BRIEFING

⟨659⟩ Packaging and Storage Requirements, *USP 42* page 6801 and *PF* 44(4) [July–Aug. 2018]. The General Chapters—Packaging and Distribution Expert Committee has canceled the *PF* 44(4) proposal and is now proposing the following revision. The purpose of the revisions will be to provide a delayed extension of the requirements specified in *Plastic Materials of Construction* ⟨661.1⟩ and *Plastic Packaging Systems for Pharmaceutical Use* ⟨661.2⟩, which otherwise were to become applicable on May 1, 2020 through this chapter, to enable early adoption of the requirements in ⟨661.1⟩ and ⟨661.2⟩ at any time during the implementation delay period in lieu of meeting the reinstated *Plastic Packaging Systems and Their Materials of Construction* ⟨661⟩ requirements.

The specific revisions are as follows:

1. Delay until December 1, 2025 the implementation of the new requirements of ⟨661.1⟩ and ⟨661.2⟩ as currently specified in this chapter.
2. To make ⟨661⟩, as referenced in this chapter, applicable until November 30, 2025.
3. In this chapter, clarify that early adoption of the requirements of ⟨661.1⟩ and ⟨661.2⟩ is permitted by USP, and that packaging systems in compliance with these requirements in advance of December 1, 2025 will no longer need to comply with ⟨661⟩ requirements to be considered by USP to be in conformance with the *USP–NF*.
4. For the "Small-volume injection" and "Large-volume injection" definitions, it was clarified that terms are also referred to as "Small-volume parenteral" and "Large-volume parenteral", respectively.

Additionally, minor editorial changes have been made to update the chapter to current *USP* style.

(GCPD: D. Hunt.)

Correspondence Number—C201835

⟨659⟩ PACKAGING AND STORAGE REQUIREMENTS

Change to read:

(A portion of the *Associated Components* section of this chapter will become official on May 1, 2019, and a portion of the *Packaging* section of this chapter will become official on ~~May 1, 2020,~~ ▲December 1, 2025▲ (USP 1-Aug-2020) as indicated. Early adoption of the requirements in this chapter and *Plastic Materials of Construction* ⟨661.1⟩ and *Plastic Packaging Systems for Pharmaceutical Use* ⟨661.2⟩ are permitted by USP.)

INTRODUCTION

The purpose of this chapter is to provide packaging definitions, auxiliary packaging information, and storage condition definitions relevant to the storage and distribution of active ingredients, excipients, and medical products, such as pharmaceuticals, devices, combination products (e.g., drug-eluting stents), and dietary supplements.

Change to read:

PACKAGING

Packaging materials must not interact physically or chemically with a packaged article in a manner that causes its safety, identity, strength, quality, or purity to fail to conform to established requirements. ▲Any plastic material used to construct a *Packaging system* must meet the applicable requirements of *Plastic Materials of Construction* ⟨661.1⟩.▲1-May-2020 All *Packaging systems* must meet the applicable requirements specified in

Containers—Glass ⟨660⟩, *Plastic Packaging Systems and Their Materials of Construction* ⟨661⟩, ▲*Plastic Packaging Systems for Pharmaceutical Use* ⟨661.2⟩,▲1-May-2020 and *Auxiliary Packaging Components* ⟨670⟩. All elastomeric closures must meet the applicable requirements in *Elastomeric Closures for Injections* ⟨381⟩.

Every monograph in *USP–NF* must have packaging and storage requirements. For the packaging portion of the statement, the choice of containers is provided in this chapter. For active pharmaceutical ingredients (APIs), the choice would be a tight, well-closed, or, where needed, light-resistant container. For excipients, given their typical presentation as large-volume commodity items (*Packaging systems* ranging from drums to tank cars), a well-closed container is an appropriate default requirement. Articles must be protected from moisture, freezing, and excessive heat (see *General Definitions*) when no specific directions or limitations are provided.

The compendial requirements for the use of specified containers apply also to articles packaged by *Dispensers*, *Repackagers*, or other individuals, unless otherwise indicated in the individual drug product monograph.

POISON PREVENTION PACKAGING ACT

This act, which is administered by the United States Consumer Product Safety Commission (CPSC), requires special packaging for most human oral prescription drugs, oral controlled drugs, certain non-oral prescription drugs, certain dietary supplements, and many over-the-counter (OTC) drug preparations, to protect the public from personal injury or illness

from misuse of these preparations [16 Code of Federal Regulations (CFR) §1700.14].

The primary packaging of substances regulated under the Poison Prevention Packaging Act (PPPA) must comply with the special packaging standards (16 CFR §1700.15). These apply to all packaging types, including reclosable, non-reclosable, and unit-dose types.

Special packaging is not required for drugs dispensed within a hospital setting for inpatient administration. Also, special packaging does not need to be used by manufacturers and packagers of bulk-packaged prescription drugs that will be repackaged by the pharmacist. PPPA-regulated prescription drugs may be dispensed in non-*Child-resistant packaging* upon the request of the purchaser or when directed in a legitimate prescription [15 United States Code (USC) §1473].

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

TEMPERATURE AND STORAGE

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 directions or limitations are provided in the article's labeling, articles must 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:

GENERAL DEFINITIONS

Packaging Definitions

Packaging system (also referred to as a Container–closure system)**:** The sum of *Packaging components* and materials that together contain and protect the article. This includes *Primary packaging components* as well as *Secondary packaging components* when such components are required to provide additional protection.

Container: A receptacle that holds an intermediate compound, API, excipient, or dosage form, and is in direct contact with the article (e.g., ampules, vials, bottles, syringes, and pen injectors).

Closure: A material that seals an otherwise open space of a *Container* and provides protection for the contents. It also provides access to the contents of the *Container* (e.g., screw caps and stoppers).

Packaging component: Any single part of the *Package* or *Container–closure system,* including: the *Container* (e.g., ampules, syringes, vials, and bottles); *Closures* (e.g., screw caps and stoppers); ferrules and overseals; *Closure* liners (e.g., tube cartridge liners); inner seals; administration ports; overwraps; administration accessories; labels; cardboard boxes; and shrink wrap.

Primary packaging component: A *Packaging component* that is in direct contact with or may come into direct contact with the article.

Secondary packaging component: A *Packaging component* that is in direct contact with a *Primary packaging component* and may provide additional protection for the article.

Tertiary packaging component: A *Packaging component* that is in direct contact with a *Secondary packaging component* and may provide additional protection for the article during transportation and/or storage.

Ancillary component: A component or entity that may come into contact with a *Tertiary packaging component* during the distribution, storage, and/or transportation of the packaged article (e.g., pallets, skids, and shrink wrap).

Associated component: A *Packaging component* that is typically intended to deliver the drug article to the patient but is not stored in contact with the article for its entire shelf life (e.g., spoons, *Dosing cups*, and dosing syringes).

Materials of construction: The materials (e.g., glass, plastic, elastomers, and metal) of which a *Packaging component* consists.

Small-volume injection ▲(also referred to as▲ (USP 1-Aug-2020) Small-volume parenteral)**:** An injectable dosage form that is packaged in *Containers* labeled as containing 100 mL or less.

Large-volume injection (also referred to as (USP 1-Aug-2020) Large-volume parenteral)**:** An injectable dosage form that is packaged in *Containers* labeled as containing more than 100 mL.

Child-resistant packaging: A *Packaging system* designed or constructed to meet CPSC standards pertaining to opening by children (16 CFR §1700.20 et seq. and 16 CFR §1700.15).

Senior-friendly packaging: A *Packaging system* designed or constructed to meet CPSC standards pertaining to opening by senior adults (16 CFR §1700.15 and 16 CFR §1700.20).

Restricted delivery system: A *Packaging system* designed or constructed to restrict (control) the amount of the drug product that may be delivered in order to limit unintended access by children and other similarly vulnerable populations. *Restricted delivery systems* should meet and may exceed CPSC standards for special packaging [*Child-resistant* and *Senior-friendly packaging* (16 CFR §1700.15 et seq.)]. For oral medicinal liquids, surface and flow characteristics vary. It is the responsibility of the manufacturer to ensure that all components of the *Restricted delivery system* provide the intended safety protection. One component of the *Restricted delivery system* is the flow restrictor, which is a *Packaging component* that restricts the flow of liquid. The flow restrictor may be used as part of a *Restricted delivery system* or as an adaptor to facilitate use of a measuring device for oral medicinal liquids. A flow restrictor should not compromise CPSC standards for special packaging [*Child-resistant* and *Senior-friendly packaging* (16 CFR §1700.15 et seq.)].

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* must be used for sterile drug products intended for ophthalmic or otic use, except where extemporaneously compounded for immediate dispensing on prescription. Drug products intended for sale without prescription are also required to comply with the *Tamper-evident packaging* and labeling requirements of the FDA where applicable (21 CFR §221.132). 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 to show evidence of any tampering with the contents.

Reclosable packaging: A package that after it has been initially opened is capable of being reclosed with a similar degree of security and is capable of being used a sufficient number of times to dispense the total contents without loss of security. *Reclosable packaging* may incorporate child-resistance capabilities.

Non-reclosable packaging: A package or part of a package that cannot be closed again after all or part of the contents have been removed. Examples of *Non-reclosable packaging* are blisters, sachets, strips, and other *Single-unit containers*. *Non-reclosable packaging* may include cold-formed foil blisters, foil strip packs, and polyvinyl chloride (PVC)/Aclar combining multilayer materials that are thermo-formed or cold-formed foil blisters. *Non-reclosable packaging* may be child resistant depending on the intended use and place of use. Household non-reclosables are subject to the PPPA as defined in 16 CFR §1700.14.

Hermetic container: A *Container–closure 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 *Container–closure 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 *Container–closure 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 ⟨671⟩.

Light-resistant container: A *Container–closure 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 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 *Plastic Packaging Systems for Pharmaceutical Use* ⟨661.2⟩*, Functionality, Spectral Transmission Requirements for Light-Resistant* ~~*Containers*~~▲*Components and Systems*.▲ (USP 1-Aug-2020)

Equivalent container–closure system: A *Container–closure system* that is as protective as or more protective than the original manufacturer's *Packaging system* in terms of moisture vapor transmission rate, oxygen transmission, light transmission, and compatibility. System equivalency extends to any special protective materials, such as those for seals or desiccants associated with the original *Packaging system*.

Table 1. Packaging Systems Definitions: Injection versus Noninjection

Injection	Noninjection
Multiple-dose	Multiple-unit
Single-dose	Single-unit
—	Unit-dose
—	Unit-of-use
Pharmacy bulk package	—
Imaging bulk package	—

Injection Packaging Systems

Multiple-dose container (also referred to as Multi-dose)**:** A *Container–closure system* that holds a sterile medication for parenteral administration (injection or infusion) that has met antimicrobial effectiveness testing

requirements, or is excluded from such testing requirements by FDA regulation. A *Multiple-dose container* is intended to contain more than one dose of a drug product. When space permits, a *Multiple-dose container* is labeled as such. *Multiple-dose containers* are generally expected to contain 30 mL or less of medications. The beyond-use date for an opened or entered (e.g., needle-punctured) *Multiple-dose container* is 28 days unless otherwise specified by the manufacturer on the label. An example of a *Multiple-dose container* is a vial.

Single-dose container: A *Container–closure system* that holds a sterile medication for parenteral administration (injection or infusion) that is not required to meet the antimicrobial effectiveness testing requirements. A *Single-dose container* is designed for use with a single patient as a single injection/infusion.[1] When space permits, a *Single-dose container* is labeled as such and should include on the label appropriate discard statements. Examples of *Single-dose containers* are vials, ampules, and prefilled syringes.

Pharmacy bulk package: A *Container–closure 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* must 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*.*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. See *Labeling* ⟨7⟩ for labeling requirements.

Imaging bulk package: A container of a sterile preparation for parenteral use that contains many single doses of a contrast agent (medical imaging drug product) for use with a medical imaging device. The contents are restricted to use in direct conjunction with a device with features to mitigate the risk of cross-contamination (i.e., an automated contrast injection system or contrast management system approved or cleared for use with an *Imaging bulk package*). The sterility assurance of the *Imaging bulk package* contents in part is dependent upon the automated contrast injection system or the contrast management system.The *Imaging bulk package* is to be used only in a room designated for radiological procedures that involve intravascular administration of a contrast agent. Using aseptic technique, the *Imaging bulk package* closure must be penetrated only one time with a suitable sterile component of the automated contrast injection system or contrast management system. If the integrity of the *Imaging bulk package* and the delivery system cannot be assured through direct continuous supervision, the *Imaging bulk package* and all associated disposables for the automated contrast injection system or contrast management system should be discarded.Designation as an *Imaging bulk package* is limited to injection, for injection, or injectable emulsion dosage forms as defined in *Nomenclature* ⟨1121⟩*, General Nomenclature Forms*. *Imaging bulk packages*, although containing more than one single dose, are exempt from the

multiple-dose container volume limit of 30 mL. The contents of the *Imaging bulk package* must have demonstrated the ability to limit the growth of microorganisms over the labeled period of use.Where a container is offered as an *Imaging bulk package*, the label must: 1) state prominently "Imaging Bulk Package" and, in juxtaposition with this statement, include the following use statement: "For use only with an automated contrast injection system or contrast management system approved or cleared for use with this contrast agent in this Imaging Bulk Package"; 2) 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; and 3) bear the statement, "See drug and device labeling for information on devices indicated for use with this Imaging Bulk Package and techniques to help assure safe use".

Noninjection Packaging Systems

Multiple-unit container: A *Container–closure system* that permits withdrawal of successive portions of a noninjection article without changing the safety, strength, quality, or purity of the remaining portion (e.g., bottle of capsules, tablets, and oral or topical liquids).

Single-unit container: A *Container–closure system* that holds a quantity of a noninjection article intended for administration as a single dose or a single finished device intended for use promptly after the *Packaging system* is opened.

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

Unit-of-use container: A *Container–closure 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 (see ⟨7⟩). It is not permitted to repackage *Unit-of-use containers* for sale.

Miscellaneous

Repackaging: The act of removing a drug product from the original manufacturer's *Packaging system* and placing it into another *Packaging system*, usually one of smaller size.

Repackager: A firm that repackages drug products or medical devices for distribution (e.g., for resale to distributors, hospitals, or pharmacies). For drug products, this applies to a function that is beyond the regular practice of a pharmacy. The distribution is not patient-specific, in that there are no prescriptions. Repackagers and relabelers of medical devices are also required to register and list and meet the provisions described in 21 CFR §807.

Contract packager/contract repackager: A firm that is contracted by another organization, such as a manufacturer, to package bulk into a marketed *Container* of a drug product. A *Contract packager* does not take ownership from the manufacturer and generally receives the assigned expiration date from the manufacturer.

Dispenser: A licensed or registered practitioner who is legally responsible for providing the patient with a preparation that is in compliance with a prescription or a medication order and contains a specific patient label. In addition, dispensers may prepare limited quantities in anticipation of a prescription or medication order from a physician. *Dispensers* are governed by the board of pharmacy of the individual state. The terms "dispenser" and "pharmacy" are used interchangeably.

Beyond-use date: See ⟨7⟩.

Expiration date: See ⟨7⟩.

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 ampule is prohibited, except for *Labeling* ⟨7⟩*, Labels and Labeling for Injectable Products, Potassium Chloride for Injection Concentrate*.

INJECTION PACKAGING

Packaging for sterile products intended for injection must be validated as meeting the containment and protection requirements that are essential for maintaining the article's quality. Refer to *Package Integrity Evaluation—Sterile Products* ⟨1207⟩, *Package Integrity Testing in the Product Life Cycle—Test Method Selection and Validation* ⟨1207.1⟩, *Package Integrity Leak Test Technologies* ⟨1207.2⟩, and *Package Seal Quality Test Technologies* ⟨1207.3⟩ for further information regarding sterile product container–closure integrity testing and validation. *Closures* for

Multiple-dose containers 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. Refer to ⟨381⟩ for *Closure* reseal tests that are useful for screening multiple-dose *Closures* for their reseal properties. Additional testing may be needed to ensure that the specific *Closure* selected for a product package is able to prevent loss of product contents and microbial contamination under anticipated conditions of multiple entry and use. Piggyback *Packaging systems* are usually intravenous infusion *Container–closure systems* that are 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 container* 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 in *Single-dose containers* only. Unless otherwise specified in the individual monograph, a *Multiple-dose container* 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:

- Injections packaged for extravascular use as irrigation solutions or peritoneal dialysis solutions
- 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 the packaging and storage requirements concerning the limitation to single-dose *Packaging systems* and the limitation on the volume of *Multiple-dose containers*.

Packaging for Constitution

Containers, including the *Closures*, for dry solids intended for injection must not interact physically or chemically with the preparation in any manner that alters 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 container* 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 3 times the volume to be withdrawn and fitted with a 21-gauge needle NLT 2.5 cm (1

inch) in length. Care must be taken to expel any air bubbles, and the contents are then discharged into a *Container* for dilution and assay.

Change to read:

MEDICAL GAS PACKAGING

Gas cylinder: A metallic *Packaging system* constructed of steel or aluminum and designed to hold medical gases under pressure; these gases may include: *Carbon Dioxide USP*, *Helium USP*, *Medical Air USP*, ~~nitric oxide,~~ (USP 1-Aug-2020)*Nitrous Oxide USP*, *Nitrogen NF*, and *Oxygen USP*. As a safety measure, for carbon dioxide, helium, medical air, nitrous oxide, and oxygen, the Pin Index Safety System of matched fittings is recommended for cylinders of Size E or smaller.

Change to read:

ASSOCIATED COMPONENTS

Many *Associated Components* are graduated for measurement and dose administration. *Associated Components* can be packaged with the drug product or sold and purchased separately. It is the responsibility of the manufacturer to ensure that the appropriate measurement and dosing component is provided or that a general purpose component, such as those described in this section, is specified for delivering the appropriate amount/dose with the intended accuracy. Liquid preparations have unique surface and flow characteristics. Consequently, the volume delivered from a measurement/dosing component may vary for each preparation.

The graduated *Associated Components* described in this section are for general use and should be composed of safe materials. Graduated markings should be legible, indelible, and on an extraoral surface that does not contact the product.

▲The associated volume markings must be in metric units only and limited to a single measurement scale that corresponds with the dosing instructions on the OTC or prescription container label (see *Prescription Container Labeling* ⟨17⟩). Under expected 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.▲ (Official 1-May-2019)

Dosing cup: A measuring device consisting of a small cup that may be packaged with oral liquid articles.

Dosing spoon: A measuring device consisting of a bowl and handle that may be packaged with oral liquid articles. 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 may be packaged with oral liquid articles.

Oral syringe: A measuring device consisting of a plunger and barrel made of transparent or translucent plastic material and a seal on the end. It may be packaged with oral liquid articles. The syringe should deliver a measured amount of a liquid drug product.

TEMPERATURE AND STORAGE DEFINITIONS

Freezer: A place in which the temperature is controlled between −25° and −10° (−13° and 14° F). It is noted that, in some instances, articles may have a recommended storage condition below −20° (−4° F). In such cases, the temperature of the storage location should be controlled to ±10°.

Refrigerator: A cold place in which the temperature is controlled 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 (also referred to as Ambient temperature)**:** The temperature prevailing in a working environment.

Controlled room temperature: The temperature maintained thermostatically that encompasses 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°, transient 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.Articles may be labeled for storage at "controlled room temperature" or at "20°–25°", or other wording based on the same mean kinetic temperature [see also *Good Storage and Distribution Practices for Drug Products* ⟨1079⟩*, Quality Management System, Environmental Management System, Mean Kinetic Temperature (MKT) Calculation*].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: 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. 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*.

Protect from freezing: The *Container* label will bear an appropriate instruction to protect the article from freezing in cases where freezing exposes an article to loss of strength or potency or to destructive alteration of its characteristics. These risks are present in addition to the risk that the *Container* may break if exposed to freezing temperatures.

Protect 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. The article must be packaged in a light-resistant *Container*.

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[1] Exceptions may be considered only under conditions described in *Pharmaceutical Compounding—Sterile Preparations* ⟨797⟩.