Add the following:

▲⟨607⟩ PHARMACEUTICAL FOAMS—PRODUCT QUALITY TESTS

INTRODUCTION

Foams are a dispersion of gas in a liquid or a semisolid continuous phase wherein the liquid or semisolid contains the drug substance and suitable excipients. Typical foam dosage forms include aqueous or nonaqueous carriers, foam structuring agents, surfactants, and propellants (for pressurized systems). Foams are produced by mechanical means or via interaction of propellant (vapor or gas) and the formulation under pressure. Foams dispensed from nonpressurized containers use mechanical forces allowing the mixing of the formulation and air, resulting in foam generation. Foams dispensed from pressurized containers use propellant present in gas phase to increase pressure inside the container. When the nozzle of the actuator is opened, the liquid phase containing a dispersed vapor or gas is emitted through an actuator. As a result, a foam is generated.

Foams are primarily used to apply drug substances to topically accessible sites. The most significant of these sites is the skin where direct application is frequently used to alleviate symptoms (e.g., inflammation, infection). An extension of this approach is to apply foams to accessible but not superficial sites such as the ear canal, or to mucosal sites such as the rectum, vagina, or oropharynx. Invasive approaches such as application at surgical sites or insertion in blood vessels extend the application of foams and their purpose.

This chapter provides a list of product quality tests that may be applied to pharmaceutical foam products. In part or in its entirety, this chapter applies when referenced in a drug product monograph (see *General Notices, 3.10 Applicability of Standards*). Manufacturers may use quality tests listed in this chapter, as appropriate, when considering the content of new drug product monographs for submission to USP.

PRODUCT QUALITY TESTS FOR PHARMACEUTICAL FOAMS

Drug product quality tests fall into two categories: 1) universal tests that are applicable to all drug products and should be included in the monograph, and 2) specific tests that should be considered for inclusion for specific types of products. Universal tests include identification, assay, and impurities and are discussed in the following *USP* chapters, based on route of administration: *Injections and Implanted Drug Products* ⟨1⟩, *Oral Drug Products—Product Quality Tests* ⟨2⟩, *Topical and Transdermal Drug Products—Product Quality Tests* ⟨3⟩, *Mucosal Drug Products—Product Quality Tests* ⟨4⟩, and *Inhalation and Nasal Drug Products—General Information and Product Quality Tests* ⟨5⟩. Pharmaceutical foams are delivered by the injection, topical, and mucosal routes. For more information on specific tests by those routes of administration, see ⟨1⟩, ⟨3⟩, and ⟨4⟩, respectively.

QUALITY TESTS FOR FOAM PRODUCTS BY ALL ROUTES OF ADMINISTRATION

- **Dispersed Content Uniformity Throughout Canister Life**

  Non-metered products: Select one container and determine its weight. Dispense quantities according to the labeled instructions separately collecting an appropriate amount, individually weighed. The sample size should be sufficient for at least one quantitative determination of the active ingredients(s) and should not exceed the maximum dose recommended by the product labeling for a single application. [Note—Refer to the labeled use instructions to determine whether or not the can is shaken prior to expelling foam and to determine the orientation (upright or inverted) when dispensing. Use the labeled content and the weights of samples collected and material discarded for the following sampling procedure.] Retain the portions of foam corresponding to: 1) an initial portion from the filled canister, 2) a portion from the middle of the canister (in the range of 40%–60% of labeled canister content), and 3) the portion corresponding to the canister contents with 85% of the labeled contents delivered. [Note—The canister should be dispensed at room temperature. If the canister cools as a result of dispensing, the canister should be warmed to room temperature before subsequent delivery. Properly discard the material removed from the canister by valve actuations required to collect specified samples. Using an appropriate sample preparation (such as outgassing) and analytical method, determine the drug substance concentration in each of the three portions.]

  Acceptance criteria: None of the three results are outside of the product assay range. The maximum difference in the amount of active ingredient(s) determined within the canister is NMT 10.0%. For example, if the three measurements within the canister are 97.0%, 95.2%, and 99.7%, the maximum difference would be 4.5% (i.e., 99.7%–95.2% = 4.5%).

  Metered-dose products: Delivered dose uniformity measures the drug substance content as dispensed over the entire unit life. Select one container. Refer to the labeled use instructions to determine whether or not the can is shaken prior to expelling foam. Using separate collection vessels, quantitatively collect delivered doses representing actuations for the initial dose, a middle dose, and the final dose from the container. [Note—Between actuations, warm the canister in a water bath at 25° for 3 min.] Discard the material removed from the canister by valve actuations required to collect specified samples. Determine the drug substance content of each of the three collected samples.

  Acceptance criteria: None of the three results are more than 10% outside of the labeled amount per dose, and the maximum difference between any of the results is NMT 10% of the claim for delivered dose.

- **Minimum Fill:** Proceed as directed for *Minimum Fill* ⟨755⟩*, Procedure for Aerosols and Sprays*. This procedure also can be applied to foams.

  Acceptance criteria: Meets the requirements

OTHER TESTS

- **Leak Rate (Aerosol Products):** Proceed as directed in *Leak Rate* ⟨604⟩.

  Acceptance criteria: Meets the requirements

- **Propellant (Aerosol Products):** Proceed as directed in *Propellants* ⟨602⟩.

  Acceptance criteria: Meets the requirements as specified in the monograph

- **Pressure in Canister (Aerosol Products):** See *Topical Aerosols* ⟨603⟩*, Pressure Test*. Pressure in the canister is only measured for products with continuous valves using a mechanism that attaches to a pressure gauge while sealing against the valve in a manner that contains the expelled gas and foam.
  Acceptance criteria: Meets the requirements for the pressure test as specified in the monograph
- **pH:** Apply *pH* ⟨791⟩ for the collapsed foam, as appropriate. In order to measure this attribute, the collapsed foam may require dilution.
- **Sterility:** If applicable, see *Sterility Tests* ⟨71⟩.
- **Microbial Limits:** Apply microbial limits tests (see *Microbial Enumeration Tests* ⟨61⟩ and *Tests for Specified Microorganisms* ⟨62⟩), as appropriate.
- **Antimicrobial Preservative Content:** If applicable, see *Antimicrobial Effectiveness Testing* ⟨51⟩ and *Antimicrobial Agents—Content* ⟨341⟩.
- **Antioxidant Content:** If applicable, see *Topical and Transdermal Drug Products—Product Quality Tests* ⟨3⟩*, Product Quality Tests for Topical and Transdermal Drug Products, Specific Tests, Antioxidant preservative content*.
- **Osmolarity and Osmolality** If applicable, see *Osmolality and Osmolarity* ⟨785⟩.

ADDITIONAL QUALITY TESTS APPLICABLE FOR TOPICAL FOAM PRODUCTS

- **Time to Break:** Rate of foam liquid drainage and collapse can be observed by dispensing a foam into a graduated cylinder maintained at an appropriate temperature. Record the foam volume as freshly dispensed and again after a period (e.g., complete collapse or as specified in the monograph). The ratio of the freshly dispensed volume to the volume of drained liquid on complete collapse of the foam or at the time specified in the monograph is as specified in the monograph.
- **Delivery Rate:** See *Topical Aerosols* ⟨603⟩*, Delivery Rate and Delivered Amount, Delivery Rate*.
  Acceptance criteria: Meets the requirements as specified in the monograph
- **Delivered Amount:** See *Topical Aerosols* ⟨603⟩*, Delivery Rate and Delivered Amount, Delivered Amount*.
  Acceptance criteria: Meets the requirements as specified in the monograph
- **Relative Density of Uncollapsed Foam:** If applicable, determine the relative foam density by weighing a mass of uncollapsed foam (*m*) and a mass of the same volume of water (*e*) in a suitable container:

$$\text{Relative density of uncollapsed foam} = m/e$$

m = mass of uncollapsed foam (g/mL)
e = volume of water (g/mL)

- **Water Content:** If applicable (where stability may be affected, primarily for nonaqueous formulations), see *Water Determination* ⟨921⟩.
- **Particle Size:** When the finished product contains a suspended drug substance or is an emulsion, the product should be examined for particle size (in case of suspended solid drug substance) or globule size (in case of an emulsion). These tests are generally formulation dependent. Therefore, such tests are not included in compendial monographs but are part of the manufacturer's approved regulatory specification for the product.▲ (USP 1-Dec-2020)