⟨1151⟩ PHARMACEUTICAL DOSAGE FORMS

Change to read:

GENERAL CONSIDERATIONS

This chapter provides general descriptions of and definitions for drug products, or dosage forms, commonly used to administer the drug substance (active pharmaceutical ingredient; API). It discusses general principles involved in the manufacture or compounding of these dosage forms. A glossary is provided as a nomenclature resource and should be used in conjunction with the *Nomenclature Guidelines*.[1]

A dosage form is a pharmaceutical preparation consisting of drug substance(s) and/or excipient(s) to facilitate dosing, administration, and delivery of the content of the drug product or placebo to the patient. The design, materials, manufacturing, and testing of all dosage forms target drug product quality. A testing protocol must consider not only the physical, chemical, microbiological, and biological properties of the dosage form as appropriate, but also the administration route and desired dosing regimen. These considerations, organized by route of administration, are detailed in *Injections and Implanted Drug Products (Parenterals)—Product Quality Tests* ⟨1⟩, *Oral Drug Products—Product Quality Tests* ⟨2⟩, *Topical and Transdermal Drug Products—Product Quality Tests* ⟨3⟩, *Mucosal Drug Products—Product Quality Tests* ⟨4⟩, *Inhalation and Nasal Drug Products—General Information and Product Quality Tests* ⟨5⟩, and *Ophthalmic Products—Quality Tests* ⟨771⟩.[2] The organization of this general information chapter is by the quality attributes of each particular dosage form, generally without specific reference to the route of administration. The following list provides the preferred dosage ▲form terms▲ (USP 1-May-2021) used in official article titles. In addition to the preferred dosage ▲form terms▲ (USP 1-May-2021) the *Glossary* contains other ▲dosage form▲ (USP 1-May-2021) terms that have been used in current official article titles but are not preferred and should not be used for new drug product titles.

Official Dosage Forms Used in Official Article Titles

- Aerosols
- Capsules
- Creams
- Emulsions
- Films
- Foams
- Gases
- Gels
- Granules
- Gums
- Implants
- Injections
- Inserts
- Irrigations
- Liquids
- Lotions
- Lozenges
- Ointments
- Pastes
- Pellets
- Pills
- Powders
- Rinses
- Shampoos
- Soaps
- Solutions
- Sprays
- Strips
- Suppositories
- Suspensions
- Systems
- Tablets

Tests to ensure compliance with *USP* standards for dosage form performance fall into one of the following areas.

Dose Uniformity

(See also *Uniformity of Dosage Units* ⟨905⟩.) Consistency in dosing for a patient or consumer requires that the variation in the drug substance content of each dosage unit be accurately controlled throughout the manufactured batch or compounded lot of drug product. Uniformity of dosage units typically is demonstrated by one of two procedures: content uniformity or weight variation. The procedure for content uniformity requires the appropriate assay of the drug substance content of individual units. The procedure for weight variation uses the weight of the individual units to estimate their content. Weight variation may be used where the underlying distribution of the drug substance in the blend is presumed to be uniform and well-controlled, as in solutions. In such cases, the content of the drug substance may be adequately estimated by the net weight. Content uniformity does not rely on the assumption of blend uniformity and can be applied in all cases. Successful development and manufacture of dosage forms requires careful evaluation of the drug substance particle or droplet size, incorporation techniques, and excipient properties.

Stability

Drug product stability involves the evaluation of chemical stability, physical stability, and performance over time. The chemical stability of the drug substance in the dosage form matrix must support the expiration dating for the commercially prepared dosage forms and a beyond-use date for a compounded dosage form. Test procedures for potency must be stability indicating (see *Validation of Compendial Procedures* ⟨1225⟩). Degradation products should be quantified. In the case of dispersed or emulsified systems, consideration must be given to the potential for settling or separation of the formulation components. Any physical changes to the dosage form must be easily reversed (e.g., by shaking) prior to dosing or administration. For tablets, capsules, oral suspensions, and implants, in vitro release test procedures such as dissolution and disintegration provide a measure of continuing consistency in performance over time (see *Dissolution* ⟨711⟩, *Disintegration* ⟨701⟩, and *Drug Release* ⟨724⟩).

[1] *Nomenclature Guidelines*, http://www.usp.org/health-quality-safety/compendial-nomenclature.
[2] Marshall K, Foster TS, Carlin HS, and Williams RL. Development of a compendial taxonomy and glossary for pharmaceutical dosage forms. *Pharm Forum.* 2003;*29*(5):1742–1752.

Bioavailability

(See also *In Vitro and In Vivo Evaluation of Dosage Forms* ⟨1088⟩ and *Assessment of Solid Oral Drug Product Performance and Interchangeability, Bioavailability, Bioequivalence, and Dissolution* ⟨1090⟩.) Bioavailability is influenced by factors such as the method of manufacture or compounding, particle size, crystal form (polymorph) of the drug substance, the properties of the excipients used to formulate the dosage form, and physical changes as the drug product ages. Assurance of consistency in bioavailability over time (bioequivalence) requires close attention to all aspects of the production (or compounding) and testing of the dosage form. With proper justification, in vitro release testing (e.g., disintegration and dissolution) may be used as a surrogate to demonstrate consistent availability of the drug substance from the formulated dosage.

Release Profile

Two principal categories of drug release are recognized: immediate-release and modified-release.

"Immediate-release" is observed when no deliberate effort has been made to modify the drug substance release profile. For example, capsules and tablets are considered immediate-release even if a disintegrating agent or a lubricant has been used.

"Modified-release" is a term used when the rate and/or time of release of the drug substance is altered as compared to what would be observed or anticipated for an immediate-release product. Two modified-release profiles, delayed-release and extended-release, are recognized. The term "modified-release" is not used for official article titles.

"Delayed-release" is used when deliberate formulation achieves a delay in the release of the drug substance for some period of time after initial administration. For oral products, expressions such as "enteric-coated" or "gastro-resistant" also have been used where release of the drug substance is prevented in the gastric environment but promoted in the intestinal environment. However, the term "delayed-release" is used for official article titles.

"Extended-release" is used when the deliberate formulation achieves prolongation of drug substance release compared to that observed or anticipated for an immediate-release dosage form. Expressions such as "prolonged-release", "repeat-action", "controlled-release", "long-acting", and "sustained-release" also have been used to describe such dosage forms. However, the term "extended-release" is used for official article titles.

The *Nomenclature Guidelines*[1] should be consulted for naming conventions for products with a single drug substance or for products with a combination of more than one drug substance displaying the combination of release profiles of immediate-release and extended-release, immediate-release and delayed-release, or extended-release and delayed-release.

Manufacture

Although detailed instructions about the manufacture of any of these dosage forms are beyond the scope of this general information chapter, general manufacturing principles have been included.[3] Information relative to extemporaneous compounding of dosage forms can be found in *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩ and *Pharmaceutical Compounding—Sterile Preparations* ⟨797⟩.

Route of Administration

The primary routes of administration for pharmaceutical dosage forms can be defined as parenteral (see ⟨1⟩), gastrointestinal (see ⟨2⟩), topical (see ⟨3⟩), mucosal (see ⟨4⟩), and inhalation (see ⟨5⟩). Each has subcategories as needed. Many tests used to ensure quality generally are applied across all of the administration routes, but some tests are specific for individual routes. For example, products intended for injection must be evaluated using *Sterility Tests* ⟨71⟩, *Bacterial Endotoxins Test* ⟨85⟩, or *Pyrogen Test* ⟨151⟩, and the manufacturing process (and sterilization technique) employed for parenterals (by injection) should ensure compliance with these tests. Tests for particulate matter may be required for certain dosage forms depending on the route of administration (e.g., by injection—*Particulate Matter in Injections* ⟨788⟩, mucosal—*Particulate Matter in Ophthalmic Solutions* ⟨789⟩, ▲or inhalation—⟨5⟩▲ (USP 1-May-2021)). Additionally, dosage forms intended for the inhalation route of administration must be monitored for particle size and spray pattern (for a metered-dose inhaler or dry powder inhaler) and droplet size (for nasal sprays). Further information regarding administration routes and suggested testing can be found in *Chapter Charts*, *Charts 4a*, *4b*, *5*, *6*, *7*, *8*, *10a*, *10b*, and *13*.

An appropriate manufacturing process and testing regimen helps ensure that a dosage form can meet the appropriate quality attributes for the intended route of administration.

Packaging and Storage

Suitable packaging is determined for each product. For additional information about meeting packaging requirements listed in the individual labeling, refer to *Packaging and Storage Requirements* ⟨659⟩, *Containers—Performance Testing* ⟨671⟩, and *Good Repackaging Practices* ⟨1178⟩. Product labeling must specify storage requirements that describe environmental conditions, limitations, and restrictions. For instance, exposure to excessive temperature, humidity, and light can influence the ability of the packaging to protect the product.

Labeling Statements

Some dosage forms or articles have mandatory labeling statements that are given in the *Code of Federal Regulations* (e.g., 21 CFR §201.320 and 21 CFR §369.21). The text of 21 CFR should be consulted to determine the current recommendations.

[3] The terms "manufacture" and "preparation" are used interchangeably in this general chapter.

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PRODUCT QUALITY TESTS, GENERAL

International Council for Harmonisation (ICH) Guidance Q6A (available at www.ich.org) recommends specifications (list of tests, references to analytical procedures, and acceptance criteria) to ensure that drug products are safe and effective at the time of release and over their shelf life. Tests that are universally applied to ensure safety, efficacy, strength, quality, and purity include description, identification, assay, and impurities.

Description

The *Definition* section (see *General Notices, 4.10 Monographs*) in a *USP* monograph describes the drug product and specifies the range of acceptable assayed content of the drug substance(s) present in the dosage form. For certain products, the *Definition* includes any relevant additional information, such as the presence or absence of other components, excipients, or adjuvants, and cautionary statements on toxicity and stability. While appearance information to aid in identification is used in a regulatory submission (e.g., a qualitative description of size, shape, color, etc.) it is typically not required as part of a *USP* monograph. This information is drug product specific.

Identification

Identification tests are discussed in *General Notices, 5.40 Identification*. Identification tests should establish the identity of the drug substance(s) present in the drug product and should discriminate between compounds of closely related structure that are likely to be present. Identification tests should be specific for the drug substance(s). For example, the infrared absorption spectrum is often used (see *Mid-Infrared Spectroscopy* ⟨854⟩ and *Spectroscopic Identification Tests* ⟨197⟩). If no suitable infrared spectrum can be obtained, other analytical methods can be used. Near-infrared (NIR) or Raman spectrophotometric methods also could be acceptable as the sole identification method of the drug product formulation (see *Near-Infrared Spectroscopy—Theory and Practice* ⟨1856⟩ and *Raman Spectroscopy—Theory and Practice* ⟨1858⟩). Identification by a chromatographic retention time from a single procedure is not regarded as specific. The use of retention times from two chromatographic procedures for which the separation is based on different principles or a combination of tests in a single procedure can be acceptable (see *Chromatography* ⟨621⟩ and *Thin-Layer Chromatographic Identification Test* ⟨201⟩).

Assay

A specific and stability-indicating test should be used to determine the strength (drug substance content) of the drug product. Some examples of these procedures are *Antibiotics—Microbial Assays* ⟨81⟩, ⟨621⟩, or *Assay for Steroids* ⟨351⟩. In cases when the use of a nonspecific assay is justified (e.g., *Titrimetry* ⟨541⟩), other supporting analytical procedures should be used to achieve specificity. When evidence of excipient interference with a nonspecific assay exists, a procedure with demonstrated specificity should be used.

Impurities

Process impurities, synthetic byproducts, and other inorganic and organic impurities may be present in the drug substance and excipients used in the manufacture of the drug product. These impurities are evaluated by tests in the drug substance and excipients monographs. Impurities arising from degradation of the drug substance or from the drug-product manufacturing process should be monitored. *Residual Solvents* ⟨467⟩ is applied to all products where relevant.

▲*Elemental Impurities—Limits* ⟨232⟩ is applied to all products where relevant.▲ (USP 1-May-2021)

In addition to the universal tests listed, the following tests may be considered on a case-by-case basis.

Physicochemical Properties

Examples include *pH* ⟨791⟩, *Viscosity—Capillary Methods* ⟨911⟩ or *Viscosity—Rotational Methods* ⟨912⟩, and *Specific Gravity* ⟨841⟩.

Particle Size

For some dosage forms, particle size can have a significant effect on dissolution rates, bioavailability, therapeutic outcome, and stability. Procedures such as those found in *Inhalation and Nasal Drug Products: Aerosols, Sprays, and Powders—Performance Quality Tests* ⟨601⟩ and *Particle Size Distribution Estimation by Analytical Sieving* ⟨786⟩ could be used.

Uniformity of Dosage Units

See the discussion of *Dose Uniformity* in the *General Considerations* section.

Water Content

A test for water content is included when appropriate (see *Water Determination* ⟨921⟩).

Microbial Limits

The type of microbial test(s) and acceptance criteria are based on the nature of the nonsterile drug product, method of manufacture, and the route of administration (see *Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests* ⟨61⟩, *Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms* ⟨62⟩, and *Microbiological Examination of Nonsterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use* ⟨1111⟩).

Antimicrobial Preservative Content

Acceptance criteria for preservative content in multidose products should be established. They are based on the levels of antimicrobial preservative necessary to maintain the product's microbiological quality at all stages throughout its proposed usage and shelf life (see *Antimicrobial Effectiveness Testing* ⟨51⟩).

Antioxidant Content

If antioxidants are present in the drug product, tests of their content should be performed to maintain the product's quality at all stages throughout its proposed usage and shelf life.

Sterility

Depending on the route of administration (e.g., ophthalmic preparations, implants, aqueous-based preparations for oral inhalation, and injections) sterility of the product is demonstrated as appropriate (see ⟨71⟩).

Dissolution

A test to measure the release of the drug substance(s) from the drug product normally is included for dosage forms such as tablets, capsules, suspensions, granules for suspensions, implants, transdermal delivery systems (TDS), and medicated chewing gums. Single-point measurements typically are used for immediate-release dosage forms. For modified-release dosage forms, appropriate test conditions and sampling procedures are established as needed (see ⟨711⟩ and ⟨724⟩). In some cases, dissolution testing may be replaced by disintegration testing (see ⟨701⟩).

Breaking Force and Friability

These parameters are evaluated as in-process controls. Acceptance criteria depend on packaging, supply chain, and intended use (see *Tablet Friability* ⟨1216⟩ and *Tablet Breaking Force* ⟨1217⟩).

Leachables

When evidence exists that leachables from the container–closure systems (e.g., rubber stopper, cap liner, or plastic bottle) have an impact on the safety or efficacy of the drug product, a test is included to evaluate the presence of leachables.

Other Tests

Depending on the type and composition of the dosage form, other tests such as alcohol content, redispersibility, particle size distribution, rheological properties, reconstitution time, endotoxins/pyrogens, particulate matter, functionality testing of delivery systems, delivered dose uniformity, viscosity, and osmolarity may be necessary.

Change to read:

DOSAGE FORMS

Aerosols

Aerosols are dosage forms packaged under pressure and contain therapeutic agent(s) and ▲propellant(s)▲ (USP 1-May-2021) that are released upon actuation of an appropriate valve system. Upon actuation of the valve system, the drug substance is released as a plume of fine particles or droplets. Only 1 dose is released from the preparation upon actuation of a metered valve. In the case of topical products and depending on the nature of the drug substance and the conditions being treated, actuation of the valve may result in a metered release of a controlled amount of the formulation or the continuous release of the formulation as long as the valve is depressed.

The aerosol dosage form refers only to those products packaged under pressure that release a fine mist of particles or droplets when actuated (see *Glossary*). Other products that produce dispersions of fine droplets or particles will be covered in subsequent sections (e.g., ▲*Sprays* and *Powders*▲ (USP 1-May-2021)).

TYPICAL COMPONENTS

Typical ▲major▲ (USP 1-May-2021) components of aerosols are the formulation containing one or more drug substance(s) and ▲propellant(s),▲ (USP 1-May-2021) the container, the valve, and the actuator. Each component plays a role in determining various characteristics of the emitted plume, such as droplet or particle size distribution, uniformity of delivery of the therapeutic agent, delivery rate, and plume velocity and geometry. The metering valve and actuator act in tandem to generate the plume of droplets or particles. The metering valve delivers an accurate volume of the pressurized liquid formulation from the container. The actuator directs the metered volume to a small orifice that is open to the atmosphere. Upon actuation, the formulation is forced through the opening, forming the fine mist of ▲droplets/▲ (USP 1-May-2021)particles that are directed to the site of administration.

Aerosol preparations may consist of either a two-phase (gas and liquid) or a three-phase (gas, liquid, and solid or liquid) formulation. The two-phase formulation consists of drug substance(s) dissolved in liquefied propellant. Co-solvents such as alcohol may be added to enhance the solubility of the drug substance(s). Three-phase inhalation and nasal aerosol systems consist of suspended drug substance(s) in propellant(s), co-solvents, and potentially other suitable excipients. The suspension or emulsion of the finely divided drug substance is typically dispersed in the liquid propellant with the aid of suitable biocompatible surfactants or other excipients.

Propellants for aerosol formulations are typically low molecular weight hydrofluorocarbons or hydrocarbons that are liquid when constrained in the container, exhibit a suitable vapor pressure at room temperature, and are biocompatible and nonirritating. Compressed gases do not supply a constant pressure over use and typically are not used as propellants.

Metal containers can withstand the vapor pressure produced by the propellant. Excess formulation may be added to the container to ensure that the full number of labeled doses can be accurately administered. The container and closure must be able to withstand the pressures anticipated under normal use conditions as well as when the system is exposed to elevated temperatures.

TYPES OF AEROSOL DOSAGE FORMS

Aerosol dosage forms can be delivered via various routes. The container, actuator, and metering valve, as well as the formulation, are designed to target the site of administration.

Inhalation aerosols, commonly known as metered-dose inhalers (MDIs), are intended to produce fine particles or droplets for inhalation through the mouth and deposition in the pulmonary tree. The design of the delivery system is intended to release measured mass and appropriate quality of the active substance with each actuation.

Nasal aerosols, commonly known as nasal MDIs, produce fine particles or droplets for delivery through the nasal vestibule and deposition in the nasal cavity. Each actuation of the valve releases a measured mass of the drug substance with appropriate quality characteristics.

Lingual aerosols are intended to produce fine particles or droplets for deposition on the surface of the tongue. The design of the delivery system releases 1 dose with each actuation.

Topical aerosols produce fine particles or droplets for application to the skin.

LABELING FOR PROPER USE

Refer to 21 CFR §201.320 and 21 CFR §369.21.

Capsules

Capsules are solid dosage forms in which the drug substance and/or excipients are enclosed within a soluble container or shell or coated on the capsule shell. The shells may be composed of two pieces (a body and a cap), or they may be composed of a single piece. Two-piece capsules are commonly referred to as hard-shell capsules, and one-piece capsules are often referred to as soft-shell capsules. This two-piece and one-piece capsule distinction, although imprecise, reflects differing levels of plasticizers in the two compositions and the fact that one-piece capsules typically are more pliable than two-piece capsules.

The shells of capsules are usually made from gelatin. However, they also may be made from cellulose polymers ▲(e.g., hypromellose)▲ (USP 1-May-2021) or other suitable material. Most capsules are designed for oral administration. When no deliberate effort has been made to modify the drug substance release rate, capsules are referred to as immediate-release.

TWO-PIECE OR HARD-SHELL CAPSULES

Two-piece capsules consist of two telescoping cap and body pieces in a range of standard sizes.

ONE-PIECE OR SOFT-SHELL CAPSULES

One-piece capsules typically are used to deliver a drug substance as a solution or suspension. Liquid formulations placed into one-piece capsules may offer advantages by comparison with dry-filled capsules and tablets in achieving content uniformity of potent drug substance(s) or acceptable dissolution of drug substance(s) with poor aqueous solubility. Because the contact between the shell wall and its liquid contents is more intimate than in dry-filled capsules, undesired interactions may be more likely to occur (including gelatin cross-linking and pellicle formation).

MODIFIED-RELEASE CAPSULES

The release of drug substance(s) from capsules can be modified in several ways. Two categories of modified-release capsule formulations are recognized by USP.

Delayed-release capsules: Capsules are sometimes formulated to include enteric-coated granules to protect acid-labile drug substances from the gastric environment or to prevent adverse events such as irritation. Enteric-coated multiparticulate capsule dosage forms may reduce variability in bioavailability associated with gastric emptying times for larger particles (i.e., tablets) and may minimize the likelihood of a therapeutic failure when coating defects occur during manufacturing. Alternatively, a coating may be applied to the capsule shell to achieve delayed release of the contents.
Extended-release capsules: Extended-release capsules are formulated in such a manner as to make the contained drug substance available over an extended period of time following ingestion. Requirements for dissolution (see ⟨711⟩) are typically specified in the individual monograph.

Methods for modifying drug substance release from capsules include coating the filled capsule shells or the contents, in the case of dry-filled capsules.

PREPARATION

Two-piece capsules: Two-piece gelatin capsules are usually formed from blends of gelatins that have relatively high gel strength in order to optimize shell clarity and toughness or from hypromellose. They may also contain colorants such as Drug & Cosmetic (D&C) and Food, Drug, & Cosmetic (FD&C) dyes[4] or various pigments, opaquing agents such as titanium dioxide, dispersing agents, plasticizers, and preservatives. Gelatin capsule shells normally contain between 12% and 16% water.

The shells are manufactured in one set of operations and later filled in a separate manufacturing process. Two-piece shell capsules are made by a process that involves dipping shaped pins into gelatin or hypromellose solutions, followed by drying, cutting, and joining steps.

Powder formulations for two-piece gelatin capsules generally consist of the drug substance and at least one excipient. Both the formulation and the method of filling can affect release of the drug substance. In the filling operation, the body and cap of the shell are separated before filling. Following the filling operation, the machinery rejoins the body and cap and ensures satisfactory closure of the capsule by exerting appropriate force on the two pieces. The joined capsules can be sealed after filling by a band at the joint of the body and cap or by a designed locking joint between the cap and body. In compounding prescription practice, two-piece capsules may be hand-filled. This permits the prescriber the choice of selecting either a single drug substance or a combination of drug substances at the exact dose level considered best for an individual patient.
One-piece capsules: One-piece capsules are formed, filled, and sealed in a single process on the same machine and are available in a wide variety of sizes, shapes, and colors. The most common type of one-piece capsule is that produced by a rotary die process that results in a capsule with a seam. The soft gelatin shell is somewhat thicker than that of two-piece capsules and is plasticized by the addition of polyols such as glycerin, sorbitol, or other suitable materials. The ratio of the plasticizer to the gelatin can be varied to change the flexibility of the shell depending on the nature of the fill material, its intended usage, or environmental conditions.

In most cases, one-piece capsules are filled with liquids. Typically, drug substances are dissolved or suspended in a liquid vehicle. Classically, an oleaginous vehicle such as a vegetable oil was used. However, nonaqueous, water-miscible liquid vehicles such as the lower molecular weight polyethylene glycols are now more common. The physicochemical properties of the vehicle can be chosen to ensure stability of the drug substance as well as to influence the release profile from the capsule shell.

Creams

(See *Emulsions*.)

Emulsions

An emulsion is a dispersed colloidal system consisting of two immiscible liquid phases generally stabilized with one or more suitable agents.

Typical pharmaceutical emulsions are prepared from immiscible aqueous and organic (oil) liquids. Complex multiple-phase systems may exist in an emulsion. Whether the organic or the aqueous phase is the dispersed phase depends on the volumes of the two phases, the emulsifier chosen, and the method of preparation. When an oil phase is dispersed in an aqueous phase, the emulsion is termed an oil-in-water (O/W) emulsion and water is referred to as the continuous phase. When water is dispersed in oil, the emulsion is referred to as a water-in-oil (W/O) emulsion. Emulsions have dispersed phases typically ranging from 0.1 to 100 µm. Emulsions are opaque while microemulsions are usually transparent or translucent. Microemulsions have dispersed phases less than 0.1 µm.

Emulsions may exhibit three types of instability: flocculation, creaming, and coalescence. Flocculation describes the process by which the dispersed phase comes out of suspension in the form of flakes. Coalescence is another form of instability—small droplets within the media continuously combine to form progressively larger droplets. Emulsions can also undergo creaming, where one of the phases migrates to the top (or the bottom, depending on the relative densities of the two phases) of the emulsion. To prevent flocculation, creaming, and coalescence of the emulsions, manufacturers commonly add surfactants, pH-modifying agents, or emulsifying agents to increase the stability of emulsions so that the emulsion does not change significantly with time.

[4] In 1960 Congress enacted the Color Additive Amendments, requiring the US FDA to regulate dyes, pigments, or other coloring agents in foods, drugs, and cosmetics separately from food additives. Under the law, color additives are deemed unsafe unless they are used in compliance with FDA regulations. The law provides a framework for the listing and certification of color additives. See FDCA §721; see FDA regulations at 21 CFR Part 70. Colors also must be listed in pertinent FDA regulations for specific uses; the list of color additives for drugs that are exempt from certification is published at 21 CFR Part 73, Subpart B. FDA also conducts a certification program for batches of color additives that are required to be certified before sale; see 21 CFR Part 74 (Subpart B re: drugs). Regulations regarding certification procedures, general specifications, and the listing of certified provisionally listed colors are at 21 CFR Part 80. FDA maintains a color additives website with links to various legal and regulatory resources at: http://www.fda.gov; search by document title.

Emulsions are widely used as pharmaceutical dosage forms. Oral emulsions have been prepared to improve taste, solubility, stability, or bioavailability. Emulsions for topical administration are referred to as creams, lotions, and sometimes ointments. Parenteral emulsions have been used for anesthetics and parenteral nutrition and to deliver poorly water-soluble drugs.

CREAMS

Creams are semisolid emulsion dosage forms. They often contain more than 20% water and volatiles, and/or typically contain less than 50% hydrocarbons, waxes, or polyols as the vehicle for the drug substance. Creams are generally intended for external application to the skin or to the mucous membranes. Creams have a relatively soft, spreadable consistency and can be formulated as either a W/O emulsion (e.g., *Cold Cream* or *Fatty Cream* as in the *European Pharmacopoeia*) or as an O/W emulsion (e.g., *Betamethasone Valerate Cream*). Creams are generally described as either nonwashable or washable, reflecting the fact that an emulsion with an aqueous external continuous phase is more easily removed than one with a nonaqueous external phase (W/O emulsion).

LOTIONS

Lotions are an emulsified liquid dosage form intended for external application to the skin. Historically, some topical suspensions such as calamine lotion have been called lotions but that nomenclature is not currently preferred. Lotions share many characteristics with creams. The distinguishing factor is that they are more fluid than semisolid and thus pourable. Due to their fluid character, lotions are more easily applied to large skin surfaces than semisolid preparations. Lotions may contain antimicrobial agents as preservatives.

INJECTABLE EMULSIONS

Injectable emulsions are sterile liquid dosage forms of drug substances dissolved or dispersed in a suitable emulsion medium. Injectable emulsions are for parenteral administration of poorly water-soluble drugs.

OINTMENTS

Ointments are sometimes semisolid emulsion dosage forms (see *Dosage Forms, Ointments*).

PREPARATION

▲▲ (USP 1-May-2021)

Creams: Creams may be formulated from a variety of oils, both mineral and vegetable, and from fatty alcohols, fatty acids, and fatty esters. Emulsifying agents include nonionic surfactants, detergents, and soaps. Soaps are usually formed in situ during the preparation of creams from a fatty acid in the oil phase hydrolyzed by a base dissolved in the aqueous phase.

Preparation usually involves separating the formula components into two portions: lipid and aqueous. The lipid portion contains all water-insoluble components and the aqueous portion contains the water-soluble components. Both phases are heated to a temperature above the melting point of the highest melting component. The phases are then mixed and the mixture is stirred until reaching ambient temperature or until the mixture has congealed. Mixing is generally continued during the cooling process to promote uniformity. Traditionally, the aqueous phase is added to the lipid phase, but comparable results have been obtained with the reverse procedure. High-shear homogenization may be employed to reduce particle or droplet size and to improve the physical stability of the resultant dosage form.

The drug substance(s) can be added to the phase in which it is soluble at the beginning of the manufacturing process, or it can be added after the cream is prepared by a suitable dispersion process such as levigation or milling with a roller mill. Creams usually require the addition of a preservative(s) unless they are compounded immediately prior to use and intended to be consumed in a relatively short period of time.

Lotions: Lotions are usually prepared by dissolving or dispersing the drug substance into the more appropriate phase (oil or water), adding the appropriate emulsifying or suspending agents, and mixing the oil and water phases to form a uniform fluid emulsion.

Injectable emulsions: Chapter ⟨1⟩ provides guidance on sterile preparations. Emulsions intended for parenteral administration can be formulated using the same principles as creams and lotions. The formulation should be designed for ease of administration. The particle size of the dispersed phase can vary by route of administration. For example, emulsions intended for intravenous administration should comply with *Globule Size Distribution in Lipid Injectable Emulsions* ⟨729⟩. The procedure to assure sterility should be validated by media fills. Preservatives are generally not used in injectable emulsions.

Ointments: (See *Dosage Forms, Ointments*.)

Films

Films are thin sheets that are placed in the oral cavity. They contain one or more layers. A layer may or may not contain the drug substance. Typically, these thin sheets are formed by casting or extrusion that results in a dispersion of the components through the film. Films are classified by the site of application. “Oral films” can be formulated to deliver medication to the mouth such as oral hygiene products or to deliver medication to the gastrointestinal tract for absorption. “Buccal films” and “sublingual films” are formulated to facilitate absorption through the proximal mucosal membranes avoiding first pass metabolism or degradation in the gastrointestinal tract and providing a quick onset of action.

Films can be formulated with edible polymers such as pullulan or with water-soluble polymers such as modified cellulose, edible gums, and copolymers. The dissolution rate of the film is controlled to facilitate incorporation of the medication into saliva or for absorption by the proximal mucosa. These films must be substantial enough to maintain their integrity during

manufacture and packaging, and permit handling by the patient. Because of the rapid dissolution, taste and mouth feel are important considerations.

Foams

Foams are dispersions of gas in a liquid or solid continuous phase wherein the liquid or solid contains the drug substance and suitable excipients. Typical excipients intended for foam dosage forms include surfactants to ensure distribution of the gas/propellant in the formulation, aqueous or nonaqueous vehicles, and propellants (for pressurized systems). Foams are produced by mechanical means or via interaction of propellant gas and the formulation under pressure. Foams dispensed from nonpressurized containers use mechanical force to mix the formulation and air resulting in foam generation. Foams dispensed from pressurized containers use the ▲propellant(s)▲ (USP 1-May-2021) present in the gas phase to increase pressure inside the container. When the nozzle of the actuator is opened, the liquid phase is pushed out through specific actuators resulting in foam generation.

▲Foams are primarily intended for application to the skin or mucous membranes. Foams can also be delivered by the injection route. Foams can be formulated to quickly break down into liquid or to remain as a foam to ensure prolonged contact.▲ (USP 1-May-2021)

Medicated foams intended to treat severely injured skin, ▲▲ (USP 1-May-2021) open wounds, ▲or administered by injection▲ (USP 1-May-2021) must be sterile.

PREPARATION

A foam may contain one or more drug substances, surfactants, and aqueous or nonaqueous liquids, and is produced with or without the aid of propellants. When a propellant is not used, mechanical work is required to generate the foam. If the propellant is in the internal (discontinuous) phase, a stable foam is discharged. If the propellant is in the external (continuous) phase, a quick-breaking foam is discharged.

Gases

Medical gases are products that are administered directly as a gas. A medical gas has a direct pharmacological action or acts as a diluent for another medical gas. Gases used as excipients for administration of aerosol products, as adjuvants in packaging, or produced by other dosage forms, are not included in this definition.

COMPONENTS

Medical gases may be single components or defined mixtures of components. Mixtures also can be extemporaneously prepared at the point of use.

ADMINISTRATION

Medical gases may be administered to the patient using several methods: nasal cannulas, face masks, atmospheric tents, and endotracheal tubes for the pulmonary route; hyperbaric chambers for the pulmonary and topical routes of administration; jetted tubes that are directed at dental tissue to promote drying in preparation for fillings and crowns; tubes for expanding the intestines to facilitate medical imaging during colonoscopy; tubes for expanding the pelvis via transuterine inflation in preparation for fallopian tubal ligation; and tubes for expanding angioplasty devices. The dose of medical gas is typically metered by a volume rate of flow under ambient temperature and pressure conditions. Administration of a highly compressed gas generally requires a regulator to decrease the pressure, a variable-volume flow controller, and suitable tubing to conduct the gas to the patient. For pulmonary administration, the gas flow will be directed to the nose or mouth by a suitable device or into the trachea through a mechanical ventilator. When medical gases are administered chronically, provision for humidification is common. Care should be exercised to avoid microbial contamination.

SPECIAL CONSIDERATIONS

The container and system fittings should be appropriate for the medical gas. Adaptors should not be used to connect containers to patient-use supply system piping or equipment. Large quantities of gases such as oxygen or nitrogen can be stored in the liquid state in a cryogenic container and converted into a gas, as needed, by evaporation. Additional rules concerning the construction and use of cryogenic containers are promulgated by governmental agencies (e.g., U.S. Department of Commerce).

Containers, tubing, and administration masks employed for gases containing oxygen are free of any compound that would be sensitive to oxidation or that would be irritating to the respiratory tract.

A significant fraction of the dose of a medical gas may be released into the general vicinity of the patient due to incomplete absorption. Adequate ventilation may be necessary to protect health care workers and others from exposure to the gas (e.g., nitrous oxide).

Gels

A gel is solid or semisolid. Gels can be classified in two groups, chemical and physical gels. Chemical gels are usually covalently cross-linked gels, while physical gels consist of small molecules or molecular chains that are physically cross-linked into networks, or solutions, or colloidal dispersions that are stiffened by a gelling agent. Typically, gels hold their form being self-supporting.

Some gels may exhibit a range of behavior under mechanical forces. Gels may be thixotropic, forming semisolids on standing and becoming less viscous on agitation. Like emulsions, gels can be characterized as having a continuous phase as well as a dispersed phase. A variety of routes are available for gel administration such as topical, mucosal, or oral. In veterinary medicine, gels also can be administered via ▲the intramammary route.▲ (USP 1-May-2021)

Gels may consist of a network of small discrete particles (e.g., *Aluminum Hydroxide Gel*, *Bentonite Magma*, or *Psyllium Hemicellulose*). Because these gels may be thixotropic, forming semisolids on standing and becoming less viscous on agitation, they should be shaken before use to ensure homogeneity and should be so labeled.

Gels can consist of organic macromolecules uniformly distributed throughout a liquid in such a manner that no apparent boundaries exist between the dispersed macromolecules and the liquid continuous phase. These gels may be made from natural or synthetic macromolecules (e.g., carbomer, hypromellose, or starch) or natural gums (e.g., tragacanth). Although these gels are commonly aqueous based, alcohols and oils may be used as the continuous phase.

Chewable gels are used to deliver drug substances or dietary supplements via the oral route. In addition to drug substances(s) or dietary supplements, chewable gels can consist of all or some of the following components: gelling agent(s), sugars, water, sweeteners, and flavoring agents. The sweeteners and flavoring are intended to enhance patient acceptance and mask the taste of the delivered labeled drug substance or dietary supplement. Chewable gels maintain their molded shape, are elastic, and yield to mastication. They are intended to be chewed before swallowing. Chewable gels are also known as "gummies" in the confectionary and dietary supplement industries but that term is not used in official article titles.

PREPARATION

Gels may be formed by dispersing the gelling agent in the continuous phase (e.g., by heating starch), by cross-linking the dispersed phase gelling agent, by changing the pH (as for *Carbomer Copolymer*), or by reducing the continuous phase by heat or vacuum (as for gels formed with sucrose).

Care should be taken to ensure uniformity of the drug substances by dispersing them by vigorous mixing or milling, or by shaking if the preparation is less viscous.

Chewable gels are formulated with one or more gelling agents (such as gelatin or starch), sugars (such as sucrose, fructose, or corn syrup), flavoring agents, sweeteners, colorants, and water. The ingredients are blended and heated to form a viscous solution that is poured into molds (e.g., corn starch molds). After cooling, the individual units are separated from the molds.

Granules

Granules are solid dosage forms that are composed of agglomerations of smaller particles. These multicomponent compositions are prepared for oral administration and are used to facilitate flexible dosing regimens as granules or as suspensions, address stability challenges, allow taste masking, or facilitate flexibility in administration (for instance, to pediatric patients, geriatric patients, or animals). Granular dosage forms may be formulated for direct oral administration and may facilitate compounding of multiple drug substances by allowing compounding pharmacists to blend various granular compositions in the retail or hospital pharmacy. More commonly, granules are reconstituted to a suspension by the addition of water or a supplied liquid diluent immediately prior to delivery to the patient. Effervescent granules are formulated to liberate gas (carbon dioxide) upon addition of water. Common examples of effervescent granules include antacid and potassium supplementation preparations. Common therapeutic classes formulated as granule dosage forms include antibiotics, certain laxatives (such as senna extract products), electrolytes, and various cough and cold remedies that contain multiple drug substances.

PREPARATION

Granules are often the precursors used in tablet compression or capsule filling. Although this application represents a pharmaceutical intermediate and not a final dosage form, numerous commercial products are based on granules. In the typical manufacture of granules, the drug substance(s) is blended with excipients (processing aids) and wetted with an appropriate pharmaceutical binding solution, solvent, or blend of solvents to promote agglomeration. This composition is dried and sized to yield the desired material properties.

Frequently, granules are used because the drug substance is unstable in aqueous environments and cannot be exposed to water for periods sufficient to accommodate manufacture, storage, and distribution in a suspension. Preparation of the liquid dosage form from the granules immediately prior to dispensing allows acceptable stability for the duration of use. Granules manufactured for this purpose are packaged in quantities sufficient for a limited time period—usually one course of therapy that typically does not exceed 2 weeks. In addition to the drug substances, other ingredients may be added to ensure acceptable stability (e.g., buffers, antioxidants, or chelating agents) or to provide color, sweetness, and flavor; and for suspensions, to provide acceptable viscosity to ensure adequate suspension of the particulate to enable uniform dosing.

Effervescent granules are typically formulated from sodium or potassium bicarbonate and an acid such as citric or tartaric acid. To prevent untimely generation of carbon dioxide, manufacturers should take special precautions to limit residual water in the product due to manufacture and to select packaging that protects the product from moisture. The manufacture of effervescent granules can require specialized facilities designed to maintain very low humidity (approximately 10% relative humidity). Effervescent powder mixtures are purposely formed into relatively ▲coarse▲ (USP 1-May-2021) granules to reduce the rate of dissolution and provide a more controlled effervescence.

Reconstitution of granules must ensure complete wetting of all ingredients and sufficient time and agitation to allow the soluble components to dissolve. Specific instructions for reconstitution provided by the manufacturer should be carefully followed.

Reconstituted suspensions should be thoroughly mixed or shaken before use to resuspend the dispersed particulates. This is especially true of suspension preparations dosed from multiple-dose containers. For particularly viscous suspensions prone to

air entrapment, instructions may advise the user how to shake the preparation to resuspend settled particulates while minimizing air entrapment.

For granules reconstituted to form suspensions for oral administration, acceptable suspension of the particulate phase depends on the particle size of the dispersed phase as well as the viscosity of the vehicle. Temperature can influence the viscosity, which influences suspension properties and the ease of removal of the dose from the bottles. In addition, temperature cycling can lead to changes in the particle size of the dispersed phase via Ostwald ripening. Thus, clear instructions should be provided regarding the appropriate storage temperature for the product.

Gums

Medicated gum is a pliable dosage form that is designed to be chewed rather than swallowed. Medicated gums release the drug substance(s) into the saliva. Medicated gums can deliver therapeutic agents for local action in the mouth or for systemic absorption via the buccal or gastrointestinal routes (e.g., nicotine or aspirin). Most gums are manufactured using the conventional melting process derived from the confectionary industry or alternatively may be directly compressed from gum powder. Medicated gums are formulated from insoluble synthetic gum bases such as polyisoprene, polyisobutylene, isobutyleneisoprene copolymer, styrene butadiene rubber, polyvinyl acetate, polyethylene, ester gums, or polyterpenes. Plasticizers and softeners such as propylene glycol, glycerin, oleic acid, or processed vegetable oils are added to keep the gum base pliable and to aid in the incorporation of the drug substance(s), sweeteners, and flavoring agents. Sugars as well as artificial sweeteners and flavorings are incorporated to improve taste, and dyes may be used to enhance appearance. Some medicated gums are coated with magnesium stearate to reduce tackiness and improve handling during packaging. A preservative may be added.

PREPARATION

Melted gum: The gum base is melted at a temperature of about 115° until it has the viscosity of thick syrup and, at that point, is filtered through a fine-mesh screen. This molten gum base is transferred to mixing tanks where the sweeteners, plasticizers, and typically the drug substance are added and mixed. Colorings, flavorings, and preservatives are added and mixed while the melted gum is cooling. The cooled mixture is shaped by extrusion or rolling and cutting. Dosage units of the desired shape and potency are packaged individually. Additional coatings such as powder coatings to reduce tackiness or film or sugar coatings may be added to improve taste or facilitate bulk packaging.

Directly compressed gum: The gum base is supplied in a free-flowing granular powder form. The powder gum base is then dry blended with sweeteners, flavors, the drug substance, and lubricant. The blend is then processed through a conventional tablet press and tableted into desired shapes. The resulting medicated gum tablets can be further coated with sugar or sugar-free excipients. These tablets can be packaged in blisters or bottles as needed.

SPECIAL CONSIDERATIONS

Medicated gums are typically dispensed in unit-dose packaging. The patient instructions also may include a caution to avoid excessive heat.

Implants

Implants are long-acting dosage forms that provide continuous release of the drug substance often for periods of months to years. They are administered by the parenteral route and are sterile. Some implants approved as animal drugs to be administered subcutaneously to the ears are not required to be sterile. Typically for systemic delivery, they may be placed subcutaneously, or for local delivery they can be placed in a specific region in the body (e.g., in the sinus, in an artery, in the eye, in the brain). Implants are usually administered by means of a suitable injector or by surgical procedure.

Polymer implants can be formed as a single-shaped mass such as a cylinder. The polymer matrix must be biocompatible (see *The Biocompatibility of Materials Used in Drug Containers, Medical Devices, and Implants* ⟨1031⟩), but it can be either bioabsorbable or nonbioabsorbable. Shaped polymer implants are administered by means of a suitable special injector. Release kinetics are typically not zero-order, but zero-order kinetics are possible. Drug substance release can be controlled by the diffusion of the drug substance from the bulk polymer matrix or by the properties of a rate-limiting polymeric membrane coating. Polymer implants are used to deliver potent small molecules like steroids (e.g., estradiol for cattle) and large molecules like peptides [e.g., luteinizing hormone-releasing hormone (LHRH)]. Example durations of drug substance release are 2 and 3 months for bioabsorbable implants and up to 3 years for nonbioabsorbable implants. An advantage of bioabsorbable implants is that they do not require removal after the release of all drug substance content. Nonbioabsorbable polymer implants can be removed before or after a drug substance release is complete or may be left in situ. An implant can have a tab with a hole in it to facilitate suturing it in place (e.g., for an intravitreal implant for local ocular delivery). Such implants may provide therapeutic release for periods as long as 2.5 years.

Drug substance-eluting stents combine the mechanical effect of the stent to maintain arterial patency with the prolonged pharmacologic effect of the incorporated drug substance (to reduce restenosis, inhibit clot formation, or combat infection). As an example, a metal stent can be coated with a nonbioabsorbable or bioabsorbable polymer-containing drug substance. The resultant coating is a polymeric matrix that controls the extended release of the drug substance.

PREPARATION

Cylindrical polymeric implants are commonly made by melt extrusion of a blend of drug substance and polymer, resulting in a rod that is cut into shorter lengths. Polymer implants also can be made by injection molding. Still other implants are assembled from metal tubes and injection-molded plastic components.

Sterility can be achieved by terminal sterilization or by employing aseptic manufacturing procedures.

Injections

(See *Emulsions*, ▲*Foams*,▲ (USP 1-May-2021)*Powders*, *Solutions*, and *Suspensions* for information on injectable dosage forms.)
Injections are not treated as a dosage form in this chapter. Chapter ⟨1⟩ provides quality and other information about injectable products. Information on specific dosage form terminology can be found in the *Glossary*. For appropriate injection nomenclature, see *Nomenclature* ⟨1121⟩.

EXCESS VOLUME IN INJECTIONS

Each container of an injection is filled with a volume in slight excess of the labeled "size" or the volume that is to be withdrawn. The excess volumes recommended in *Table 1* are usually sufficient to permit withdrawal and administration of the labeled volumes.

Table 1

Labeled Size (mL)	Recommended Excess Volume	
	For Mobile Liquids (mL)	For Viscous Liquids (mL)
0.5	0.10	0.12
1.0	0.10	0.15
2.0	0.15	0.25
5.0	0.30	0.50
10.0	0.50	0.70
20.0	0.60	0.90
30.0	0.80	1.20
50.0 or more	2%	3%

Inserts

Inserts are solid dosage forms that are inserted into a naturally occurring (nonsurgical) body cavity other than the mouth or rectum (see *Suppositories*). The drug substance in inserts is delivered for local or systemic action. Vaginal inserts are usually globular or oviform and weigh about 5 g each. Inserts intended to dissolve in vaginal secretions are usually made from water-soluble or water-miscible vehicles such as polyethylene glycol or glycerinated gelatin.

PREPARATION

▲▲ (USP 1-May-2021) Inserts vary considerably in their preparation. Inserts may be molded (using technology similar to that used to prepare lozenges, suppositories, or plastics), compressed from powders (as in tableting), or formulated as special applications of capsules (soft gelatin capsules and hard gelatin capsules have been employed for extemporaneously compounded preparations). Inserts may be formulated to melt at body temperature or disintegrate upon insertion. Design of the dosage form should take into consideration the fluid volume available at the insertion site and minimize the potential to cause local irritation. Most inserts are formulated to ensure retention at the site of administration.

Irrigations

(See *Solutions*.)

Liquids

As a dosage form, a liquid consists of a pure chemical in its liquid state. Examples include mineral oil, isoflurane, and ether. This dosage form term is not applied to solutions.

Lotions

(See *Emulsions*.)

Lozenges

Lozenges are solid oral dosage forms that are designed to dissolve or disintegrate slowly in the mouth. They contain one or more drug substances that are slowly liberated from the typically flavored and sweetened base. They are frequently intended to provide local action in the oral cavity or the throat but also include those intended for systemic absorption after dissolution.

The typical therapeutic categories of drug substances delivered in lozenges are antiseptics, analgesics, decongestants, antitussives, and antibiotics. Molded lozenges are called cough drops or pastilles but these terms are not used in official article titles. Lozenges prepared by compression or by stamping or cutting from a uniform bed of paste are sometimes known as troches (a term not used in official article titles). Compressed or stamped lozenges are often produced in a circular shape.

Lozenges can be made using sugars such as sucrose and dextrose, or can provide the benefits of a sugar-free formulation that is usually based on sorbitol or mannitol. Polyethylene glycols and hypromellose are sometimes included to slow the rate of dissolution.

PREPARATION

Excipients used in molded lozenge manufacture include gelatin, fused sucrose, sorbitol, or another carbohydrate base.

Molded lozenges can be prepared by mixing the ingredients with water and heating to reduce the water content. The viscous solution is then poured into molds (e.g., corn starch molds). The lozenges are quickly cooled in the molds to trap the base in the glassy state. Once formed, the lozenges are removed from the molds and packaged. Care is taken to avoid excessive moisture during storage to prevent crystallization of the sugar base.

Compressed lozenges are made using excipients that may include a filler, binder, sweetening agent, flavoring agent, and lubricant. Sugars such as sucrose, sorbitol, and mannitol are often included because they can act as a filler and binder as well as serve as sweetening agents. Approved FD&C and D&C dyes or lakes (dyes adsorbed onto insoluble aluminum hydroxide) also may be present.

The manufacturing of compressed lozenges is essentially the same as that for conventional tableting, with the exception that a tablet press capable of making larger tablets and exerting greater force to produce harder tablets may be required (see *Tablets*).

The paste used to produce lozenges manufactured by stamping or cutting contains a moistening agent, sucrose, and flavoring and sweetening agents. The homogenous paste is spread as a bed of uniform thickness, and the lozenges are cut or stamped from the bed and are allowed to dry. Some lozenges are prepared by forcing dampened powders under low pressure into mold cavities and then ejecting them onto suitable trays for drying at moderate temperatures.

Ointments

Ointments are semisolid preparations generally intended for external application to the skin or mucous membranes. Drug substances delivered in ointments are intended for local action or for systemic absorption. Ointments usually contain less than 20% water and volatiles and more than 50% hydrocarbons, waxes, or polyols as the vehicle. Ointment bases recognized for use as vehicles fall into four general classes: hydrocarbon bases, absorption bases, water-removable bases, and water-soluble bases.

HYDROCARBON BASES

Also known as oleaginous ointment bases, hydrocarbon bases allow the incorporation of only small amounts of an aqueous component. Ointments prepared from hydrocarbon bases act as occlusive dressings and provide prolonged contact of the drug substance with the skin. They are difficult to remove and do not change physical characteristics upon aging.

ABSORPTION BASES

Absorption bases allow the incorporation of aqueous solutions. Such bases include only anhydrous components (e.g., *Hydrophilic Petrolatum*) or W/O emulsions (e.g., *Lanolin*). Absorption bases are also useful as emollients.

WATER-REMOVABLE BASES

O/W emulsions (e.g., *Hydrophilic Ointment*) are sometimes referred to as creams (see *Emulsions*). Water-removable bases may be readily washed from the skin or clothing with water, making them acceptable for cosmetic reasons. Other advantages of the water-removable bases are that they can be diluted with water and that they favor the absorption of serous discharges in dermatological conditions.

WATER-SOLUBLE BASES

Also known as greaseless ointment bases, they are formulated entirely from water-soluble constituents. *Polyethylene Glycol Ointment* is the only official preparation in this group. Water-soluble bases offer many of the advantages of the water-removable bases and, in addition, contain no water-insoluble substances such as petrolatum, anhydrous lanolin, or waxes. They are more correctly categorized as gels (see *Gels*).

The choice of an ointment base depends on the action desired, the characteristics of the incorporated drug substance, and the latter's bioavailability if systemic action is desired. The product's stability may require the use of a base that is less than ideal in meeting other quality attributes. Drug substances that hydrolyze rapidly, for example, are more stable in hydrocarbon bases than in bases that contain water.

PREPARATION

Ointments are typically prepared by either direct incorporation into a previously prepared ointment base or by fusion (heating during the preparation of the ointment). A levigating agent is often added to facilitate the incorporation of the medicament into the ointment base by the direct incorporation procedure. In the fusion method, the ingredients are heated. Homogenization

is often necessary. The rate of cooling is an important manufacturing detail because rapid cooling can impart increased structure to the product of the fusion method.

Pastes

Pastes are semisolid preparations of stiff consistency and contain a high percentage (20%–50%) of finely dispersed solids. Pastes are intended for application to the skin, oral cavity, or mucous membranes. Pastes ordinarily do not flow at body temperature and thus can serve as occlusive, protective coatings. As a consequence, pastes are more often used for protective action than are ointments.

Fatty pastes that have a high proportion of hydrophilic solids appear less greasy and are more absorptive than ointments. They are used to absorb serous secretions and are often preferred for acute lesions that have a tendency toward crusting, vesiculation, or oozing.

Dental pastes are applied to the teeth. Other orally administered pastes may be indicated for adhesion to the mucous membrane for a local effect. ▲Although rare, pastes can be administered orally, for example to evaluate pharyngeal function.▲ (USP 1-May-2021)

In veterinary medicine, pastes are typically administered orally and are intended for systemic delivery of drug substances. The paste is squeezed into the mouth of the animal, generally at the back of the tongue, or is spread inside the mouth.

Pellets

The use of the term "pellet" for implantable dosage forms is no longer preferred (see *Implants*). In veterinary medicine, medicated articles and feeds may be pelletized but are not considered dosage forms (see *Animal Drugs for Use in Animal Feeds* ⟨1152⟩).

Pellets are small solid dosage forms that can be designed as single or multiple entities. They can have a spherical or nearly spherical shape, although such a shape is not required. Spherical pellets are sometimes referred to as beads. Pellets used in veterinary medicine may instead be cylindrical in shape. Pellets can provide several advantages, including physical separation for chemically or physically incompatible materials and for control of the release of drug substance. Pellets may be designed with the drug substance dispersed in a matrix or the pellets may be coated with an appropriate polymer. Pellets may be administered by the oral (gastrointestinal) route. ▲Depending on the design, pellets▲ (USP 1-May-2021) for oral administration can:

1. Protect stomach tissues from irritation
2. Sometimes minimize variability associated with gastric retention of larger dosage forms
3. Solely extend the release of the drug substance
4. Solely delay the release
5. Both extend and delay the release of the drug substance

Some pellets can be sprinkled on food. In the case of delayed-release formulations, the coating polymer is chosen to resist dissolution at the lower pH of the gastric environment but to dissolve in the higher pH of the intestinal environment.

Pellets may be administered by injection. One or several pellets can be injected or surgically administered to provide continuous therapy for periods of months or years (see *Implants*).

In veterinary medicine, pellets may be used to improve palatability of the drug product and pellets for oral administration may be delivered on top of an individual animal's food or feed.

PREPARATION

The desired performance characteristics determine the manufacturing method chosen. In general, pellet dosage forms are manufactured by compression, or by wet or dry extrusion processes sometimes followed by spheronization, or followed by wet or dry coating processes. Manufacture of pellets by wet coating usually involves the application of successive coatings upon nonpareil seeds. This manufacturing process is frequently conducted in fluid-bed processing equipment. Dry powder coating or layering processes are often performed in specialized rotor granulation equipment. The extent of particle growth achievable in wet coating processes is generally more limited than the growth that can be obtained with dry powder layering techniques, but either method allows the formulator to develop and apply multiple layers of coatings to achieve the desired release profile. The manufacture of pellets by compression is largely restricted to the production of material for subcutaneous implantation. This method of manufacture provides the necessary control to ensure dose uniformity and is generally better suited to aseptic processing requirements.

Alternatively, microencapsulation techniques can be used to manufacture pellets. Coacervation coating techniques typically produce coated particles that are much smaller than those made by other techniques.

Pills

Pills are drug substance-containing small, spherical, solid bodies intended for oral administration. The pill dosage form has been largely replaced by compressed tablets and by capsules. Unlike tablets, pills are usually prepared by a wet massing, piping, and molding technique. This term is frequently incorrectly used as a general term to describe solid oral dosage forms, such as tablets and capsules.

PREPARATION

Excipients are selected on the basis of their ability to produce a mass that is firm and plastic. The drug substance is triturated with powdered excipients in serial dilutions to attain a uniform mixture. Liquid excipients that act to bind and provide plasticity to the mass are subsequently added to the dry materials. The mass is formed by kneading. The properties of firmness and plasticity are necessary to permit the mass to be worked and retain the shape produced. Cylindrical pill pipes are produced from portions of the mass. The pill pipe is cut into individual lengths corresponding to the intended pill size, and the pills are rolled to form the final shape. Pill-making machines can automate the preparation of the mass, production of pill piping, and the cutting and rolling of pills.

Plasters

A plaster is a semisolid substance for external application that is supplied on a support material. Plasters are applied for prolonged periods to provide protection, support, or occlusion (maceration). This term is not preferred and should not be used for new drug product titles ▲(see *Systems*).▲ (USP 1-May-2021) Plasters consist of an adhesive layer that may contain active substances. This layer is spread uniformly on an appropriate support that is usually made of a rubber base or synthetic resin. Unmedicated plasters are designed to provide protection or mechanical support to the site of application. Plasters are available in a range of sizes or cut to size to effectively provide prolonged contact to the site of application. They adhere firmly to the skin but can be peeled off the skin without causing injury.

Powders

Powders are defined as a single solid or a mixture of solids in a finely divided state. Powders used as pharmaceutical dosage forms may contain one or more drug substances and can be used as is or can be mixed with a suitable vehicle for administration (see *Solutions* or *Suspensions*). Powders can be intended for internal or external use. Powders for external use are typically dusted onto the skin or applied to bandages or clothing. Powders for internal use can be applied to accessible mucous membranes with suitable applicators or are entrained in air streams for application to the nose or lungs.

The performance of powder dosage forms can be affected by the physical characteristics of the powder. Selection of relevant and appropriate powder characteristics depends on the dosage form and its route of administration. For example, particle size can influence the dissolution rate of the particles and thus the bioavailability and/or effectiveness at the site of action. Externally applied powders should have a particle size of 150 µm or less (typically in the 50–100-µm range to prevent a gritty feel on the skin that could further irritate traumatized skin). The particle size of powders delivered to the lung or nose influences where the powder is deposited. Particle size may influence the mixing, segregation, and aggregation of the particles, which can affect the delivery and uniformity of the dosage form. For more information, see *Powder Fineness* ⟨811⟩ and ⟨5⟩.

▲In veterinary medicine, a powder that needs to be reconstituted prior to administration previously has been called a concentrate. The term "concentrate" is no longer preferred.▲ (USP 1-May-2021)

INHALATION POWDERS AND NASAL POWDERS

Inhalation powders and nasal powders consist of an appropriately finely divided solid and a suitable container–closure delivery system. For additional information, see ⟨5⟩ and ⟨601⟩.

PREPARATION

Powder dosage forms can be produced by the combination of multiple components into a uniform blend. This preparation can also involve particle size reduction, a process referred to as comminution. Milling, spray drying, supercritical fluid, high-pressure homogenization, precipitation technologies, and porous microparticle fabrication techniques may be used to reduce the particle size of powders. As the particle size is decreased, the number of particles and the surface area increase, which can increase the dissolution rate and bioavailability, and/or the rate and extent of local action, of the drug substance.

Blending of powders may be accomplished by different techniques. Industrial processes may employ sifting or tumbling the powders in a rotating container. One of the most common tumble blenders is a V-blender, which is available in a variety of sizes suitable for small-scale and large-scale compounding and industrial production. Depending on the particle size of the drug substance, a random mixture of powders may be employed. Blending techniques for powders include those used in compounding pharmacy such as spatulation and trituration. ▲▲ (USP 1-May-2021)

Powder flow can be influenced by both particle size and shape. Larger particles generally flow more freely than do fine particles. Powder flow is an important attribute that can affect the packaging or dispensing of a powder.

Rinses

(See *Solutions*.)

Soaps and Shampoos

Soaps and shampoos are solid or liquid preparations intended for topical application to the skin or scalp followed by subsequent rinsing with water. Soaps and shampoos are emulsions, suspensions, or surface-active compositions that readily form emulsions, micelles, or foams upon the addition of water followed by rubbing. Incorporation of drug substances in soaps and shampoos combines the cleansing/degreasing abilities of the vehicle and facilitates the topical application of the drug substance to affected areas, even large areas, of the body. The surface-active properties of the vehicle facilitate contact of the

drug substance with the skin or scalp. Medicated soap and shampoo formulations frequently contain suitable antimicrobial agents to protect against bacteria, yeast, and mold contamination.

PREPARATION

The preparation of medicated soaps and shampoos follows techniques frequently used for the preparation of emulsified systems. To ensure uniformity, the drug substance(s) must be added to the vehicle prior to congealing (in the case of soaps) followed by thorough mixing. If the medication is present as a suspension, the particle size must be controlled to promote uniform distribution of the drug substance and possibly optimize performance. Because soap manufacture frequently involves processing the ingredients at an elevated temperature, care must be exercised to avoid excessive degradation of the drug substance during processing.

Solutions

A solution is a preparation that contains one or more dissolved chemical substances in a suitable solvent or mixture of mutually miscible solvents. Because molecules of a drug substance in solution are uniformly dispersed, the use of solutions as dosage forms generally provides assurance of uniform dosage upon administration and good accuracy when the solution is diluted or otherwise mixed.

Substances in solutions are more susceptible to chemical instability than they are in the solid state and, dose-for-dose, are generally heavier and more bulky than solid dosage forms. These factors increase the cost of packaging and shipping relative to that of solid dosage forms. Some solutions are prepared and ready for use, and others are prepared as powders or other solids intended for reconstitution with an appropriate vehicle just before use (see *Powders*). Solution dosage forms can be administered by injection, inhalation, and the mucosal, topical, and gastrointestinal routes. A solution administered by injection is officially titled "injection" (see ⟨1⟩).

Some solutions are designed to form a mass in situ. These solutions comprise polymer, drug substance, and solvent for the polymer. The polymer solvent can be water or an organic solvent. After administration of the solution to a patient by subcutaneous or intramuscular administration, it forms a gel or a solid polymeric matrix that traps the drug substance and extends the drug substance release for days or months.

Solutions intended for oral administration usually contain flavorings and colorants to make the medication more attractive and palatable for the patient or consumer. When needed, they also may contain stabilizers to maintain chemical and physical stability and preservatives to prevent microbial growth.

Solutions are sometimes placed on devices such as swabs, cloths, or sponges, that aid application.

▲▲ (USP 1-May-2021) A solution that needs to be diluted prior to administration ▲previously▲ (USP 1-May-2021) has been called a concentrate. ▲▲ (USP 1-May-2021) The term "concentrate" is no longer preferred.

Sprays

Spray preparations may deliver either accurately metered or nonmetered amounts of formulation.

A spray drug product is a dosage form that contains a drug substance in the liquid state as a solution or suspension and is intended for administration as a mist. Sprays are distinguished from aerosols in that spray containers are not pressurized. Most of the sprays are generated by manually squeezing a flexible container or actuation of a pump that generates the mist by discharging the contents through a nozzle.

Depending on the design of the formulation and the valve system, the droplets generated may be intended for immediate inhalation through the mouth and deposition in the pulmonary tree, or for inhalation into the nose and deposition in the nasal cavity.

The mechanism for droplet generation and the intended use of the preparation distinguish various ▲types of spray drug products.▲ (USP 1-May-2021) A spray ▲drug product▲ (USP 1-May-2021) may be composed of a pump, container, actuator, valve, nozzle, or mouthpiece in addition to the formulation containing the drug(s), solvent(s), and any excipient(s). The design of each component plays a role for the appropriate performance of the drug product and in determining the critical characteristics of the droplet size distribution. Droplet and particle size distributions, delivered dose uniformity, plume geometry, and droplet velocity are critical parameters that influence the efficiency of drug delivery. When the preparation is supplied as a multidose container, the addition of a suitable antimicrobial preservative may be necessary. Spray formulations intended for local or systemic effect typically have an aqueous base and may contain excipients to control pH and viscosity. In addition, depending on the route of administration, the formulation may be isotonic. For additional information, see ⟨5⟩ and ⟨601⟩.

LABELING AND USE

Refer to the Center for Drug Evaluation and Research (CDER) *Guidance for Industry: Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products—Chemistry, Manufacturing, and Controls Documentation*.

Strips

A strip is a dosage form or device in the shape of a long, narrow, thin, absorbent, solid material such as filter paper. Typically it is sterile and it may be impregnated with a compound or be gauged to allow measurements for diagnostic purposes, such as in measuring tear production. The term "strip" should not be used when another term such as "film" is more appropriate.

Suppositories

Suppositories are dosage forms adapted for application into the rectum. They melt, soften, or dissolve at body temperature. A suppository may have a local protectant or palliative effect, or may deliver a drug substance for systemic or local action.

Suppository bases typically include cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, mixtures of polyethylene glycols of various molecular weights, and fatty acid esters of polyethylene glycol. The suppository base can have a notable influence on the release of the drug substance(s). Although cocoa butter melts quickly at body temperature, it is immiscible with body fluids, and this inhibits the diffusion of fat-soluble drug substances to the affected sites. Polyethylene glycol is a suitable base for some antiseptics. In cases when systemic action is desired, incorporating the ionized rather than the nonionized form of the drug substance may help maximize bioavailability. Although nonionized drug substances partition more readily out of water-miscible bases such as glycerinated gelatin and polyethylene glycol, the bases themselves tend to dissolve very slowly, which slows drug substance release. Cocoa butter and its substitutes (e.g., *Hard Fat*) perform better than other bases for allaying irritation in preparations intended for treating internal hemorrhoids. Suppositories for adults are tapered at one or both ends and usually weigh about 2 g each.

PREPARATION

Cocoa butter suppositories have cocoa butter as the base and can be made by incorporating the finely divided drug substance into the solid oil at room temperature and suitably shaping the resulting mass, or by working with the oil in the melted state and allowing the resulting suspension to cool in molds. A suitable quantity of hardening agents may be added to counteract the tendency of some drug substances (such as chloral hydrate and phenol) to soften the base. The finished suppository melts at body temperature.

A variety of vegetable oils, such as coconut or palm kernel, modified by esterification, hydrogenation, or fractionation, are used as cocoa butter substitutes to obtain products that display varying compositions and melting temperatures (e.g., *Hydrogenated Vegetable Oil* and *Hard Fat*). These products can be designed to reduce rancidity while incorporating desired characteristics such as narrow intervals between melting and solidification temperatures, and melting ranges to accommodate formulation and climatic conditions.

Drug substances can be incorporated into glycerinated gelatin bases by addition of the prescribed quantities to a vehicle consisting of about 70 parts of glycerin, 20 parts of gelatin, and 10 parts of water.

Several combinations of polyethylene glycols that have melting temperatures that are above body temperature are used as suppository bases. Because release from these bases depends on dissolution rather than on melting, there are significantly fewer problems in preparation and storage than is the case for melting-type vehicles. However, high concentrations of higher molecular weight polyethylene glycols may lengthen dissolution time, resulting in problems with retention.

Several nonionic surface-active agents closely related chemically to the polyethylene glycols can be used as suppository vehicles. Examples include polyoxyethylene sorbitan fatty acid esters and the polyoxyethylene stearates. These surfactants are used alone or in combination with other suppository vehicles to yield a wide range of melting temperatures and consistencies. A notable advantage of such vehicles is their water dispersibility. However, care must be taken with the use of surfactants because they may either increase the rate of drug substance absorption or interact with the drug substance to reduce therapeutic activity.

Compounding suppositories using a suppository base typically involves melting the suppository base and dissolution or dispersion of the drug substance in the molten base (see ⟨795⟩). When compounding suppositories, the compounding professional prepares an excess amount of total formulation to allow the prescribed quantity to be accurately dispensed. In compounding suppositories, avoid caustic or irritating ingredients, carefully select a base that will allow the drug substance to provide the intended effect, and in order to minimize abrasion of the rectal membranes, reduce solid ingredients to the smallest reasonable particle size.

Suspensions

A suspension is a biphasic preparation consisting of solid particles dispersed throughout a liquid phase. Suspension dosage forms may be formulated for specific routes of administration such as oral, topical, inhalation, ophthalmic, otic, and injection. ▲In veterinary medicine, suspensions also can be administered via the intramammary route.▲ (USP 1-May-2021) Some suspensions are prepared and ready for use, and others are prepared as powders or other solids intended for reconstitution with an appropriate vehicle just before use (see *Powders*).

Inhalation suspensions (see ⟨5⟩), ophthalmic suspensions, injectable suspensions, and some otic suspensions are prepared in sterile form. Suspensions are generally not injected intravenously, epidurally, or intrathecally unless the product labeling clearly specifies these routes of administration.

Some liposomal drug products are referred to as suspensions because they can settle and require resuspension prior to administration (see ⟨1⟩).

Resorbable microparticles can provide extended release of a drug substance over periods varying from a few weeks to months. They can be administered subcutaneously or intramuscularly for systemic delivery, or they may be deposited in a desired location in the body for site-specific delivery. Resorbable microparticles (or microspheres) generally range from 20 to 100 µm in diameter. They are composed of a drug substance dispersed within a biocompatible, bioabsorbable polymeric excipient (matrix). Poly(lactide-co-glycolide) polymers have been used frequently. These excipients typically resorb by hydrolysis of ester linkages. The microparticles are typically administered by suspension in an aqueous vehicle followed by injection with a conventional syringe and needle. Release of the drug substance from the microparticles begins after physiological fluid enters the polymer matrix, dissolving some of the drug substance that is then released by a diffusion-controlled process. Drug release also can occur as the bioresorbable polymer molecular weight decreases and as the matrix erodes.

Some suspensions are designed to form a mass in situ. These suspensions comprise polymer, drug substance, and solvent for the polymer. The polymer solvent can be water or an organic solvent. After administration of the suspension to a patient

by subcutaneous or intramuscular administration, it forms a gel or a solid polymeric matrix that traps the drug substance and extends the drug substance release for days or months.

Historically, the term "milk" was sometimes used for suspensions in aqueous vehicles intended for oral administration (e.g., *Milk of Magnesia*). The term "magma" is often used to describe suspensions of inorganic solids, such as clays in water, that display a tendency toward strong hydration and aggregation of the solid, giving rise to gel-like consistency and thixotropic rheological behavior (e.g., *Bentonite Magma*). In the past, the term "lotion" referred to both topical suspensions and topical emulsions. Now the term only refers to topical emulsions (see *Emulsions*).

Limited aqueous solubility of the drug substance(s) is the most common rationale for developing a suspension. Other potential advantages of an oral suspension include taste masking and improved patient compliance because of the more convenient dosage form. When compared to solutions, suspensions can have improved chemical stability. Ideally, a suspension should contain small uniform particles that are readily suspended and easily redispersed following settling. Unless the dispersed solid is colloidal, the particulate matter in a suspension will likely settle to the bottom of the container upon standing. Such sedimentation may lead to caking and solidification of the sediment and difficulty in redispersing the suspension upon agitation. To prevent such problems, manufacturers commonly add ingredients to increase viscosity and the gel state of the suspension or flocculation, including clays, surfactants, polyols, polymers, or sugars. Frequently, thixotropic vehicles are used to counter particle-settling tendencies, but these vehicles must not interfere with pouring or redispersal. Additionally, the density of the dispersed phase and continuous phase may be modified to further control settling rate. For topical suspensions, rapid drying upon application is desirable.

Temperature can influence the viscosity (and thus suspension properties and the ease of removing the dose from the bottle), and temperature cycling can lead to changes in the particle size of the dispersed phase via Ostwald ripening. When manufacturers conduct stability studies to establish product shelf life and storage conditions, they should cycle conditions (freeze/thaw) to investigate temperature effects.

Unless studies confirm that the formulation will not support microbial growth, suspension preparations packaged to provide multiple doses should contain suitable antimicrobial agents to protect against bacterial, yeast, and mold contamination (see ⟨51⟩) or other appropriate measures should be taken to avoid microbial contamination.

Suspensions for reconstitution are dry powder or granular mixtures that require the addition of water or a supplied formulated diluent before administration. This formulation approach is frequently used when the chemical or physical stability of the drug substance or suspension does not allow sufficient shelf life for a preformulated suspension. Typically, these suspensions are refrigerated after reconstitution to increase their shelf life. For this type of suspension, the powder blend is uniform and the powder readily disperses when reconstituted.

Injectable suspensions are generally intended for either subcutaneous or intramuscular routes of administration and should have a controlled particle size, typically in the range of 5 µm and smaller. The rationale for the development of injectable suspensions may include poor drug substance solubility, improved chemical stability, prolonged duration of action, and avoidance of first-pass metabolism. Care is needed in selecting the sterilization technique because it may affect product stability or alter the physical properties of the material.

▲▲ (USP 1-May-2021) A suspension that needs to be diluted prior to administration ▲previously▲ (USP 1-May-2021) has been called a concentrate. ▲▲ (USP 1-May-2021) The term "concentrate" is no longer preferred.

PREPARATION

Suspensions are prepared by adding suspending agents or other excipients and purified water or oil to solid drug substances and mixing to achieve uniformity. In the preparation of a suspension, the characteristics of both the dispersed phase and the dispersion medium should be considered. During development, manufacturers should define an appropriate particle size distribution for the suspended material to achieve the desired effectiveness and to minimize the likelihood of particle size changes during storage.

In some instances, the dispersed phase has an affinity for the vehicle and is readily wetted upon its addition. For some materials, the displacement of air from the solid surface is difficult, and the solid particles may clump together or float on top of the vehicle. In the latter case, a wetting agent may be used for certain types of suspensions to facilitate displacement of air from the powder surface. Surfactants, alcohol, glycerin, and other hydrophilic liquids can be used as wetting agents when an aqueous vehicle will be used as the dispersion phase. These agents function by displacing the air in the crevices of the particles and dispersing the particles. In the large-scale preparation of suspensions, wetting of the dispersed phase may be aided by the use of high-energy mixing equipment such as colloid mills or other rotor–stator mixing devices.

After the powder has been wetted, the dispersion medium (containing the soluble formulation components such as colorants, flavorings, and preservatives) is added in portions to the powder, and the mixture is thoroughly blended before subsequent additions of the vehicle. A portion of the vehicle is used to wash the mixing equipment free of suspended material, and this portion is used to bring the suspension to final volume and ensure that the suspension contains the desired concentration of solid matter. The final product may be passed through a colloid mill or other blender or mixing device to ensure uniformity.

Suspensions are resuspended before the dose is dispensed. Because of the viscosity of many suspension vehicles, air entrainment may occur during dosing. The formulation process allows evaluation of this possibility; adjustments in vehicle viscosity or the incorporation of low levels of antifoaming agents are common approaches to minimize air entrainment. Alternatively, specific instructions for resuspending the formulation may be provided to minimize air incorporation and ensure accurate dosing.

Systems

Systems are preparations of drug substance(s) in carrier devices, often containing adhesive backing, that are applied topically or inserted into body cavities. The drug substance is designed to be released in a controlled manner over a specified period of time or the drug substance is released based on its concentration in the formulation. Unless otherwise stated in the labeling,

the carrier device is removed after use. The term "system" should not be used when another dosage form term is more appropriate (e.g., inserts and implants).

The notation of strength is either defined in terms of the amount of the drug substance released from the system over a specific period of time or as the drug concentration within the formulation (e.g., the percentage of the drug). Various routes of administration are possible, so the route must always be indicated in the compendial name when a specific location for application is essential for proper use (e.g., "intrauterine", "ocular", or "periodontal" as the route of administration). For example, systems applied to the eye are called ocular systems. The route is named "transdermal" when, for example, systemic absorption of the drug substance may take place through the dermis without specifying the region of the body to which the system is applied.

The term "patch" has sometimes been used but is not preferred for use in drug product monograph nomenclature when referring to a system.

Intrauterine systems are intended for placement in the uterus. Release of the drug substance can be up to 5 years.

Ocular systems are intended for placement in the lower conjunctival fornix from which the drug diffuses through a membrane at a constant rate.

Periodontal systems are intended for placement in the pocket between the tooth and the gum. In some cases, periodontal systems may be formed in situ in the periodontal pocket and release the drug substance(s) for several weeks.

TDSs are placed onto intact skin to deliver the drug to the systemic circulation. They are designed for prolonged release (up to 7 days). Specific quality tests for TDS are found in ⟨3⟩.

Tablets

Tablets are solid dosage forms in which the drug substance is generally blended with excipients and compressed into the final dosage. Tablets are the most widely used dosage form in the United States. Tablet presses use steel punches and dies to prepare compacted tablets by the application of high pressures to powder blends or granulations. Tablets can be produced in a wide variety of sizes, shapes, and surface markings. Capsule-shaped tablets are commonly referred to as caplets, although the term is not used in official article titles. Specialized tablet presses may be used to produce tablets with multiple layers or with specially formulated core tablets placed in the interior of the final dosage form. These specialized tablet presentations can delay or extend the release of the drug substance(s) or physically separate incompatible drug substances. Tablets may be coated by a variety of techniques to provide taste masking, protection of photo-labile drug substance(s), extended or delayed release, or unique appearance (colors). When no deliberate effort has been made to modify the drug substance release rate, tablets are referred to as immediate-release.

BUCCAL TABLETS

Intended to be inserted in the buccal pouch, where the drug substance is absorbed directly through the oral mucosa. Few drug substances are readily absorbed in this way (examples are nitroglycerin and certain steroid hormones).

CHEWABLE TABLETS

Formulated and manufactured to produce a pleasant-tasting residue in the mouth and to facilitate swallowing. Hard chewable tablets are typically prepared by compaction, usually utilizing mannitol, sorbitol, or sucrose as binders and fillers, and contain colors and flavors to enhance their appearance and taste. Soft chewable tablets are typically made by a molding or extrusion process, frequently with more than 10% water to help maintain a pliable, soft product. Hard chewable tablets in veterinary medicine often have flavor enhancers like brewer's yeast or meat/fish-based flavors.

Tablets for human use that include "chewable" in the title must be chewed or crushed prior to swallowing to ensure reliable release of the drug substance(s) or to facilitate swallowing. If tablets are designed so that they may be chewed (but chewing is not required for drug substance release or ease of swallowing), the title should not include a reference to "chewable". In that case, the product may still be described as "chewable" in the ancillary labeling statement.

Tablets for veterinary use that are intended to be chewed will include "chewable" in the title. However, it is understood that for veterinary products it is not possible to ensure that tablets are chewed prior to ingestion. Chewable tablets may be broken into pieces and fed to animals that normally swallow treats whole.

EFFERVESCENT TABLETS

Prepared by compaction and contain, in addition to the drug substance(s), mixtures of acids (e.g., citric acid or tartaric acid) and carbonates, and/or sodium bicarbonate. Upon contact with water, these formulations release carbon dioxide, producing the characteristic effervescent action.

HYPODERMIC TABLETS

Molded tablets made from completely and readily water-soluble ingredients; formerly intended for use in making preparations for hypodermic injection. They may be administered orally or sublingually when rapid drug substance availability is required.

MODIFIED-RELEASE TABLETS

Two categories of modified-release tablet formulations are recognized by USP.

Delayed-release tablets: Tablets are sometimes formulated with acid-resistant or enteric (also called "gastro-resistant") coatings to protect acid-labile drug substances from the gastric environment or to prevent adverse events such as irritation.

Extended-release tablets: Extended-release tablets are formulated in such a manner as to make the drug substance available over an extended period of time following ingestion. Requirements for dissolution (see ⟨711⟩) are typically specified in the individual monographs.

ORALLY DISINTEGRATING TABLETS

Orally disintegrating tablets are intended to disintegrate rapidly within the mouth to provide a dispersion before the patient swallows the resulting slurry where the drug substance is intended for gastrointestinal delivery and/or absorption. Some of these dosage forms have been formulated to facilitate rapid disintegration and are manufactured by conventional means or by using lyophilization or molding processes. Further details may be found in the CDER *Guidance for Industry: Orally Disintegrating Tablets*.

SUBLINGUAL TABLETS

Sublingual tablets are intended to be inserted beneath the tongue, where the drug substance is absorbed directly through the oral mucosa. As with buccal tablets, few drug substances are extensively absorbed in this way, and much of the drug substance is swallowed and is available for gastrointestinal absorption.

TABLETS FOR ORAL SOLUTION

Before administration, tablets for oral solution are intended to be solubilized in a liquid diluent. In some cases, tablets for oral solution also may be chewed or swallowed.

TABLETS FOR ORAL SUSPENSION

Tablets for oral suspension are intended to be dispersed in a liquid before administration as a suspension. The dosage form is tablets for oral suspension when either the drug substance or the excipients do not dissolve when dispersed in a liquid. In some cases, tablets for oral suspension also may be chewed or swallowed.

TABLET TRITURATES

Small, usually cylindrical, molded or compacted tablets. Tablet triturates traditionally were used as dispensing tablets in order to provide a convenient, measured quantity of a potent drug substance for compounding purposes, but they are rarely used today.

PREPARATION

Most compacted (compressed) tablets consist of the drug substance(s) and a number of excipients. These excipients may include fillers (diluents), binders, disintegrating agents, lubricants, and glidants. Approved FD&C and D&C dyes or lakes, flavors, and sweetening agents also may be present.

Fillers or diluents are added when the quantity of drug substance(s) is too small or the properties of the drug substance do not allow satisfactory compaction in the absence of other ingredients. Binders impart adhesiveness to the powder blend and promote tablet formation and maintenance of drug substance uniformity in the tableting mixture. Disintegrating agents facilitate reduction of the tablet into small particles upon contact with water or biological fluids. Lubricants reduce friction during the compaction and ejection cycles. Glidants improve powder fluidity, powder handling properties, and tablet weight control. Colorants are often added to tablet formulations for aesthetic value or for product identification.

Tablets are prepared from formulations that have been processed by one of three general methods: wet granulation, dry granulation (roll compaction or slugging), or direct compression.

Wet granulation: Involves the mixing of dry powders with a granulating liquid to form a moist granular mass that is dried and sized prior to compression. It is particularly useful in achieving uniform blends of low-dose drug substances and facilitating the wetting and dissolution of poorly soluble, hydrophobic drug substances.

Dry granulation: Can be produced by passing powders between rollers at elevated pressure (roll compaction). Alternatively, dry granulation also can be carried out by the compaction of powders at high pressures on tablet presses, a process also known as slugging. In either case, the compacts are sized before compression. Dry granulation improves the flow and handling properties of the powder formulation without involving moisture in the processing.

Direct compression: Tablet processing involves dry blending of the drug substance(s) and excipients followed by compression. The simplest manufacturing technique, direct compression, is acceptable only when the drug substance and excipients possess acceptable flow and compression properties without prior process steps.

Tablets may be coated to protect the ingredients from air, moisture, or light; to mask unpleasant tastes and odors; to improve tablet appearance; and to reduce dustiness. In addition, coating may be used to protect the drug substance from acidic pH values associated with gastric fluids or to control the rate of drug release in the gastrointestinal tract.

The most common coating in use today is a thin film coating composed of a polymer that is derived from cellulose. Sugar coating is an alternative, less common approach. Sugar-coated tablets have considerably thicker coatings that are primarily sucrose with a number of inorganic diluents. A variety of film-coating polymers are available and enable the development of specialized release profiles. These formulations are used to protect acid-labile drug substances from the acidic stomach environment as well as to prolong the release of the drug substance to reduce dosing frequency (see ⟨711⟩ or ⟨701⟩).

Tapes

A tape is a dosage form suitable for delivering drug substances to the skin. It consists of a drug substance(s) impregnated into a durable yet flexible woven fabric or extruded synthetic material that is coated with an adhesive agent. Typically the impregnated drug substance is present in the dry state. The adhesive layer is designed to hold the tape securely in place without the aid of additional bandaging. Unlike TDSs, tapes are not designed to control the release rate of the drug substance. The term "tape" is not preferred and should not be used for new official article titles ▲(see *Systems*).▲ (USP 1-May-2021)

The drug substance content of tapes is expressed as amount per surface area with respect to the tape surface exposed to the skin. The use of an occlusive dressing with the tape enhances the rate and extent of delivery of the drug substance to deeper layers of the skin and may result in greater systemic absorption of the drug substance.

Change to read:

GLOSSARY

This glossary provides definitions for terms in use in medicine and serves as a source of official titles for official articles, except when the definition specifically states that the term is not to be used in drug product titles. Examples of general nomenclature forms for the more frequently encountered categories of dosage forms appear in ⟨1121⟩. In an attempt to be comprehensive, this glossary was compiled without the limits imposed by current preferred nomenclature conventions. To clearly identify/distinguish preferred from not preferred terms, entries indicate when a term is not preferred and generally direct the user to the current preferred term. ▲Terms are also used to modify dosage forms, and such terms can be used in the naming of dosage forms.▲ (USP 1-May-2021) For example, ▲a tablet can be called a chewable tablet. The term "chewable" designates that the tablet▲ (USP 1-May-2021) must be chewed prior to swallowing.

Aerosol: A dosage form consisting of a liquid or solid preparation packaged under pressure and intended for administration as a fine mist. When not used in naming, the term "aerosol" also refers to the fine mist of small droplets or solid particles that are emitted from the product.

Aromatic water (not used in official titles; see *Solution*)**:** A clear, saturated, aqueous solution of volatile oils or other aromatic or volatile substances.

Aural (Auricular) (not used in official titles; see *Otic*)**:** For administration into, or by way of, the ear.

Bead (not used in official titles; see *Pellet*)**:** A solid dosage form in the shape of a small sphere. In most products a unit dose consists of multiple beads.

Bolus (not preferred; see *Tablet*)**:** A large tablet intended for administration to large animals. Occasionally, the term "bolus" is used to describe a method of administration.

Buccal: Administration directed toward the cheek, generally from within the mouth.

Caplet (not used in official titles; see *Tablet*)**:** Tablet dosage form in the shape of a capsule.

Capsule: A solid dosage form in which the drug substance, with or without other ingredients, is filled into either a hard or soft shell or coated on the capsule shell. Most capsule shells are composed mainly of gelatin.

Chewable: A term for a solid dosage form that is intended to be chewed or crushed before swallowing.

Chewable gel: Formed or molded oral gel dosage forms that maintain their shape, are elastic, and yield to mastication. Chewable gels are also known as "gummies," but this term is not used for official article titles.

Coating (Coated) (not used in official titles)**:** A term for the outer solid covering applied to a solid dosage form. This outer deposit is also referred to as a film. Coatings are applied for functional or aesthetic purposes such as taste masking, stability, modifying release characteristics, product identification, and appearance.

Collodion (not preferred; see *Solution*)**:** A preparation that is a solution dosage form composed of pyroxilin dissolved in a solvent mixture of alcohol and ether, and applied externally.

Colloidal dispersion: A term for a preparation or formulation in which particles of colloidal dimension (i.e., typically between 1 nm and 1 µm) are distributed uniformly throughout a liquid.

Concentrate (not a preferred term for human or veterinary drug products)**:** The current use is for drug substances that are not intended for direct administration to humans or animals. The use in drug product nomenclature is being phased out (see ⟨1121⟩ and *Nomenclature Guidelines*[1]).

Conventional-release (not used in official titles; see *Immediate-release*)**:** A term describing a dosage form in which no deliberate effort has been made to modify the release rate of the drug substance. In the case of capsules and tablets, the inclusion or exclusion of a disintegrating agent is not interpreted as a modification.

Cough drop (not used in official titles; see *Lozenge*)

Cream: A semisolid emulsion dosage form often containing more than 20% water and volatiles, and/or containing less than 50% hydrocarbons, waxes, or polyols as the vehicle for the drug substance. Creams are generally intended for external application to the skin or mucous membranes.

Delayed-release: A type of modified-release dosage form. When used in naming dosage forms, this term denotes a dosage form deliberately formulated to delay release of the drug substance for some period of time after initial administration. For oral products, expressions such as "enteric-coated" or "gastro-resistant" have been used where release of the drug substance is prevented in the gastric environment but promoted in the intestinal environment. However, the term "delayed-release" is used for official article titles.

Dental: When used in naming dosage forms, this term denotes a preparation that is applied to the teeth for localized action.

Dip (not preferred; see *Immersion*)

Disintegrating tablet (not used in official titles; see *Tablet*, *Tablet for oral suspension*, or *Tablet for oral solution*; see also *Orally disintegrating*)

Dispersible tablet (not used in official titles; see *Tablet*, *Tablet for oral suspension*, or *Tablet for oral solution*)

Dosage form (not used in official titles)**:** A combination of drug substance(s) and/or excipient(s) in quantities and physical form designed to allow the accurate and efficient administration of the drug substance to the human or animal patient.

Dry powder inhaler (not used in official titles)**:** A device used to administer an inhalation powder in a finely divided state suitable for oral inhalation by the patient.

Effervescent: A term for an oral dosage form, frequently tablets or granules, containing ingredients that, when in contact with water, rapidly release carbon dioxide. The dosage form is dissolved or dispersed in water to initiate the effervescence prior to ingestion.

Elixir (not preferred; see *Solution*)**:** A preparation that typically is a clear, flavored, sweetened hydroalcoholic solution intended for oral use. The term should not be used for new drug products in *USP–NF* but is commonly encountered in compounding pharmacy practice.

Emollient (not used in official titles)**:** A term for a cream or ointment indicating an increase in the moisture content of the skin following application of bland, fatty, or oleaginous substances.

Emulsion: A dosage form consisting of a two-phase system composed of at least two immiscible liquids, one of which is dispersed as droplets (internal or dispersed phase) within the other liquid (external or continuous phase), generally stabilized with one or more emulsifying agents. "Emulsion" is not used as a dosage form term if a more specific term is applicable (e.g., *Cream*, *Lotion*, or *Ointment*).

Enteric-coated (not used in official titles; see *Delayed-release*)**:** A term for a solid dosage form in which a polymer coating has been applied to prevent the release of the drug substance in the gastric environment.

Excipient (not used in official titles)**:** An ingredient of a dosage form other than a drug substance. The term “excipient” is synonymous with inactive ingredient.

Extended-release: A term denoting a dosage form that is deliberately formulated to prolong the release of the drug substance compared to that observed for an immediate-release dosage form. Expressions such as “prolonged release”, “repeat action”, “controlled release”, “long acting”, and “sustained release” also have been used to describe such dosage forms. However, the term “extended-release” is used for official article titles.

Extended-release injectable suspension: Liquid preparations of solids suspended in a suitable vehicle and formulated to allow the drug substance to be available over an extended period of time. The term "for extended-release injectable suspension" indicates dry solids that, upon the addition of a suitable vehicle, yield a preparation that conforms in all respects to the requirements for extended-release injectable suspensions.

Film: A term used to describe a thin sheet of material, usually composed of a polymer. Films are used in various routes of administration including as a means of oral administration of material in a rapidly dissolving form.

Foam: A dosage form containing gas dispersed in a liquid or solid continuous phase. Foams are formed at the time of application by dispensing product from the canister or other appropriate container and can be formulated to quickly break down into a liquid or to remain as a foam to ensure prolonged contact.

Gas (not used in official titles)**:** One of the states of matter having no definite shape or volume and occupying the entire container when confined.

Gastro-resistant (not used in official titles; see *Delayed-release*)**:** A term for a solid dosage form in which a polymer coating has been applied to prevent release in the gastric environment.

Gel: A dosage form that is a semisolid dispersion of small particles or a solution of large molecules interpenetrated by a solution containing a gelling agent to provide stiffness.

Gelcap (not used in official titles)**:** A capsule that is coated is sometimes referred to as a gelcap.

Geltab/Filmtab (not used in official titles)**:** A tablet that is coated is sometimes referred to as a geltab or filmtab.

Granules: A dosage form composed of dry aggregates of powder particles that may contain one or more drug substances, with or without other ingredients. They may be swallowed as such, dispersed in food, or dissolved in water. Granules are frequently compacted into tablets or filled into capsules, with or without additional ingredients. More commonly, granules are reconstituted as suspensions.

Gum: A dosage form in which the base consists of a pliable material that, when chewed, releases the drug substance into the oral cavity.

Gummies (not used in official titles; see *Chewable gel*)

Hard-shell capsule (not preferred; see *Capsule*)**:** A type of capsule in which one or more drug substances, with or without other ingredients, are filled into a two-piece shell. Most hard-shell capsules are composed mainly of gelatin and are fabricated prior to the filling operation.

Immediate-release (not used in official titles)**:** A term for a dosage form in which no deliberate effort has been made to modify the drug substance release rate.

Immersion: A veterinary route of administration via partial or complete submersion in a specified environment such as liquid or air.

Implant: A dosage form that is a solid or semisolid material containing the drug substance that is placed into the body. The implantation process is invasive, and the material is intended to reside at the site for a period consistent with the design release kinetics or profile of the drug substance(s).

Inhalation (By Inhalation): A route of administration for aerosols characterized by dispersion of the drug substance into the airways during inspiration.

Injection (By Injection): A route of administration of a liquid or semisolid deposited into a body cavity, fluid, or tissue by use of a needle.

Injection: Liquid preparations that may contain drug substances and/or excipients or solutions thereof. The term “for injection” indicates dry solids that, upon the addition of a suitable vehicle, yield solutions conforming in all respects to the requirements for injections.

Injectable emulsion: Liquid preparations of drug substances dissolved or dispersed in a suitable emulsion medium.

Injectable suspension: Liquid preparations of solids suspended in a liquid medium. The term “for injectable suspension” indicates dry solids that, upon the addition of a suitable vehicle, yield preparations conforming in all respects to the requirements for injectable suspensions. For extended-release preparations, see *Extended-release injectable suspension*.

Insert: A solid dosage form that is inserted into a naturally occurring (nonsurgical) body cavity other than the mouth or rectum. It should be noted that a suppository is intended for application into the rectum and is not classified as an insert (see *Suppository*).

▲Intramammary: Administration of a drug product into the mammary gland, including via the teat canal.▲ (USP 1-May-2021)

Intraocular: A route of administration to deliver a sterile preparation within the eye.

Irrigation: A sterile solution or liquid intended to bathe or flush open wounds or body cavities.

Jelly (not preferred; see *Gel*)**:** A semisolid dispersion of small particles or a solution of large organic molecules interpenetrated by a solution containing a gelling agent to promote stiffness.

Liposomes: A term for preparations of amphiphilic lipids that have low water solubility (see ⟨1⟩).

Liquid (not used in official titles)**:** A dosage form consisting of a pure chemical in its liquid state. This dosage form term should not be applied to solutions. When not used in dosage form naming, the term, "liquid" is used to indicate a material that is pourable and conforms to its container at room temperature.

Lotion: An emulsion liquid dosage form applied to the outer surface of the body. Historically, this term was applied to topical suspensions and topical emulsions. The current definition of a lotion is restricted to an emulsion.

Lozenge: A solid dosage form intended to disintegrate or dissolve slowly in the mouth.

Modified-release: A term for a dosage form with a drug substance release pattern that has been deliberately changed from that observed for the immediate-release dosage form of the same drug substance. The two types of modified-release are extended-release and delayed-release. The term "modified-release" is not used in official article titles.

Molded tablet (not used in official titles)**:** A tablet that has been formed by dampening the ingredients and pressing into a mold, then removing and drying the resulting solid mass.

Mouthwash (not used in official titles; see *Rinse*)**:** Term applied to a solution preparation used to rinse the oral cavity.

Nasal: Route of administration (mucosal) characterized by administration to the nose or by way of the nose for local or systemic effect.

Ocular (not preferred; see *Intraocular*)**:** Route of administration indicating deposition of the drug substance within the eye.

Ointment: A semisolid dosage form, usually containing less than 20% water and volatiles and more than 50% hydrocarbons, waxes, or polyols as the vehicle. This dosage form generally is for external application to the skin or mucous membranes.

Ophthalmic: A route of administration characterized by application of a sterile preparation to the external parts of the eye.

Oral: Route of administration characterized by application to the mouth or delivery to the gastrointestinal tract through the mouth.

Orally disintegrating: When used in naming a dosage form, this term denotes a solid oral dosage form that disintegrates rapidly in the mouth prior to swallowing. The drug substance is intended for gastrointestinal delivery and/or absorption. See also CDER *Guidance for Industry: Orally Disintegrating Tablets*.

Orodispersible (not used in official titles; see *Orally disintegrating*)

Oro-pharyngeal: A route of administration characterized by deposition of a preparation into the oral cavity and/or pharyngeal region to exert a local or systemic effect.

Otic: A route of administration characterized by deposition of a preparation into, or by way of, the ear. Sometimes referred to as *Aural* (*Aural* not preferred).

Parenteral: General route of administration which is characterized by injection through the skin or other external boundary tissue or implantation within the body. Specific parenteral routes include intravenous, intraventricular, intra-arterial, intra-articular, subcutaneous, intramuscular, intrathecal, intracisternal, and intraocular (see ⟨1⟩).

Paste: A semisolid dosage form containing a high percentage (20%–50%) of finely dispersed solids with a stiff consistency. This dosage form is intended for application to the skin, oral cavity, or mucous membranes.

Pastille (not used in official titles; see *Lozenge*)

Patch (not preferred; see *System*)**:** Frequently incorrectly used to describe a *System*.

Pellet: A small solid dosage form of uniform, sometimes spherical, shape intended for direct administration. Spherical pellets are sometimes referred to as *Beads*. Pellets used in veterinary medicine are typically cylindrical in shape. Pellets intended as implants must be sterile, except for some ear implants used in animal drugs. The use of the term "pellet" for implantable dosage forms is no longer preferred (see *Implant*).

Periodontal: A term for a preparation that is applied around a tooth for localized action.

Pill: A solid, spherical dosage form usually prepared by a wet massing, piping, and molding technique. This term is frequently incorrectly used as a general term to describe solid oral dosage forms such as tablets or capsules.

Plaster (not preferred; ▲see *System*)▲ (USP 1-May-2021)**:** A dosage form containing a semisolid composition supplied on a support material for external application. Plasters are applied for prolonged periods of time to provide protection, support, or occlusion (for macerating action).

Powder: A dosage form composed of a solid or mixture of solids reduced to a finely divided state and intended for internal or external use.

Powder, inhalation: A powder containing a drug substance for oral inhalation. The powder is used with a device that aerosolizes and delivers an accurately metered amount.

Premix (not preferred; see Animal Drugs for Use in Animal Feeds ⟨1152⟩, Scope, Type A Medicated Articles and Type B Medicated Feeds)

Prolonged-release (not used in official titles; see *Extended-release*)

Rectal: A route of administration characterized by deposition into the rectum to provide local or systemic effect.

Rinse (see *Solution*)**:** A liquid preparation used to cleanse by flushing. A rinse is used to swish in the mouth and then expectorated. The nonpreferred term "mouthwash" sometimes has been used for "rinse".

Semisolid (not used in official titles)**:** A term for a material that exhibits plastic flow behavior. A semisolid material is not pourable, does not readily conform to its container at room temperature, and does not flow at low shear stress.

Shampoo: A solution, emulsion, or suspension dosage form used to clean the hair and scalp. May contain a drug substance intended for topical application to the scalp.

Soap: The alkali salt(s) of a fatty acid or mixture of fatty acids used to cleanse the skin. Soaps used as dosage forms may contain a drug substance intended for topical application to the skin. Soaps also have been used as liniments and enemas.

Soft gel capsule (not preferred; see *Capsule*)**:** A specific capsule type characterized by increased levels of plasticizers producing a more pliable and thicker-walled material than hard gelatin capsules. Soft gel capsules are further distinguished because they are single-piece sealed dosages. Frequently used for delivering liquid compositions.

Soluble tablet (not used in official titles; see *Tablet* and *Tablet for oral solution*)**:**

Solution: A clear, homogeneous liquid dosage form that contains one or more chemical substances dissolved in a solvent or mixture of mutually miscible solvents.

Spirit (not preferred; see *Solution*)**:** A liquid dosage form composed of an alcoholic or hydroalcoholic solution of volatile substances.

Spot on (Pour On) (not used in official titles)**:** A method of delivering liquid veterinary drug products by administering them onto the animal's skin, usually between the shoulder blades (spot on) or down the back (pour on).

Spray: A spray is a dosage form that contains drug substance(s) in the liquid state, either as a solution or as a suspension, and is intended for administration as a mist. Sprays are distinguished from aerosols in that spray containers are not pressurized. Most of the sprays are generated by manually squeezing a flexible container or actuation of a pump that generates the mist by discharging the contents through a nozzle.

When not used in the naming of a dosage form, the term "spray" describes the generation of droplets of a liquid or solution to facilitate application to the intended area.

Stent, drug-eluting: A specialized form of implant used for extended local delivery of the drug substance to the immediate location of stent placement.

Strip (only used for diagnostic products, otherwise not preferred; see *Film*)**:** A dosage form or device in the shape of a long, narrow, thin, absorbent, solid material such as filter paper.

Sublingual: A route of administration characterized by placement underneath the tongue and for release of the drug substance for absorption in that region.

Suppository: A solid dosage form in which one or more drug substances are dispersed in a suitable base and molded or otherwise formed into a suitable shape for insertion into the rectum to provide local or systemic effect.

Suspension: A liquid dosage form that consists of solid particles dispersed throughout a liquid phase.

Syrup (not preferred; see *Solution*)**:** A solution containing high concentrations of sucrose or other sugars. This term is commonly used in compounding pharmacy.

System: A preparation of drug substance(s) in a carrier device that is applied topically or inserted into a body cavity. The drug substance is designed to be released in a controlled manner over a specified period of time or the drug substance is released based on its concentration in the formulation. Unless otherwise stated in the labeling, the carrier device is removed after use.

Tablet: A solid dosage form prepared from powders or granules by compaction.

Tablet for oral solution: A tablet that is intended to be dispersed in a liquid before administration. When dispersed in the liquid, a solution results.

Tablet for oral suspension: A tablet that is intended to be dispersed in a liquid before administration. When dispersed in the liquid, a suspension results.

Tape (not preferred; ▲see *System*)▲ (USP 1-May-2021)**:** A dosage form or device composed of a woven fabric or synthetic material onto which a drug substance is placed, usually with an adhesive on one or both sides to facilitate topical application. The rate of release of the drug substance is not controlled.

Tincture (not preferred; see *Solution*)**:** An alcoholic or hydroalcoholic solution prepared from vegetable materials or from chemical substances.

Topical: A route of administration characterized by application to the external surface of the body.

Transdermal: A route of administration characterized by drug product application to the skin where the drug substance passes through the dermal layer with the intent to achieve a systemic effect.

Troche (not used in official titles; see *Lozenge*)**:** A solid dosage form intended to disintegrate or dissolve slowly in the mouth and usually prepared by compaction in a manner similar to that used for tablets.

Urethral: A route of administration characterized by deposition into the urethra.

Vaginal: A route of administration characterized by deposition into the vagina.

Vehicle (not used in official titles)**:** A term commonly encountered in compounding pharmacy that refers to a component for internal or external use that is used as a carrier or diluent in which liquids, semisolids, or solids are dissolved or suspended. Examples include water, syrups, elixirs, oleaginous liquids, solid and semisolid carriers, and proprietary products (see *Excipient*).

Veterinary: A term for dosage forms intended for nonhuman use.