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BRIEFING

⟨**1662**⟩ **Materials and Manufacturing Processes for Metallic Packaging Systems.** A previous proposal for this new general chapter was published in *PF* 50(4) [Jul.–Aug. 2024]. This chapter is intended to support the new general test chapter, Metallic Packaging Systems and Their Materials and Components ⟨662⟩, by providing information on the materials of construction, manufacture, and processing of metallic packaging containers used in pharmaceutical packaging/delivery systems for inhalation, nasal, topical, mucosal, and oral dosage forms.

No revisions are being proposed based on the *PF* 50(4) proposal, but the General Chapters—Packaging and Distribution Expert Committee has requested that it be republished along with ⟨662⟩ to give stakeholders another opportunity to provide feedback.

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

(GCPD: D. Hunt)

Case ID—SUB-2307

Add the following:

▲⟨1662⟩ MATERIALS AND MANUFACTURING PROCESSES FOR METALLIC PACKAGING SYSTEMS

1. INTRODUCTION

Packaging systems, also referred to as container–closure systems, are defined in *Packaging and Storage Requirements* ⟨659⟩. These systems are the sum of components that together contain and protect the drug product and, in some cases, deliver the drug product to the patient. Drug products can chemically interact with their associated packaging system's metallic materials of construction. The magnitude of these interactions should not adversely affect the suitability of the packaged drug product, which includes both quality aspects and performance aspects such as efficacy, stability, purity, and compendial compliance. Suitability for use, as determined by the impact of the interaction between a drug product and its packaging system, is assessed and established via the appropriate testing of the materials of construction and the packaging/delivery systems. *USP* chapter *Metallic Packaging Systems and Their Materials and Components* ⟨662⟩ establishes the tests and acceptance criteria that are necessary and appropriate for ensuring that such systems are suitable for use.

2. SCOPE

This chapter provides information on the materials of construction, manufacture, and processing of metallic packaging containers used in pharmaceutical packaging/delivery systems for inhalation, nasal, topical, mucosal, and oral dosage forms.

3. METALLIC MATERIALS OF CONSTRUCTION

The two metallic materials of construction commonly used in primary packaging components for pharmaceutical products are 1) aluminum alloys for aerosol cans, soft tubes, and foil; and 2) aluminum and stainless steel alloys for canisters (cans) for inhalation delivery systems. For requirements for these packaging systems, consult ⟨662⟩ and FDA Guidance on Container Closure Systems (*1*).

3.1 Stainless Steel Alloys for Metered Dose Inhaler Canisters

Super austenitic stainless steel alloys, which contain high levels of chromium and nickel along with molybdenum and copper, offer enhanced strength and exhibit resistance to pitting. These alloys, such as 316L and 904L, are representative examples of stainless steel alloys used to manufacture canisters for metered dose inhalers. See *Table 1* for their elemental composition.

Table 1. Elemental Composition of Representative Examples of Commonly Used Stainless Steel Alloys for Inhalation Canisters (*2–3*)

Elemental Composition	Stainless Steel Canisters Alloy 316L (Mass Fraction/%)[a]	Stainless Steel Canisters Alloy 904L (Mass Fraction/%)[a]
Carbon	0.03	0.02
Copper	—	1.0–2.0
Chromium	16.00–18.00	19.0–23.0
Manganese	2.00	2.00

Elemental Composition	Stainless Steel Canisters Alloy 316L (Mass Fraction/%)[a]	Stainless Steel Canisters Alloy 904L (Mass Fraction/%)[a]
Molybdenum	2.00–3.00	4.0–5.0
Nickel	10.00–13.00	23.0–28.0
Nitrogen	0.10	0.15
Phosphorus	0.045	0.045
Silicon	0.75	0.70
Sulfur	0.03	0.035
Iron	Balance	Balance

[a] Values are maxima unless otherwise stated.

3.2 Aluminum Alloys for Metered Dose Inhaler Canisters, Aerosol Cans, and Soft Tubes

While aluminum can be produced with up to 99.99% purity, it is both more expensive and mechanically weaker than aluminum alloys. These alloys, containing other elements such as iron, copper, manganese, magnesium, and zinc, offer better rigidity and corrosion resistance. The composition of aluminum alloys is tailored to their application in pharmaceutical primary packaging, including canisters for metered dose inhalers, aerosol cans, soft tubes for topical pharmaceuticals, and foil for solid oral dosage forms. See *Table 2* for the elemental composition of commonly used aluminum alloys for manufacturing canisters, aerosol cans, and soft tubes.

Table 2. Elemental Composition of Representative Examples of Aluminum Alloys Commonly Used for Pharmaceutical Inhalation Canisters, Aerosol Cans, and Soft Tubes (*4–5*)

	Inhalation Canisters		Aerosol Cans	Soft Tubes
Elemental Composition	Aluminum Alloy 1050A (Mass Fraction/%)[a]	Aluminum Alloy 5052 (Mass Fraction/%)[a]	Aluminum Alloy 1050A (Mass Fraction/%)[a]	Aluminum Alloy 1070A (Mass Fraction/%)[a]
Silicon	0.25	0.25	0.25	0.20
Iron	0.40	0.40	0.40	0.25
Copper	0.05	0.10	0.05	0.03
Manganese	0.05	0.10	0.05	0.03
Magnesium	0.05	2.2–2.8	0.05	0.03
Chromium	—	0.15–0.35	—	—
Zinc	0.07	0.10	0.07	0.07
Titanium	0.05	—	0.05	0.03
Other (individual)	0.03	0.05	0.03	0.03
Other (total)	—	0.15	—	—
Aluminum	Remainder	Remainder	Remainder	99.70

[a] Values are maxima unless otherwise stated.

3.3 Aluminum Alloys for Foil

Aluminum foil is widely used for packaging pharmaceutical solid oral dosage forms, primarily because its physical properties make it an effective barrier to bacteria, light, moisture, and oxygen. It also has good mechanical properties of hardness and high tensile strength, combined with a low tear strength, and its smooth surface characteristics enable good printability.

Aluminum foil can be soft-tempered, semi-hard, or hard-tempered, representing the range of the foil's hardness or elasticity. Tempering is designated as the letter O. The foil is strengthened beyond its basic strengths by strain hardening, indicated by H1; the next digit, up to 8, indicates the degree of hardening (e.g., H18). A range of foil thicknesses is available for each alloy, generally between 0.01 mm and 0.2 mm.

Both soft- and hard-tempered foil are used as pharmaceutical primary packaging. Soft-tempered foil is typically used in laminations and in applications where the foil needs to be stretched. All pouching, child-resistant lidding, cold form, and suppository applications use soft foil. Hard foil is used for unsupported push-through lidding applications only. Soft foil can also be used in these applications; however, it isn't as

common because soft foil has higher elongation properties, which are less desirable for push-through lidding.

The elemental composition of the aluminum alloys will vary slightly in the selection and amount of the minor ingredients. Alloys used for soft-tempered foil include 1100, 1200, 1235, 8011, 8021, and 8079 (e.g., 8079-O), while hard-tempered foil alloys are typically 1200-H18. Thus, the alloy selected for a particular application is optimized by both composition and the degree of tempering. Aluminum foil is also used as secondary packaging to provide additional protection to packaged drug products (e.g., aluminum pouches).

See *Table 3* for the elemental composition of representative examples of aluminum alloys commonly used for manufacturing pharmaceutical foil.

Table 3. Elemental Composition of Representative Examples of Aluminum Alloys Commonly Used for Pharmaceutical Foil (*4–5*)

Elemental Composition	Aluminum Alloy 1100 (Mass Fraction/%)[a]	Aluminum Alloy 1200 (Mass Fraction/%)[a]	Aluminum Alloy 1235 (Mass Fraction/%)[a]	Aluminum Alloy 8011 (Mass Fraction/%)[a]	Aluminum Alloy 8021B (Mass Fraction/%)[a]	Aluminum Alloy 8079 (Mass Fraction/%)[a]
Silicon				0.50–0.90	0.40	0.05–0.30
Iron	0.95	1.00	0.65	0.60–1.0	1.1–1.7	0.17–1.3
Copper	0.05–0.20	0.05	0.05	0.10	0.05	0.05
Manganese	0.05	0.05	0.05	0.20	0.03	—
Magnesium	—	—	0.05	0.05	0.01	—
Chromium	—	—	—	0.05	0.03	—
Zinc	0.10	0.10	0.10	0.10	0.05	0.10
Titanium	—	0.05	0.06	0.08	0.05	—
Vanadium	—	—	0.05	—	—	—
Other (each)	0.05	0.05	0.03	0.05	0.03	0.05
Other (total)	0.15	0.15	—	0.15	0.10	0.15
Aluminum	99.00	99.00	99.35	Remainder	97.6	Remainder

[a] Values are maxima unless otherwise stated.

4. METALLIC PACKAGING/DELIVERY SYSTEMS

An understanding of the manufacturing process for the different metallic packaging/delivery systems as well as the alloy elemental composition will assist in determining the appropriate physicochemical tests for a metallic packaging/delivery system. The metallic container is formed and the inner surfaces may be coated with an organic lining to prevent chemical reactions with the drug product and corrosion of the inner layers. Polymers such as acrylics, vinyls, polyesters, and alkyds are used to produce such coatings. Coatings are also applied to the exterior surfaces to allow text to be printed on the exterior surfaces when required.

4.1 Manufacturing Process

4.1.1 STAINLESS STEEL CANISTERS, ALUMINUM CANISTERS, AEROSOL CANS, AND SOFT TUBES

The manufacture of stainless steel canisters, aluminum canisters, aerosol cans, and soft tubes all begin with a circular disc of metal (a blank or slug). In general terms, the manufacturing process produces the required container shape, cleans the container, and adds inner and outer surface coatings.

To manufacture inhalation canisters, a lubricated stainless steel or aluminum blank is formed into a canister by, for example, a deep-draw process. The formed canisters are thoroughly washed to remove lubricants and then dried with heat to remove residual aqueous and nonaqueous solvents. An interior coating (if required) is added to aluminum canisters by methods such as:

- *Anodized coating:* electrochemical process utilizing acids
- *Polymer coating:*
  - Fluorinated ethylene propylene (FEP) using solvents and heating
  - Gas plasma process to produce the treatment without solvents

Aluminum aerosol cans are formed by impact extrusion from a lubricated aluminum slug and then undergo shaping of the base, if required. The formed aerosol can is thoroughly washed and then dried with heat to remove residual aqueous and nonaqueous solvents. An interior coating is added and cured. An external lacquer is then applied, cured, and printing added. Formation of the aerosol can's neck to the desired configuration completes the manufacturing process.

Aluminum soft tubes are extruded from a slug with a lubricant (e.g., zinc stearate), trimmed to size, and then a cap thread is created. The tubes are then annealed (softened) before the addition of an internal coating, which is then cured. An external lacquer is then applied, cured,

and printing added. A cap is attached with an appropriate torque setting. A sealant can be added to assist closure of the fold-end seal to prevent product seepage after filling.

4.1.2 ALUMINUM FOIL

Aluminum foil is manufactured by reducing foil stock to the required thickness in a rolling mill where the sheets are squeezed thinner. Lubricants are added to facilitate the rolling process, and the aluminum may be annealed to maintain its workability. This process produces both bright and matte surface finishes, with the bright finish produced when the foil comes in contact with the work roll surfaces. When two sheets are packed together and rolled simultaneously between the rolls, this produces a matte finish on the two sides touching each other. The foil can then be coated with a wide range of materials, such as polymers and resins, for protective or heat-sealing purposes.

4.2 Surface Coatings

Applying coatings to metal surfaces contacting the drug product is a critical safety criterion for many metallic packaging/delivery systems, even though noncoated aluminum and stainless steel aerosol inhalation canisters are still significantly used. For aerosol inhalation canisters, internal coatings protect against drug product contact with the metal alloy and minimize drug product deposition on the internal surface wall. Commonly used coatings for aerosol inhalation canisters include fluorinated ethylene propylene (FEP) and epoxy phenolic lacquer. Since epoxy phenolic lacquer contains bisphenol A (BPA), it is being replaced by bisphenol A non-intended lacquers (BPA-NI). Similar internal coatings are used for aluminum aerosol cans, while aluminum soft tubes commonly use BPA, BPA-NI, and polyester resins. Polymer coatings can be applied by spraying, or they can be applied electrostatically as powders where the coating material and the canisters are oppositely charged with electricity. This process may also require heating the canisters to 400°. Gas plasma processing is carried out under vacuum using constant or pulsed excitation of gas, either by radio frequency or microwave field at low temperature to produce an energetic plasma that deposits an internal thin treatment layer.

Aluminum foil is typically coated on both sides with a primer, heat seal coating, or extrusion coating as well as possibly an adhesive or another layer of extrusion coating, enabling it to be laminated to film or paper. Numerous coating combinations are available, such as:

- A solvent or water-based primer on one side and a solvent or water-based heat seal coating on the other side
- A primer on one side and an extrusion coating with a resin on the other side; a water-based primer can be used under the resin
- A primer on one side and a solvent or water-based adhesive laminate on the other side
- An adhesive laminate on both sides
- An extrusion coating on one side and a water-based or ethylene acrylic acid copolymer primer extrusion adhesive laminate on the other side
- Extrusion laminates on both sides
- An adhesive laminate on one side and an extrusion coating or laminate on the other side

Quality issues to be addressed for surface coatings include the quality of the coating materials, achievement of 100% coating of the drug product contact surfaces, resistance to coating degradation or loss, the presence of potential extractables and leachables, and pinholes. However, because both sides of the foil are generally coated, as detailed above, any pinholes will be sealed.

5. REFERENCES

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▲ (USP 1-Dec-2026)

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Topic/Question	Contact	Expert Committee
<1662> MATERIALS AND MANUFACTURING PROCESSES FOR METALLIC PACKAGING SYSTEMS	Desmond G. Hunt Principal Scientific Liaison	GCPD2025 Packaging and Distribution

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REFERENCE STANDARDS SUPPORT	RS Technical Services RSTECH@usp.org	GCPD2025 Packaging and Distribution

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