The average of not less than four consecutive readings that lie within a range of 0.2° constitutes the congealing temperature. These readings lie about a point of inflection or a maximum, in the temperature-time curve, that occurs after the temperature becomes constant or starts to rise and before it again begins to fall. The average to the nearest 0.1° is the congealing temperature.

(659) PACKAGING AND STORAGE REQUIREMENTS

(Chapter to become official May 1, 2016)

Delete the following:

Every monograph in the USP and NF shall have packaging and storage requirements. For the packaging portion of the statement, the choice of containers is given in this chapter. For drug product packaging requirements, definitions are provided to guide selection and adaptation. For active pharmaceutical ingredients (APIs), the choice would be tight, well-closed or, where needed, a light-resistant container. For excipients, given their typical presentation as large-volume commodity items (containers ranging from drums to tank cars), a well-closed container is an appropriate default.

Where no specific directions or limitations are provided in the article’s labeling, articles shall be protected from moisture, freezing, and excessive heat and, where necessary, from light during shipping and distribution. Drug substances are exempt from this standard.

Change to read:

PACKAGING

Packaging must not interact physically or chemically with official articles in any way that causes their safety, identity, strength, quality, or purity to fail to conform to requirements.

Packaging container choices are given in this chapter. For drug products and active pharmaceutical ingredients (APIs), the container choices are tight, well-closed, or, where needed, light-resistant. For excipients, given their typical presentation as large-volume commodity items (containers ranging from drums to tank cars), a well-closed container is an appropriate default.

For articles other than drug substances and drug products, where no specific directions or limitations are provided, articles shall be protected from moisture, freezing, and excessive heat, and, where necessary, from light during shipping and distribution.

The compendial requirements for the use of specified containers apply also to articles as packaged by the pharmacist or other dispenser, unless otherwise indicated in the individual monograph.

Change to read:

GENERAL DEFINITIONS

Packaging system (also referred to as a container–closure system): The sum of packaging components that together contain and protect the article. This includes primary packaging components and secondary packaging components, if the latter is intended to provide additional protection.

Container: A receptacle that holds an intermediate compound, active pharmaceutical ingredient, excipient, or dosage form and is or may be in direct contact with the articles. 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.

Packaging component: Any single part of the package or container–closure system including the container (e.g., ampuls, prefilled syringes, vials, bottles); container liners (e.g., tube cartridge liners); closures (e.g., screw caps, stoppers); ferrules and overseals; closure liners; inner seals; administration ports; overwraps; administration accessories; and labels.

Primary packaging component: Packaging components that are in direct contact or may become in direct contact with the article.

Secondary packaging component: Packaging components that are not and will not be in direct contact with the article.

Tertiary packaging: Packaging components that are not in direct contact with the article but facilitate the handling and transport in order to prevent damage from physical handling and storage conditions to which the article is subjected.

Materials of construction: Refers to the materials (e.g., glass, plastic, elastomers, metal) used to manufacture a packaging component.
Multiple-dose container: A packaging system that permits withdrawal of successive portions of an article for parenteral administration without changing the safety, strength, quality, or purity of the remaining portion. See *Multi-Dose Containers in Container Content for Injections (697).*

Multiple-unit container: A packaging system that permits withdrawal of successive portions of an article without changing the safety, strength, quality, or purity of the remaining portion.

Single-unit container: A packaging system that holds a quantity of an article intended for administration as a single dose or a single finished device intended for use promptly after the container is opened. Preferably, the immediate container and/or the outer container or protective packaging shall be so designed as to show evidence of any tampering with the contents.

Single-dose container: A single-dose container is a container of sterile medication for parenteral administration (injection or infusion) that is not required to meet the antimicrobial effectiveness testing criteria. [Note—For this definition only, container is synonymous with packaging system and container–closure system.] A single-dose container is designed for use with a single patient as a single injection/infusion. A single-dose container is labeled as such and, when space permits, should include appropriate discard instructions on the label. Examples of single-dose containers are vials, ampuls, and prefilled syringes.

Unit-dose container: A single-unit packaging system for an article intended for administration by other than the parenteral route as a single dose.

Unit-of-use container: A packaging system that contains a specific quantity of an article that is intended to be dispensed as such without further modification except for the addition of appropriate labeling. Unit-of-use packaging may not be repackaged for sale.

Pharmacy bulk package: A packaging system of a sterile preparation for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for infusion or, through a sterile transfer device, for the filling of empty sterile syringes.

The closure shall be penetrated only one time after constitution, if necessary, with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents. The Pharmacy bulk package is to be used only in a suitable work area such as a laminar flow hood (or an equivalent clean-air compounding area).

Designation as a Pharmacy bulk package is limited to Injection, for Injection, or Injectable Emulsion dosage forms as defined in Nomenclature (1121), General Nomenclature Forms (USP38).

Pharmacy bulk package, although containing more than one single dose, is exempt from the multiple-dose container volume limit of 30 mL and the requirement that it contains a substance or suitable mixture of substances to prevent the growth of microorganisms. See Labeling (7) for labeling requirements.

Small-volume injections: An injection that is packaged in containers labeled as containing 100 mL or less.

Large-volume injections: An injection that is intended for intravenous use, and is packaged in containers labeled as containing more than 100 mL.

Child-resistant packaging: A packaging system designed or constructed to meet Consumer Product Safety Commission standards pertaining to opening by children (16 CFR §1700.20).

Senior-friendly packaging: A packaging system designed or constructed to meet Consumer Product Safety Commission standards pertaining to opening by senior adults (16 CFR §1700.20).

Tamper-evident packaging: A packaging system that may not be accessed without obvious destruction of the seal or some portion of the packaging system. Tamper-evident packaging shall be used for a sterile article intended for ophthalmic or otic use, except where extemporaneously compounded for immediate dispensing on prescription. Articles intended for sale without prescription are also required to comply with the tamper-evident packaging and labeling requirements of the FDA where applicable. Preferably, the immediate container and/or the outer container or protective packaging used by a manufacturer or distributor for all dosage forms that are not specifically exempt is designed so as to show evidence of any tampering with the contents.

Hermetic container: A packaging system that is impervious to air or any other gas under the ordinary or customary conditions of handling, shipment, storage, and distribution.

Tight container: A packaging system that 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. Where a tight container is specified, it may be replaced by a hermetic container for a single dose of an article. [Note—Where packaging and storage in a tight container or well-closed container is specified in the individual monograph, the container used for an article when dispensed on prescription meets the requirements in Containers—Performance Testing (671)].

Well-closed container: A packaging system that protects the contents from contamination by extraneous solids and from loss of the article under the ordinary or customary conditions of handling, shipment, storage, and distribution. See Containers—Performance Testing (671).

Light-resistant container: A packaging system that 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. A clear and colorless or a translucent container may be made light-resistant by means of an opaque covering or by use of secondary packaging, in which case the label of the container bears a statement that the opaque covering or secondary packaging is needed until the articles are dispensed as such without further modification except for the addition of appropriate labeling. Unit-of-use packaging may not be repackaged for sale.

* Exceptions may be considered only under conditions described in Pharmaceutical Compounding—Sterile Preparations (797).
are to be used or administered. Where it is directed to “protect from light” in an individual monograph, preservation in a light-resistant container is intended. See Containers—Performance Testing (671), Light Transmission Test.

**Black closure system or black bands:** The use of a black closure system on a vial (e.g., a black cap overseal and a black ferrule to hold the elastomeric closure) or the use of a black band or series of bands above the constriction on an ampul is prohibited, except for Potassium Chloride for Injection Concentrate. See Labeling (7).

*Add the following:*

### INJECTION PACKAGING

Validation of container–closure integrity must demonstrate no penetration of microbial contamination or chemical or physical impurities. In addition, the solutes and the vehicle must maintain their specified total and relative quantities or concentrations when exposed to anticipated extreme conditions of manufacturing and processing, storage, shipment, and distribution. Closures for multiple-dose packaging systems permit the withdrawal of the contents without removal or destruction of the closure. The closure permits penetration by a needle and, upon withdrawal of the needle, closes at once, protecting the contents against contamination. Validation of the multiple-dose container–closure integrity must include verification that such a package prevents microbial contamination or loss of product contents under anticipated conditions of multiple entry and use.

Piggyback packaging systems are usually intravenous infusion container–closure systems used to administer a second infusion through a connector of some type or an injection port on the administration set of the first fluid, thereby avoiding the need for another injection site on the patient’s body. Piggyback packaging systems also are known as secondary infusion containers.

The volume of injection in a single-dose packaging system provides the amount specified for one-time parenteral administration and in no case is more than sufficient to permit the withdrawal and administration of 1 L.

Preparations intended for intraspinal, intracisternal, or peridural administration are packaged only in single-dose packaging systems.

Unless otherwise specified in the individual monograph, a multiple-dose packaging system contains a volume of injection sufficient to permit the withdrawal of NMT 30 mL.

The following injections are exempt from the 1-L restriction of the foregoing requirements relating to packaging:

1. Injections packaged for extravascular use as irrigation solutions or peritoneal dialysis solutions.
2. Injections packaged for intravascular use as parenteral nutrition or as replacement or substitution fluid to be administered continuously during hemofiltration.

Injections packaged for intravascular use that may be used for intermittent, continuous, or bolus replacement fluid administration during hemodialysis or other procedures, unless excepted above, must conform to the 1-L restriction. Injections labeled for veterinary use are exempt from packaging and storage requirements concerning the limitation to single-dose packaging systems and the limitation on the volume of multiple-dose containers.

**Sterile solids packaging:** Containers, including the closures, for dry solids intended for injection do not interact physically or chemically with the preparation in any manner to alter the strength, quality, or purity beyond the official requirements under the ordinary or customary conditions of handling, shipment, storage, sale, and use. A packaging system for a sterile solid permits the addition of a suitable solvent and withdrawal of portions of the resulting solution or suspension in such manner that the sterility of the product is maintained. Where the Assay in a monograph provides a procedure for the Sample solution, in which the total withdrawable contents are to be withdrawn from a single-dose packaging system with a hypodermic needle and syringe, the contents are to be withdrawn as completely as possible into a dry hypodermic syringe of a rated capacity not exceeding three times the volume to be withdrawn and fitted with a 21-gauge needle NLT 2.5 cm (1 inch) in length, with care being taken to expel any air bubbles, and discharged into a container for dilution and assay.

### MEDICAL GAS PACKAGING

**Gas cylinder:** A gas cylinder is a metallic packaging system constructed of steel or aluminum designed to hold medical gases under pressure. Medical gases include Carbon Dioxide USP, Helium USP, Medical Air USP, nitric oxide, Nitrous Oxide USP, Nitrogen NF, and Oxygen USP. As a safety measure, for carbon dioxide, cyclopropane, helium, medical air, nitrous oxide, and oxygen, the Pin-Index Safety System of matched fittings is recommended for cylinders of Size E or smaller.

### ASSOCIATED COMPONENTS

Many associated components are graduated for dose administration. It is the responsibility of the manufacturer to ensure that the appropriate dosing component is provided or that a general purpose component, such as those described in this section, is specified for delivering the appropriate dose with the intended accuracy. The graduations should be legible and indelible.

Graduated associated components described in this section are for general use. Graduated markings should be legible, indelible, and on an extraoral nonproduct contact surface. Under ideal conditions of use, the volume error incurred in measuring liquids for individual dose administration by means of such graduated components should be NMT 10% of the indicated
amount of the liquid preparation with which the graduated component will be used. Few liquid preparations have the same surface and flow characteristics. Therefore, the volume delivered varies materially from one preparation to another.

Polymers and ingredients added to polymers that are used in the fabrication of associated components must conform to the requirements in the applicable sections of the Code of Federal Regulations, Title 21, Indirect Food Additives.

Dosing cup: A measuring device consisting of a small cup that is packaged with oral liquid articles or that may be sold and purchased separately.

Dosing spoon: A measuring device consisting of a bowl and a handle that is packaged with oral liquid articles or that may be sold and purchased separately. The handle may be a graduated tube.

Medicine dropper: A measuring device consisting of a transparent or translucent barrel or tube that is generally fitted with a collapsible bulb. It is packaged with oral liquid articles or may be sold and purchased separately.

Droppers typically vary in capacity; however, the delivery end should be a round opening having an external diameter of about 3 mm. The barrel may be graduated. [Note—Few medicinal liquids have the same surface and flow characteristics as water, and therefore the size of drops varies materially from one preparation to another.]

Oral syringe: A measuring device consisting of a plunger and barrel made of suitable rigid, transparent or translucent plastic material and a seal on the end. It is packaged with oral liquid articles or may be sold and purchased separately. The syringe should expel a measured amount of a liquid article directly into the patient’s mouth. Finger grips located at the open end of the barrel should be the appropriate size, shape, and strength, and should allow the syringe to be held securely during use. The barrel may be graduated.

Teaspoon: A measuring device consisting of a shallow bowl, oval or round, at the end of a handle. A teaspoon has been established as containing 4.93 ± 0.24 mL. For the practice of administering articles, the teaspoon may be regarded as representing a volume of 5 mL.

Articles intended for administration by teaspoon should be formulated on the basis of dosage in 5-mL units, such that any component used to administer liquid articles should deliver 5 mL wherever a teaspoon calibration is indicated. A household spoon is not an acceptable alternative to the graduated teaspoon described herein.

POISON PREVENTION PACKAGING ACT (PPPA)

This act requires special packaging of most human oral prescription drugs, oral controlled drugs, certain non-oral prescription drugs, certain dietary supplements, and many over-the-counter (OTC) drug preparations in order to protect the public from personal injury or illness from misuse of these preparations (16 CFR §1700.14).

The immediate packaging of substances regulated under the PPPA must comply with the special packaging standards (16 CFR §1700.15 and 16 CFR §1700.16) and applies to all packaging types including reclosable, nonclosable, and unit-dose types.

Special packaging is not required either for drugs dispensed within a hospital setting for inpatient administration or by manufacturers and packagers of bulk-packaged prescription drugs repackaged by the pharmacist. PPPA-regulated prescription drugs may be dispensed in nonchild-resistant packaging upon the request of the purchaser or when directed in a legitimate prescription (15 U.S.C. §1473).

Manufacturers or packagers of PPPA-regulated OTC preparations are allowed to package one size in nonchild-resistant packaging as long as popular-size, special packages are also supplied. The nonchild-resistant packaging requires special labeling (16 CFR §1700.5).

Change to read:

STORAGE CONDITIONS

Specific directions are stated in some monographs with respect to storage conditions, e.g., the temperature or humidity at which an article must be stored and shipped. Such directions apply, except where the label on the article has different storage conditions that are based on stability studies. Where no specific storage conditions are provided in the individual monograph, but the label of an article states storage conditions based on stability studies, such labeled storage directions apply.

Freezer: A place in which the temperature is maintained between −25° and −10° (−13° and 14 °F).

Refrigerator: A place in which the temperature is maintained between 2° and 8° (36° and 46 °F).

Cold: Any temperature not exceeding 8° (46 °F).

Cool: Any temperature between 8° and 15° (46° and 59 °F). [Note—An article for which storage in a cool place is directed may, alternatively, be stored and shipped as refrigerated, unless otherwise specified by the individual monograph.]

Controlled room temperature: The temperature maintained thermostatically that encompasses at the usual and customary working environment of 20°–25° (68°–77 °F). The following conditions also apply.

Mean kinetic temperature not to exceed 25°. Excursions between 15° and 30° (59° and 86 °F) that are experienced in pharmacies, hospitals, and warehouses, and during shipping are allowed. Provided the mean kinetic temperature does not exceed 25°, transients spikes up to 40° are permitted as long as they do not exceed 24 h. Spikes above 40° may be permitted only if the manufacturer so instructs.

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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.

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

Warm: Any temperature between 30° and 40° (86° and 104 °F).

Excessive heat: Any temperature above 40° (104 °F).

Dry place: The term “dry place” denotes a place that does not exceed 40% average relative humidity at 20° (68 °F) 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 NLT 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 does not exceed 40% relative humidity. Storage in a container validated to protect the article from moisture vapor, including storage in bulk, is considered a dry place.

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

Protection from light: Where light subjects an article to loss of strength or potency, or to destructive alteration of its characteristics, the container label bears an appropriate instruction to protect the article from light.

〈659〉 PACKAGING AND STORAGE REQUIREMENTS

(Current chapter official through April 30, 2016)

Every monograph in the USP and NF shall have packaging and storage requirements. For the packaging portion of the statement, the choice of containers is given in this chapter. For drug product packaging requirements, definitions are provided to guide selection and adaptation. For active pharmaceutical ingredients (APIs), the choice would be tight, well-closed, or, where needed, a light-resistant container. For excipients, given their typical presentation as large-volume commodity items (containers ranging from drums to tank cars), a well-closed container is an appropriate default.

Where no specific directions or limitations are provided in the article’s labeling, articles shall be protected from moisture, freezing, and excessive heat, and where necessary, from light during shipping and distribution. Drug substances are exempt from this standard.

PACKAGING

Packaging must not interact physically or chemically with official articles in any way that causes their safety, identity, strength, quality, or purity to fail to conform to requirements. This chapter provides definitions of both packaging and storage.

GENERAL DEFINITIONS

Packaging System (also referred to as a container–closure system): The sum of packaging components that together contains and protects the article. This includes primary packaging components and secondary packaging components, if the latter is intended to provide additional protection.

Container: A receptacle that holds an intermediate compound, active pharmaceutical ingredient, excipient, or dosage form and is in direct contact with the articles.

Packaging Component: Any single part of the package or container–closure system including the container (e.g., ampolles, prefilled syringes, vials, bottles); container liners (e.g., tube cartridge liners); closures (e.g., screw caps, stoppers); ferrules and overseals; closure liners; inner seals; administration ports; overwraps; administration accessories; and labels.

Primary Packaging Component: Packaging components that are in direct contact or may become in direct contact with the article.

Secondary Packaging Component: Packaging components that are not and will not be in direct contact with the article but may provide additional protection.

Tertiary Packaging: Packaging components that are not in direct contact with the article but facilitate the handling and transport in order to prevent damage from physical handling and storage conditions to which the article is subjected.

Materials of Construction: Refers to the materials (e.g., glass, plastic, elastomers, metal) used to manufacture a packaging component.

Multiple-Dose (also referred to as multi-dose): A packaging system that permits withdrawal of successive portions of an article for parenteral administration without changing the safety, strength, quality, or purity of the remaining portion. See Multi-Dose Containers in Injections (1), Determination of Volume of Injection in Containers.
Multiple-Unit: A packaging system that permits withdrawal of successive portions of an article without changing the safety, strength, quality, or purity of the remaining portion.

Single-Unit: A packaging system that holds a quantity of an article intended for administration as a single dose or a single finished device intended for single use.

Single-Dose (see also Injections (1), Containers for Injections): A single-unit package for an article intended for parenteral administration. Examples of single-dose containers include prefilled syringes, cartridges, fusion-sealed containers, and closure-sealed containers when so labeled.

Unit-Dose: A single-unit packaging system for an article intended for administration by other than the parenteral route as a single dose.

Unit-of-Use: A packaging system that contains a specific quantity of an article that is intended to be dispensed as such without further modification except for the addition of appropriate labeling. Unit-of-Use packaging may not be repackaged for sale.

Pharmacy Bulk Package: A container of a sterile preparation for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for infusion or, through a sterile transfer device, for the filling of empty sterile syringes.

After constitution, the closure shall be penetrated only one time with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents. The Pharmacy Bulk Package is to be used only in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area).

Designation as a Pharmacy Bulk Package is limited to Injections, for Injection, or Injectable Emulsion as defined under Injections (1), Nomenclature.

Pharmacy Bulk Packages, although containing more than one single dose, are exempt from the multiple-dose container volume limit of 30 mL and the requirement that they contain a substance or suitable mixture of substances to prevent the growth of microorganisms. Where a container is offered as a Pharmacy Bulk Package, the label shall (a) state prominently “Pharmacy Bulk Packages—Not for direct infusion,” (b) contain or refer to information on proper techniques to help assure safe use of the product, and (c) bear a statement limiting the time frame in which the container may be used once it has been entered, provided it is held under the labeled storage conditions.

Small-Volume Injections: A single-dose injection that is intended for intravenous use and is packaged in containers labeled as containing 100 mL or less.

Large-Volume Injections: A single-dose injection that is intended for intravenous use and is packaged in containers labeled as containing more than 100 mL.

Child-Resistant: A packaging system designed or constructed to meet Consumer Product Safety Commission standards pertaining to opening by children (16 CFR §1700.20).

Senior-Friendly: A packaging system designed or constructed to meet Consumer Product Safety Commission standards pertaining to opening by senior adults (16 CFR §1700.20).

Tamper-Evident: A packaging system that may not be accessed without obvious destruction of the seal or some portion of the packaging system.

Tight: A packaging system that protects the articles 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. See Containers—Performance Testing (671).

Well-Closed: A packaging system that protects the articles from contamination by extraneous solids and liquids and from loss of the article under the ordinary or customary conditions of handling, shipment, storage, and distribution. See Containers—Performance Testing (671).

Light-Resistant: A packaging system that protects 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. A clear and colorless or a translucent container may be made light-resistant by means of an opaque covering or by use of secondary packaging, in which case the label of the container bears a statement that the opaque covering or secondary packaging is needed until the articles are to be used or administered. See Containers—Performance Testing (671), Light Transmission Test.

MEDICAL GAS PACKAGING

Gas Cylinder: A gas cylinder is a metallic packaging system constructed of steel or aluminum designed to hold medical gases under pressure. Medical gases include Carbon Dioxide USP, Helium USP, Medical Air USP, nitric oxide, Nitrous Oxide USP, Nitrogen NF, and Oxygen USP. As a safety measure, for carbon dioxide, cyclopropane, helium, medical air, nitrous oxide, and oxygen, the Pin-Index Safety System of matched fittings is recommended for cylinders of Size E or smaller.

ASSOCIATED COMPONENTS

Many associated components are graduated for dose administration. It is the responsibility of the manufacturer to ensure the appropriate dosing component is provided or a general purpose component, such as those described in this section, is specified for delivering the appropriate dose with the intended accuracy. The graduations should be legible and indelible.

Graduated associated components described in this section are for general use. Graduated markings should be legible, indelible, and on an extraoral nonproduct contact surface. Under ideal conditions of use, the volume error incurred in measuring
liquids for individual dose administration by means of such graduated components should be not greater than 10% of the indicated amount of the liquid preparation with which the graduated component will be used. Few liquid preparations have the same surface and flow characteristics. Therefore, the volume delivered varies materially from one preparation to another.

Polymers and ingredients added to polymers that are used in the fabrication of associated components must conform to the requirements in the applicable sections of the Code of Federal Regulations, Title 21, Indirect Food Additives.

**Dosing Cup:** A measuring device consisting of a small cup that is packaged with oral liquid articles or that may be sold and purchased separately.

**Dosing Spoon:** A measuring device consisting of a bowl and a handle that is packaged with oral liquid articles or that may be sold and purchased separately. The handle may be a graduated tube.

**Medicine Dropper:** A measuring device consisting of a transparent or translucent barrel or tube that is generally fitted with a collapsible bulb. It is packaged with oral liquid articles or may be sold and purchased separately.

Droppers typically vary in capacity; however, the delivery end should be a round opening having an external diameter of about 3 mm. The barrel may be graduated. [Note—Few medicinal liquids have the same surface and flow characteristics as water, and therefore the size of drops varies materially from one preparation to another.]

**Oral Syringe:** A measuring device consisting of a plunger and barrel made of suitable rigid transparent or translucent plastic material and a seal on the end. It is packaged with oral liquid articles or may be sold and purchased separately. The syringe should expel a measured amount of a liquid article directly into the patient’s mouth. Finger grips located at the open end of the barrel should be the appropriate size, shape, and strength and should allow the syringe to be held securely during use. The barrel may be graduated.

**Teaspoon:** A measuring device consisting of a shallow bowl, oval or round, at the end of a handle. A teaspoon has been established as containing 4.93 ± 0.24 mL. For the practice of administering articles, the teaspoon may be regarded as representing 5 mL.

Articles intended for administration by teaspoon should be formulated on the basis of dosage in 5-mL units, such that any component used to administer liquid articles should deliver 5 mL wherever a teaspoon calibration is indicated. A household spoon is not an acceptable alternative to the graduated teaspoon described herein.

**POISON PREVENTION PACKAGING ACT (PPPA)**

This act requires special packaging of most human oral prescription drugs, oral controlled drugs, certain non-oral prescription drugs, certain dietary supplements, and many over-the-counter (OTC) drug preparations in order to protect the public from personal injury or illness from misuse of these preparations (16 CFR §1700.14).

The immediate packaging of substances regulated under the PPPA must comply with the special packaging standards (16 CFR §1700.15 and 16 CFR §1700.16) and applies to all packaging types including reclosable, nonclosable, and unit-dose types.

Special packaging is not required either for drugs dispensed within a hospital setting for inpatient administration or by manufacturers and packagers of bulk-packaged prescription drugs repackaged by the pharmacist. PPPA-regulated prescription drugs may be dispensed in nonchild-resistant packaging upon the request of the purchaser or when directed in a legitimate prescription (15 U.S.C. §1473).

Manufacturers or packagers of PPPA-regulated OTC preparations are allowed to package one size in nonchild-resistant packaging as long as popular-size, special packages are also supplied. The nonchild-resistant packaging requires special labeling (16 CFR §1700.5).

**STORAGE CONDITIONS**

Specific directions are stated in some monographs with respect to storage conditions, e.g., the temperature or humidity at which an article must be stored and shipped. Such directions apply, except where the label on the article has different storage conditions that are based on stability studies. Where no specific storage conditions are provided in the individual monograph, but the label of an article states storage conditions based on stability studies, such labeled storage directions apply. Current storage conditions for articles are defined by the following terms.

**Freezer:** A place in which the temperature is maintained between −25° and −10° (−13° and 14 °F).

**Refrigerator:** A place in which the temperature is maintained between 2° and 8° (36° and 46 °F).

**Cold:** Any temperature not exceeding 8° (46 °F).

**Cool:** Any temperature between 8° and 15° (46° and 59 °F). [Note—An article for which storage in a cool place is directed may, alternatively, be stored and shipped as refrigerated, unless otherwise specified by the individual monograph.]

**Room Temperature:** The temperature prevailing in a work area.

**Controlled Room Temperature:** The temperature maintained at the usual and customary working environment of 20° to 25° (68° to 77 °F). The following conditions also apply.

The mean kinetic temperature shall not exceed 25°. The mean kinetic temperature is a calculated value that may be used as an isothermal storage temperature that simulates the nonisothermal effects of storage temperature variations.

Excursions between 15° and 30° (59° and 86 °F) that are experienced in pharmacies, hospitals, and warehouses, and during shipping are allowed, provided the mean kinetic temperature does not exceed 25°.
Transient spikes up to 40° are permitted as long as they do not last for more than 24 hours. Spikes above 40° may be permitted only 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.

An article for which storage at Controlled Room Temperature is directed may, alternatively, be stored and shipped in a cool place or refrigerated, unless otherwise specified in the individual monograph or on the label.

**Warm:** Any temperature between 30° and 40° (86° and 104 °F).

**Excessive Heat:** Any temperature above 40° (104 °F).

**Dry Place:** The term “dry place” denotes a place that does not exceed 40% average relative humidity at 20° (68 °F) 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 does not exceed 40% relative humidity. Storage in a container validated to protect the article from moisture vapor, including storage in bulk, is considered a dry place.

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

**Protection from Light:** Where light subjects an article to loss of strength or potency, or to destructive alteration of its characteristics, the container label bears an appropriate instruction to protect the article from light.

### CONTAINERS—GLASS

**DESCRIPTION**

Glass containers for pharmaceutical use are intended to come into direct contact with pharmaceutical products. Glass used for pharmaceutical containers is either borosilicate (neutral) glass or soda-lime-silica glass. Borosilicate glass contains significant amounts of boric oxide, aluminum oxide, and alkali and/or alkaline earth oxides in the glass network. Borosilicate glass has a high hydrolytic resistance and a high thermal shock resistance due to the chemical composition of the glass itself; it is classified as Type I glass. Soda-lime-silica glass is a silica glass containing alkaline metal oxides, mainly sodium oxide, and alkaline earth oxides, mainly calcium oxide, in the glass network. Soda-lime-silica glass has a moderate hydrolytic resistance due to the chemical composition of the glass itself; it is classified as Type III glass. Suitable treatment of the inner surface of Type III soda-lime-silica glass containers will raise the hydrolytic resistance from a moderate to a high level, changing the classification of the glass to Type II.

The following recommendations can be made as to the suitability of the glass type for containers for pharmaceutical products, based on the tests for hydrolytic resistance. Type I glass containers are suitable for most products for parenteral and non-parenteral uses. Type II glass containers are suitable for most acidic and neutral aqueous products for parenteral and non-parenteral uses. Type II glass containers may be used for alkaline parenteral products where stability data demonstrate their suitability. Type III glass containers usually are not used for parenteral products or for powders for parenteral use, except where suitable stability test data indicate that Type III glass is satisfactory.

The inner surface of glass containers may be treated to improve hydrolytic resistance. The outer surface of glass containers may be treated to reduce friction or for protection against abrasion or breakage. The outer surface treatment is such that it does not contaminate the inner surface of the container.

Information on chemical composition of glass types, the formation of glass containers, and factors that influence inner surface durability of glass containers is provided in Evaluation of the Inner Surface Durability of Glass Containers (660). This chapter also contains recommended approaches to evaluate the potential of a drug product to cause the formation of glass particles and delamination. Glass may be colored to provide protection from light by the addition of small amounts of metal oxides and is tested as described in Spectral Transmission for Colored Glass Containers. A clear and colorless container that is made light resistant by means of an opaque enclosure (see Packaging and Storage Requirements (659), Light-Resistant) is exempt from the requirements for spectral transmission.