prepared from ingredients or Food Chemicals Codex standards. Where such standards do not exist, substances may be used in dietary supplements if they have been shown to be of acceptable food grade quality using other suitable procedures.

3.20. Indicating Conformance

A drug product, drug substance, or excipient may use the designation “USP,” “NF,” or “USP±NF” in conjunction with official title or elsewhere on the label only when (1) a monograph is provided in the specified compendium and (2) the article complies with the identity prescribed in the specified compendium.

When a drug product, drug substance, or excipient differs from the relevant USP or NF standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.

When a drug product, drug substance, or excipient fails to comply with the identity prescribed in USP or NF or contains an added substance that interferes with the prescribed tests and procedures, the article shall be designated by a name that is clearly distinguishing and differentiating from any name recognized in USP or NF.

A medical device, dietary supplement, or ingredient or component of a medical device or dietary supplement may use the designation “USP” or “NF” in conjunction with its official title or elsewhere on the label only when (1) a monograph is provided in the specified compendium and (2) the article complies with the monograph standards and other applicable standards in the compendium.

The designation “USP” or “NF” on the label may not and does not constitute an endorsement by USP and does not represent assurance by USP that the article is known to comply with the relevant standards. USP may seek legal redress if an article purports to be or is represented as an official article in one of USP’s compendia and such claim is determined by USP not to be made in good faith.

The designation “USP-NF” may be used on the label of an article provided that the label also bears a statement such as “Meets NF standards as published by USP,” indicating the particular compendium to which the article purports to apply.

When the letters “USP,” “NF,” or “USP-NF” are used on the label of an article to indicate compliance with compendial standards, the letters shall appear in conjunction with the official title of the article. The letters are not to be enclosed in any symbol such as a circle, square, etc., and shall appear in capital letters.

If a dietary supplement does not comply with all applicable compendial requirements but contains one or more dietary ingredients or other ingredients that are recognized in USP or NF, the individual ingredient(s) are designated as complying with USP or NF standards or being of USP or NF quality provided that the designation is limited to the individual ingredient(s) and does not suggest that the dietary supplement complies with USP standards.

4. MONOGRAPHS AND GENERAL CHAPTERS

4.10. Monographs

Monographs set forth the article’s name, definition, specification, and other requirements related to packaging, storage, and labeling. The specification consists of tests, procedures, and acceptance criteria that help ensure the identity, strength, quality, and purity of the article. For general requirements relating to specific monograph sections, see section 5, Monograph Components.

Because monographs may not provide standards for all relevant characteristics, some official substances may con-
form to the USP or NF standard but differ with regard to nonstandardized properties that are relevant to their use in specific preparations. To assure interchangeability in such instances, users may wish to ascertain functional equivalence or determine such characteristics before use.

4.10.10. Applicability of Test Procedures

A single monograph may include several different tests, procedures, and/or acceptance criteria that reflect attributes of different manufacturers’ articles. Such alternatives may be presented for different polymorphic forms, impurities, hydrides, and dissolution cases. Monographs indicate the tests, procedures, and/or acceptance criteria to be used and the required labeling. A test in a monograph may contain and require multiple procedures. However, multiple procedures may be included in particular monographs specifically for the purpose of assuring the availability of an appropriate procedure for a particular product. In such cases, a labeling statement to indicate the appropriate application of the procedure(s) will be included in the monograph. A labeling statement is not required if Test 1 is used.

4.10.11. Dissolution, Disintegration, and Drug Release Tests

Multiple Dissolution, Disintegration, or Drug Release tests may be present in the monograph. The order in which the tests are listed in the monograph is based on the order in which they are approved by the relevant Expert Committee for inclusion in the monograph. Test 1 is not necessarily the test for the innovator or for the reference product. Compliance with any of the tests does not assure bioequivalence or bioavailability.

4.10.20. Acceptance Criteria

The acceptance criteria allow for analytical error, for unavoidable variations in manufacturing and compounding, and for deterioration to an extent considered acceptable under practical conditions. The existence of compendial acceptance criteria does not constitute a basis for a claim that an official substance that more nearly approaches 100 percent purity “exceeds” compendial quality. Similarly, the fact that an article has been prepared to tighter criteria than those specified in the monograph does not constitute a basis for a claim that the article “exceeds” the compendial requirements.

An official product shall be formulated with the intent to provide 100 percent of the quantity of each ingredient declared on the label. Where the minimum amount of a substance present in a dietary supplement is required by law to be higher than the lower acceptance criterion allowed for in the monograph, the upper acceptance criterion contained in the monograph may be increased by a corresponding amount.

The acceptance criteria specified in individual monographs and in the general chapters for compounded preparations are based on such attributes of quality as might be expected to characterize an article compounded from suitable bulk drug substances and ingredients, using the procedures provided or recognized principles of good compounding practice, as described in these compendia.

4.20. General Chapters

Each general chapter is assigned a number that appears in angle brackets adjacent to the chapter name (e.g., Chromatography (621)). General chapters may contain the following:

- Descriptions of tests and procedures for application through individual monographs,
- Descriptions and specifications of conditions and practices for pharmaceutical compounding,
- General information for the interpretation of the compendial requirements,
- Descriptions of general pharmaceutical storage, dispensing, and packaging practices, or
- General guidance to manufacturers of official substances or official products.

When a general chapter is referenced in a monograph, acceptance criteria may be presented after a colon.

Some 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.

Change to read:

5. MONOGRAPH COMPONENTS

5.10. Molecular Formula

The use of the molecular formula for the active ingredient(s) named in defining the required strength of a compendial article is intended to designate the chemical entity or entities, as given in the complete chemical name of the article, having absolute (100 percent) purity.

5.20. Added Substances

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

The air in a container of an official article may, where appropriate, be evacuated or be replaced by carbon dioxide, helium, argon, or nitrogen, or by a mixture of these gases. The use of such gas need not be declared in the labeling.

5.20.10. Added Substances, Excipients, and Ingredients in Official Substances

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

5.20.20. Added Substances, Excipients, and Ingredients in Official Products

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

Added substances and excipients employed solely to impart color may be incorporated into official products other than those intended for parenteral or ophthalmic use, in accordance with the regulations pertaining to the use of colors issued by the U.S. Food and Drug Administration (FDA), provided such added substances or excipients are otherwise appropriate in all respects. (See also Injections (1), Ingredients, Vehicles and Added Substances, Added Substances.)

The proportions of the substances constituting the base in ointment and suppository products and preparations may be varied to maintain a suitable consistency under different climatic conditions, provided that the concentrations of active ingredients are not varied and provided that the bioavailability, therapeutic efficacy, and safety of the preparation are not impaired.

5.20.20.1. In Compounded Preparations

Compounded preparations for which a complete composition is given shall contain only the ingredients named in the formulas unless specifically exempted herein or in the individual monograph. Deviation from the specified processes or methods of compounding, although not from the ingredients or proportions thereof, may occur provided...
that the finished preparation conforms to the relevant stan-
dards and to preparations produced by following the speci-
fied process.
Where a monograph for a compounded preparation calls
for an ingredient in an amount expressed on the dried ba-
sis, the ingredient need not be dried before use if due al-
lowance is made for the water or other volatile substances
present in the quantity taken.
Specially denatured alcohol formulas are available for use
in accordance with federal statutes and regulations of the
Internal Revenue Service. A suitable formula of specially de-
natured alcohol may be substituted for Alcohol in the man-
ufacture of official preparations intended for internal or top-
cical use, provided that the denaturant is volatile and does
not remain in the finished product. A preparation that is
intended for topical application to the skin may contain
specially denatured alcohol, provided that the denaturant is
either a usual ingredient in the preparation or a permissible
added substance; in either case the denaturant shall be
identified on the label of the topical preparation. Where a
process is given in the individual monograph, any prepara-
tion compounded using denatured alcohol shall be identi-
cal to that prepared by the monograph process.

5.20. Assay

Assay tests for compounded preparations are not int-
tended for evaluating a compounded preparation before
dispensing, but instead are intended to serve as the official
test in the event of a question or dispute regarding the
preparation’s conformance to official standards.

5.20.10. Units of Potency (Biological)

For substances that cannot be completely characterized
by chemical and physical means, it may be necessary to
express quantities of activity in biological units of potency,
each defined by an authoritative, designated reference
standard.

Units of biological potency defined by the World Health
Organization (WHO) for International Biological Standards
and International Biological Reference Preparations are
termed International Units (IU). Monographs refer to the
units defined by USP Reference Standards as “USP Units.”
For biological products, units of potency are defined by the
corresponding U.S. Standard established by FDA, whether
or not International Units or USP Units have been defined
(see Biologicals (1041)).

5.60. Impurities and Foreign Substances

Tests for the presence of impurities and foreign sub-
stances are provided to limit such substances to amounts
that are unobjectionable under conditions in which the article
is customarily employed (see also Impurities in Drug Sub-
stances and Drug Products (1086)).

Nonmonograph tests and acceptance criteria suitable for
detecting and controlling impurities that may result from a
change in the processing methods or that may be intro-
duced from external sources should be employed in addi-
tion to the tests provided in the individual monograph,
where the presence of the impurity is inconsistent with ap-
plicable good manufacturing practices or good pharmaceu-
tical practices.

5.60.10. Other Impurities in USP and NF Articles

If a USP or NF monograph includes an assay or organic
impurity test based on chromatography, other than a test
for residual solvents, and that monograph procedure does
not detect an impurity present in the substance, the
amount and identity of the impurity, where both are
known, shall be stated in the labeling (certificate of analy-
sis) of the official substance, under the heading Other
Impurity(ies).

The presence of any unlabeled other impurity in an offi-
cial substance is a variance from the standard if the content
is 0.1% or greater. The sum of all Other Impurities com-
bined with the monograph-detected impurities may not ex-
ced 2.0% (see Ordinary Impurities (466)), unless otherwise
stated in the monograph.

The following categories of drug substances are excluded
from Other Impurities requirements:

- Fermentation products and semi-synthetics derived therefrom,
- Radiopharmaceuticals,
- Biologics,
- Biotechnology-derived products,
- Peptides,
- Herbals, and
- Crude products of animal or plant origin.

Any substance known to be toxic shall not be listed under
Other Impurities.

5.60.20. Residual Solvents in USP and NF Articles

All USP and NF articles are subject to relevant control of
residual solvents, even when no test is specified in the indi-
vidual 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 Residual Solvents (467), using the general methods presented therein or other suitable methods.

6.60.30. Elemental Impurities in USP Drug Products and Dietary Supplements

*Effective January 1, 2018, elemental impurities will be controlled in official drug products according to the principles defined and requirements specified in Elemental Impurities—Limits (232). Effective January 1, 2018, elemental contaminants are controlled in official dietary supplements according to the principles defined and requirements specified in Elemental Contaminants in Dietary Supplements (2232). Also effective January 1, 2018, general chapter Heavy Metals (231) will be omitted from all references to it in general chapters and monographs and deleted. Early adoption of the requirements in (232) and (2232) are permitted by USP, and if (232) or (2232), as applicable, is fully implemented with respect to a particular drug product or dietary supplement in advance of the January 1, 2018 date, that product and its ingredients will no longer need to comply with requirements (231) requirements to be considered by USP to be in conformance with USP–NF requirements.† (RB 1-Apr-2015)

5.70. Performance Tests

Where content uniformity determinations have been made using the same analytical methodology specified in the Assay, with appropriate allowances made for differences in sample preparation, the average of all of the individual content uniformity determinations may be used as the Assay value. 5.80. USP Reference Standards

USP Reference Standards are authentic specimens that have been approved as suitable for use as comparison standards in USP or NF tests and assays. (See USP Reference Standards (11).) Where USP or NF tests or assays call for the use of a USP Reference Standard, only those results obtained using the specified USP Reference Standard are conclusive. Where a procedure calls for the use of a compendial article rather than for a USP Reference Standard as a material standard of reference, a substance meeting all of the compendial monograph requirements for that article shall be used. If any new USP or NF standard requires the use of a new USP Reference Standard that is not yet available, that portion of the standard containing the requirements shall not be official until the specified USP reference material is available.

Unless a Reference Standard label bears a specific potency or content, assume the Reference Standard is 100.0% pure in the official application. Unless otherwise directed in the procedure in the individual monograph or in a general chapter, USP Reference Standards are to be used in accordance with the instructions on the label of the Reference Standard.

Change to read:

6. TESTING PRACTICES AND PROCEDURES

6.10. 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 a procedure described in the compendia, the analyst should be aware of the hazards associated with the chemicals and the techniques and means of protecting against them. These compendia are not designed to describe such hazards or protective measures.

6.20. Automated Procedures

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

6.30. 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 Validation of Compendial Procedures (1225) 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 should be submitted to USP for evaluation as a potential replacement or addition to the standard (see section 4.10, Monographs).

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 a substance or preparation is found to comply with a requirement using an interchange method or procedure from one of the pharmacopoeias, it should comply with the requirements of the USP–NF. When a difference appears, or in the event of dispute, only the result obtained by the method and/or procedure given in the USP–NF is conclusive.

6.40. Dried, Anhydrous, Ignited, 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 or unignited substance and the results calculated on the dried, anhydrous, or ignited basis, provided a test for Loss on Drying, or Water Determination, or Loss on Ignition, 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 Residual Solvents (467) 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 Loss on Drying (731) or Water Determination (921) (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. 6.40.10. Ignite to Constant Weight

“Ignite to constant weight” means that ignition shall be continued at 800 ± 25°C, unless otherwise indicated, until two consecutive weighings, the second of which is taken after an additional period appropriate to the nature and quantity of the residue, do not differ by more than 0.50 mg per g of substance taken.

6.40.20. 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 per g of substance taken.

6.50. Preparation of Solutions

6.50.10. 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.

6.50.20. Solutions

Unless otherwise specified, all solutions shall be prepared with Purified Water. Solutions for quantitative measures shall be prepared using accurately weighed or accurately measured analytes (see section 8.20, 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, by volume of the designated liquids shall be mixed, unless otherwise indicated.

6.50.20.1. 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.

Proportionately larger or smaller quantities than the specified weights and volumes of assay or test substances, Reference Standards, or USP±NF may be taken, provided the measurement is made with at least equivalent accuracy.

Unless otherwise indicated, analytic concentrations shall be prepared to within ten percent (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 ten percent (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.

6.50.20.2. Test Solutions

Information on Test Solutions (TS) is provided in the Test Solutions portion of the Reagents, Indicators, and Solutions section of the USP±NF. Use of an alternative Test Solution or a change in the Test Solution used may require validation.

6.50.20.3. Indicator Solutions

Where a procedure specifies the use of an indicator TS, approximately 0.2 mL, or 3 drops, of the solution shall be added unless otherwise directed.

6.60. Units Necessary to Complete a Test

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

6.60.10. Tablets

Where the procedure of a Tablet monograph directs to weigh and finely powder not fewer than a given number of Tablets, a counted number of Tablets shall be weighed and reduced to a powder. The portion of the powdered Tablets taken shall be representative of the whole Tablets and shall, in turn, be weighed accurately.

6.60.20. Capsules

Where the procedure of a Capsule monograph gives direction to remove, as completely as possible, the contents of not fewer than a given number of the Capsules, a counted number of Capsules shall be carefully opened and the contents quantitatively removed, combined, mixed, and weighed accurately. The portion of mixed Capsules contents taken shall be representative of the contents of the Capsules and shall, in turn, be weighed accurately.

6.70. 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, comparable specifications for reagents of acceptable quality are provided (see the Reagents, Indicators, and Solutions section of the USP±NF). Reagents not covered by any of these specifications shall be of a grade suitable to the proper performance of the method of assay or test involved.

Listing of these reagents, including the indicators and solutions employed as reagents, in no way implies that they have therapeutic utility; furthermore, any reference to USP or NF in their labeling shall include also the term "reagent" or "reagent grade." OSP may supply reagents if they otherwise may not be generally commercially available.

6.80. 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.

6.80.10. 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.

6.80.10.1. Pipet/Pipette

Where a pipet/pipette is specified, a suitable buret may be substituted. Where a "to contain" pipet/pipette is specified, a suitable volumetric flask may be substituted.

6.80.10.2. Light Protection

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

6.80.20. 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.

6.80.20.1. Chromatographic Tubes and Columns

The term "diameter" refers to internal diameter (ID).

6.80.20.2. Tubing

The term "diameter" refers to outside diameter (OD).

6.80.20.3. Steam Bath

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

6.80.20.4. Water Bath

A water bath requires vigorously boiling water unless otherwise specified.

6.80.30. Temperature Reading Devices

Temperature reading devices suitable for pharmaceutical tests conform to specifications that are traceable to an National Institute of Standards and Technology (NIST) standard or equivalent. Temperature reading devices may be of the liquid-in-glass type or an analog or digital temperature indicator type, such as a resistance temperature device, thermometer, or thermocouple. Standardization of thermometers is performed on an established testing frequency with a temperature standard traceable to NIST. For example, refer to the current issue of American Society of Testing and Materials (ASTM) standards E1 for liquid-in-glass thermometers.
7. TEST RESULTS

7.10. 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.

7.10.5. 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 Standard. For other procedures, correction for assayed content, potency, or both is made prior to using the concentration in the equation provided in the monograph.

7.10.10. 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 Titrimetry (541)).

7.20. 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.

8. TERMS AND DEFINITIONS

Illustration of Rounding Numerical Values for Comparison with Requirements

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

8.10. Abbreviations

- RS refers to a USP Reference Standard.
- CS refers to a Colorimetric Solution.
- TS refers to a Test Solution.
- VS refers to a Volumetric Solution that is standardized in accordance with directions given in the individual monograph or in the Reagents, Indicators, and Solutions section of USP–NF.

8.20. 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 Volumetric Apparatus (31) and Balances (41), respectively.

8.30. Alcohol Content

Percentages of alcohol, such as those under the heading Alcohol Content, refer to percentage by volume of C₂H₅OH at 15.56 °. Where a formula, test, or assay calls for alcohol, ethyl alcohol, or ethanol, the USP monograph article Alcohol shall be used. Where reference is made to “C₂H₅OH,” absolute (100 percent) ethanol is intended. Where a procedure calls for dehydrated alcohol, alcohol absolute, or anhydrous alcohol, the USP monograph article Dehydrated Alcohol shall be used.

8.40. Atomic Weights

Atomic weights used in computing molecular weights and the factors in the assays and elsewhere are those established by the IUPAC Commission on Atomic Weights and Isotopic Abundances.

8.50. 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.

8.60. Concomitantly

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

8.70. 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 8.220, Vacuum Desiccator.

8.80. Logarithms

Logarithms are to the base 10.

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8.90. 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.

8.100. Negligible
“Negligible” indicates a quantity not exceeding 0.50 mg.

8.110. NLT/NMT
“NLT” means “not less than.” “NMT” means “not more than.”

8.120. Odor
“Odorless,” “practically odorless,” “a faint characteristic odor,” and variations thereof indicate evaluation of a suitable quantity of freshly opened material after exposure to the air for 15 minutes. An odor designation is descriptive only and should not be regarded as a standard of purity for a particular lot of an article.

8.130. 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 percent 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.

8.140. 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 the 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.

8.150. 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.

8.160. Reaction Time
Reaction time is 5 minutes unless otherwise specified.

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

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

8.190. Time
Unless otherwise specified, rounding rules, as described in section 7.20, Rounding Rules, apply to any time specified.

8.200. Transfer
“Transfer” indicates a quantitative manipulation.

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

8.220. 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 kPas) or at the pressure designated in the individual monograph.

8.230. Water
8.230.10. Water as an Ingredient in an Official Product
As an ingredient in an official product, water meets the requirements of the appropriate water monograph in USP or NF.

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

8.230.30. Water in a Compendial Procedure
When water is called for in a compendial procedure, the USP article Purified Water shall be used unless otherwise specified. Definitions for High-Purity Water and Carbon Dioxide-Free Water are provided in Containers—Glass (660). Definitions of other types of water are provided in Water for Pharmaceutical Purposes (1231).

8.240. 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. For compendial purposes, the term “weight” is considered to be synonymous with “mass.”

Molarity is designated by the symbol M preceded by a number that represents the number of moles of the designated solute contained in 1 kilogram 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 liter of solution.

Normality is designated by the symbol N preceded by a number that represents the number of equivalents of the designated solute contained in an amount of the designated solvent that is sufficient to prepare 1 liter of solution.

Chart of Symbols and Prefixes commonly employed for SI metric units and other units:

<table>
<thead>
<tr>
<th>Units</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length</td>
<td></td>
<td></td>
</tr>
<tr>
<td>meter</td>
<td>m</td>
<td>Previously referred to as a micron</td>
</tr>
<tr>
<td>centimeter</td>
<td>cm</td>
<td></td>
</tr>
<tr>
<td>millimeter</td>
<td>mm</td>
<td></td>
</tr>
<tr>
<td>micrometer</td>
<td>µm</td>
<td>Previously the symbol µ (for millimicron) was used</td>
</tr>
<tr>
<td>nanometer</td>
<td>nm</td>
<td></td>
</tr>
<tr>
<td>Ångstrom</td>
<td>Å</td>
<td>Equal to 0.1 nm</td>
</tr>
<tr>
<td>Mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>kilogram</td>
<td>kg</td>
<td>The symbol µg is used in the USP and NF to represent micrograms, but</td>
</tr>
<tr>
<td>gram</td>
<td>g</td>
<td>micrograms may be represented as “mcg” for labeling and prescribing</td>
</tr>
<tr>
<td>milligram</td>
<td>mg</td>
<td>The term “gamma,” symbolized by γ, frequently is used to represent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>micrograms in biochemical literature.</td>
</tr>
<tr>
<td>microgram</td>
<td>µg</td>
<td></td>
</tr>
</tbody>
</table>
Units | Symbol | Notes
--- | --- | ---
nanogram | ng | Also referred to as the unified atomic mass unit and is equal to 1/12 times the mass of the free carbon 12 atom.
picogram | pg |
dalton | Da |
kilodalton | kDa |
time | | seconds: s, minutes: min, hours: h

Volume

<table>
<thead>
<tr>
<th>Unit</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>liter</td>
<td>L</td>
<td>1 L is equal to 1000 cm³ (cubic centimeters)</td>
</tr>
<tr>
<td>deciliter</td>
<td>dL</td>
<td></td>
</tr>
<tr>
<td>milliliter</td>
<td>mL</td>
<td>1 mL is equal to 1 cm³, sometimes referred to as cc</td>
</tr>
<tr>
<td>microliter</td>
<td>µL</td>
<td></td>
</tr>
</tbody>
</table>

Temperature

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celsius</td>
<td>°C</td>
<td></td>
</tr>
</tbody>
</table>

Amount of Substance

<table>
<thead>
<tr>
<th>Substance</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>mole</td>
<td>mol</td>
<td>Historically referred to as gram-molecular weight or gram-atomic weight</td>
</tr>
<tr>
<td>millimole</td>
<td>mmol</td>
<td></td>
</tr>
<tr>
<td>micromole</td>
<td>µmol</td>
<td></td>
</tr>
<tr>
<td>femtomole</td>
<td>fmol</td>
<td></td>
</tr>
</tbody>
</table>

Pressure

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>pascal</td>
<td>Pa</td>
<td></td>
</tr>
<tr>
<td>kilopascal</td>
<td>kPa</td>
<td></td>
</tr>
<tr>
<td>pounds per square inch</td>
<td>psi</td>
<td></td>
</tr>
<tr>
<td>millimeter of mercury</td>
<td>mmHg</td>
<td>Equal to 133.322 Pa</td>
</tr>
</tbody>
</table>

Electrical Units

<table>
<thead>
<tr>
<th>Units</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ampere</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>volt</td>
<td>V</td>
<td></td>
</tr>
<tr>
<td>millivolt</td>
<td>mV</td>
<td></td>
</tr>
<tr>
<td>hertz</td>
<td>Hz</td>
<td>Unit of frequency</td>
</tr>
<tr>
<td>kilohertz</td>
<td>kHz</td>
<td></td>
</tr>
<tr>
<td>megahertz</td>
<td>MHz</td>
<td></td>
</tr>
<tr>
<td>electron volt</td>
<td>eV</td>
<td></td>
</tr>
<tr>
<td>kilo-electron volt</td>
<td>keV</td>
<td></td>
</tr>
<tr>
<td>mega-electron volt</td>
<td>MeV</td>
<td></td>
</tr>
</tbody>
</table>

Radiation

<table>
<thead>
<tr>
<th>Units</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>becquerel</td>
<td>Bq</td>
<td>SI unit of activity for radionuclides</td>
</tr>
<tr>
<td>kilobecquerel</td>
<td>kBq</td>
<td></td>
</tr>
<tr>
<td>megabecquerel</td>
<td>MBq</td>
<td></td>
</tr>
<tr>
<td>gigabecquerel</td>
<td>GBq</td>
<td></td>
</tr>
<tr>
<td>curie</td>
<td>Ci</td>
<td>Non-SI unit of activity for radionuclides</td>
</tr>
<tr>
<td>millicurie</td>
<td>mCi</td>
<td></td>
</tr>
<tr>
<td>microcurie</td>
<td>µCi</td>
<td></td>
</tr>
<tr>
<td>nanocurie</td>
<td>nCi</td>
<td></td>
</tr>
</tbody>
</table>

Other

<table>
<thead>
<tr>
<th>Unit</th>
<th>Symbol</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>acceleration due to gravity</td>
<td>g</td>
<td></td>
</tr>
<tr>
<td>revolutions per minute</td>
<td>rpm</td>
<td>Used to express rate of centrifugation</td>
</tr>
</tbody>
</table>

Selected SI Prefixes

<table>
<thead>
<tr>
<th>Prefix</th>
<th>Symbol</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>giga</td>
<td>G</td>
<td>10⁹</td>
</tr>
<tr>
<td>mega</td>
<td>M</td>
<td>10⁶</td>
</tr>
<tr>
<td>kilo</td>
<td>k</td>
<td>10³</td>
</tr>
<tr>
<td>deci</td>
<td>d</td>
<td>10⁻¹</td>
</tr>
<tr>
<td>centi</td>
<td>c</td>
<td>10⁻²</td>
</tr>
<tr>
<td>milli</td>
<td>m</td>
<td>10⁻³</td>
</tr>
<tr>
<td>micro</td>
<td>µ</td>
<td>10⁻⁶</td>
</tr>
<tr>
<td>nano</td>
<td>n</td>
<td>10⁻⁹</td>
</tr>
<tr>
<td>pico</td>
<td>p</td>
<td>10⁻¹²</td>
</tr>
<tr>
<td>femto</td>
<td>f</td>
<td>10⁻¹⁵</td>
</tr>
</tbody>
</table>

9. PRESCRIBING AND DISPENSING

9.10 Use of Metric Units

Prescriptions for compendial articles shall be written to state the quantity and/or strength desired in metric units unless otherwise indicated in the individual monograph (see also Units of Potency [Biological], section 5.50.10 above). If an amount is prescribed by any other system of measurement, only an amount that is the metric equivalent of the prescribed amount shall be dispensed. Apothecary unit designations on labels and labeling shall not be used.

9.20 Changes in Volume

In the dispensing of prescription medications, slight changes in volume owing to variations in room temperatures may be disregarded.
10. PRESERVATION, PACKAGING, STORAGE, AND LABELING

[NOTE—Storage- and packaging-related provisions previously addressed in the General Notices have been omitted, except for the brief provision proposed to be established below in 10.10; see general chapter Packaging and Storage Requirements (659) for packaging components and storage conditions. Labeling-related provisions are also in the process of being moved to a new general chapter Labeling (7), and will be featured in the future.]

10.10. Packaging and Storage

All articles in USP or NF are subject to the packaging and storage requirements specified in general chapter (659), unless different requirements are provided in a specific monograph.

10.40. 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 it 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 product identification (except for controlled articles), lot number, expiration date, and conditions for storage and distribution.

Articles in these compendia are subject to compliance with such labeling requirements as may be promulgated by governmental bodies in addition to the compendial requirements set forth for the articles.

10.40.10. Amount of Ingredient Per Dosage Unit

The strength of a drug product is expressed on the container label in terms of micrograms or milligrams or grams or percentage of the therapeutically active moiety or drug substance, whichever form is used in the title, unless otherwise indicated in an individual monograph. Both the active moiety and drug substance names and their equivalent amounts are then provided in the labeling.

Official articles in capsule, tablet, or other unit dosage form shall be labeled to express the quantity of each active ingredient or recognized nutrient contained in each such unit, except that, in the case of unit-dose oral solutions or suspensions, whether supplied as liquid preparations or as solid preparations that are constituted from solids upon addition of a designated volume of a specific diluent, the label shall express the quantity of each active ingredient or recognized nutrient delivered under the conditions prescribed in Deliverable Volume (698). Official drug products not in unit dosage form shall be labeled to express the quantity of each active ingredient in each milliliter or in each gram, or to express the percentage of each such ingredient (see 8.140, Percentage Concentrations), except that oral liquids or solids intended to be constituted to yield oral liquids may, alternatively, be labeled in terms of each 5-mL portion of the liquid or resulting liquid. Unless otherwise indicated in a monograph or chapter, such declarations of strength or quantity shall be stated only in metric units. See also 5.50.10, Units of Potency (Biological).

10.40.20. Use of Leading and Terminal Zeros

To help minimize the possibility of errors in the dispensing and administration of drugs, the quantity of active ingredient when expressed in whole numbers shall be shown without a decimal point that is followed by a terminal zero (e.g., express as 4 mg [not 0.4 mg]). The quantity of active ingredient when expressed as a decimal number smaller than 1 shall be shown with a zero preceding the decimal point (e.g., express as 0.2 mg [not .2 mg]).

10.40.30. Labeling of Salts of Drugs

It is an established principle that official articles shall have only one official title. For purposes of saving space on labels and because chemical symbols for the most common inorganic salts of drugs are well known to practitioners as synonymous with the written forms, the following alternatives are permitted in labeling official articles that are salts: HCl for hydrochloride; HBr for hydrobromide; Na for sodium; and K for potassium. The symbols Na and K are intended for use in abbreviating names of the salts, but these symbols are not used where the word Sodium or Potassium appears at the beginning of an official title (e.g., Phenobarbital Na is acceptable, but Na Salicylate is not to be written).

10.40.40. Labeling Vitamin-Containing Products

The vitamin content of an official drug product shall be stated on the label in metric units per dosage unit. The amounts of vitamins A, D, and E may be stated also in USP Units. Quantities of vitamin A declared in metric units refer to the equivalent amounts of retinol (vitamin A alcohol). The label of a nutritional supplement shall bear an identifying lot number, control number, or batch number.

10.40.50. Labeling Botanical-Containing Products

The label of an herb or other botanical intended for use as a dietary supplement bears the statement, “If you are pregnant or nursing a baby, seek the advice of a health professional before using this product.”

10.40.60. Labeling Parenteral and Topical Preparations

The concentration and dosage of electrolytes for replacement therapy (e.g., sodium chloride or potassium chloride) shall be stated on the label in milliequivalents (mEq). The label of the product shall also indicate the quantity of ingredient(s) in terms of weight or percentage concentration.

10.40.70. Labeling Electrolytes

The concentration and dosage of electrolytes for replacement therapy (e.g., sodium chloride or potassium chloride) shall be stated on the label in milliequivalents (mEq). The label of the product shall indicate also the quantity of ingredient(s) in terms of weight or percentage concentration.

10.40.80. Labeling Alcohol

The content of alcohol in a liquid preparation shall be stated on the label as a percentage (v/v) of C₂H₅OH.

10.40.90. Special Capsules and Tablets

The label of an herb or other botanical intended for use as a dietary supplement bears the statement, “If you are pregnant or nursing a baby, seek the advice of a health professional before using this product.”
tended for sale without prescription and the labeling of which states no dosage limitations, and which is stable for not less than 3 years when stored under the prescribed conditions.

Where an official article is required to bear an expiration date, such article shall be dispensed solely in, or from, a container labeled with an expiration date, and the date on which the article is dispensed shall be within the labeled expiry period. The expiration date identifies the time during which the article may be expected to meet the requirements of the compendial monograph, provided it is kept under the prescribed storage conditions. The expiration date limits the time during which the article may be dispensed or used. Where an expiration date is stated only in terms of the month and the year, it is a representation that the intended expiration date is the last day of the stated month. The beyond-use date is the date after which an article shall not be used. The dispense shall place on the label of the prescription container a suitable beyond-use date to limit the patient’s use of the article based on any information supplied by the manufacturer and the General Notices. The beyond-use date placed on the label shall not be later than the expiration date on the manufacturer’s container.

For articles requiring constitution before use, a suitable beyond-use date for the constituted product shall be identified in the labeling.

For all other dosage forms, in determining an appropriate period of time during which a prescription drug may be retained by a patient after its dispensing, the dispense shall take into account, in addition to any other relevant factors, the nature of the drug; the container in which it was packaged by the manufacturer and the expiration date thereon; the characteristics of the patient’s container, if the article is repackaged for dispensing; the expected storage conditions to which the article may be exposed; any unusual storage conditions to which the article may be exposed; and the expected length of time of the course of therapy. The dispense shall, on taking into account the foregoing, place on the label of a multiple-unit container a suitable beyond-use date to limit the patient’s use of the article. Unless otherwise specified in the individual monograph, or in the absence of stability data to the contrary, such beyond-use date shall be not later than (a) the expiration date on the manufacturer’s container, or (b) 1 year from the date the drug is packaged, whichever is earlier. For nonsterile solid and liquid dosage forms that are packaged in single-unit and unit-dose containers, the beyond-use date shall be 1 year from the date the drug is packaged into the single-unit or unit-dose container or the expiration date on the manufacturer’s container, whichever is earlier, unless stability data or the manufacturer’s labeling indicates otherwise.

The dispense shall maintain the facility where the dosage forms are packaged and stored, at a temperature such that the mean kinetic temperature is not greater than 25°C. The plastic material used in packaging the dosage forms shall afford better protection than polyvinyl chloride, which does not provide adequate protection against moisture permeation. Records shall be kept of the temperature of the facility where the dosage forms are stored, and of the plastic materials used in packaging.

10.40.100.1. Compounded Preparations

The label on the container or package of an official compounded preparation shall bear a beyond-use date. The beyond-use date is the date after which a compounded preparation is not to be used. Because compounded preparations are intended for administration immediately or following short-term storage, their beyond-use dates may be assigned based on criteria different from those applied to assigning expiration dates to manufactured drug products.

The monograph for an official compounded preparation typically includes a beyond-use requirement that states the time period following the date of compounding during which the preparation, properly stored, may be used. In the absence of stability information that is applicable to a specific drug and preparation, recommendations for maximum beyond-use dates have been devised for nonsterile compounded drug preparations that are packaged in tight, light-resistant containers and stored at controlled room temperature unless otherwise indicated (see the general test chapter Pharmaceutical Compounding—Nonsterile Preparations (795), Stability Criteria and Beyond-Use Dating).