Change to read:

▲⟨661.1⟩ PLASTIC MATERIALS OF CONSTRUCTION

(This chapter will become official on December 1, 2025. Early adoption of the requirements in this chapter and its companion chapter *Plastic Packaging Systems for Pharmaceutical Use* ⟨661.2⟩ **are permitted by USP. When early adoption is not used,** *Plastic Packaging Systems and Their Materials of Construction* ⟨661⟩ **will apply. If** ⟨661.1⟩ **or** ⟨661.2⟩ **are referenced elsewhere in the *USP-NF* prior to December 1, 2025, the standards in** ⟨661⟩ **will apply if early adoption of** ⟨661.1⟩ **or** ⟨661.2⟩ **has not occurred.)**

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INTRODUCTION

The use of well-characterized materials to construct packaging systems is a primary means of ensuring that the packaging system is suited for its intended use. Materials are characterized so that their properties and characteristics can be matched to the performance requirements of the packaging system, thus facilitating the intentional selection of appropriate materials. For the purposes of this chapter, a plastic material of construction is considered to be well characterized for its intended use if the following characteristics have been adequately established: its identity, biological reactivity, general physicochemical properties, and composition (i.e., additives likely to be present). Extractable elements may also be relevant to the selection of a packaging system's materials of construction and therefore a relevant aspect of material characterization. Materials of construction can vary widely in terms of their intentionally and unintentionally added elements and their potential use. Because of this, it is challenging to provide universally effective and efficient tests methodologies, lists of target elements and reporting requirements. It is the material user's responsibility to evaluate the need for extractable elements testing and, if such testing is necessary, to establish and justify the means by which testing is accomplished, taking into account extraction conditions, target elements, and reporting requirements.

SCOPE

The purpose of this chapter is to provide test methods for determining the suitability of plastic materials of construction used in packaging systems for drug products. Individual plastic materials of construction are considered to be well characterized if they meet the requirements in this chapter or are used in a packaging system that meets the requirements in *Plastic Packaging Systems for Pharmaceutical Use* ⟨661.2⟩. The testing and qualification of plastic packaging systems and components for pharmaceutical use are covered in ⟨661.2⟩.

This chapter contains tests, methods, and acceptance criteria for the following materials: cyclic olefins; polyamide 6; polycarbonate; polyethylene; polyethylene terephthalate; polyethylene terephthalate G; poly(ethylene-vinyl acetate); polypropylene; polyvinyl chloride; and polyvinyl chloride, plasticized.

Plastic packaging systems could be constructed from materials that are not specifically addressed in this chapter; such materials of construction are termed "unaddressed materials". For an unaddressed material to be considered compliant with this chapter, it must be characterized and meet acceptance criteria established in ways that are comparable to those used for the materials specified in this chapter. Specifically, the unaddressed material of construction must be identified by appropriate methodology and be tested with consideration of the dosage forms for which it is used (e.g., biological reactivity, physicochemical properties, and plastic additives; see ⟨1661⟩).

Table 1 provides the appropriate application of the chemical and biological tests.

Table 1. Application of Tests

Test Parameter	Oral and Topical Dosage Forms[a]	All Other Dosage Forms
Identification	X	X
Physicochemical		
UV absorbance	X	X
Acidity/alkalinity	X	X
Total organic carbon (TOC)	X	X
Extractable elements	—[b]	—[b]
Plastic additives	—[c]	X
Biological Reactivity		

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Table 1. Application of Tests *(continued)*

Test Parameter	Oral and Topical Dosage Forms[a]	All Other Dosage Forms
In vitro per *Biological Reactivity Tests, In Vitro* ⟨87⟩[d]	—	X

[a] For aqueous-based oral drug products that contain cosolvents (or if, for any reason, it may be expected to extract greater amounts of substances from plastic packaging components than water), additional extractables information may be needed to determine suitability. If additional information is required, perform ▲Plastic additives▲ (RB 1-Mar-2021) tests as directed in this table.

[b] As deemed necessary and appropriate by end-user. See ⟨1661⟩ for additional information.

[c] Provide appropriate reference to the Indirect Food Additive regulations in 21 CFR 174–186, specifically those addressing the purity criteria and limitations pertaining to use.

[d] Biological reactivity testing in support of plastic packaging materials used for final pharmaceutical product packaging/delivery systems (drugs and drug/device combination products) provides baseline information and will often not be sufficient to assess the final suitability for use expectations of regulatory authorities. Thus, it is important to work with the appropriate regulatory authority for guidance regarding a product specific application.

CYCLIC OLEFINS

Identification

- **A. Infrared Spectrophotometry**

Refer to *Mid-Infrared Spectroscopy* ⟨854⟩.

Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.

Sample preparation

Transmission mode: Prepare a specimen of appropriate thickness without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Procedure: Place the mounted specimen sections in the sample compartment of the infrared spectrophotometer or the internal reflectance accessory, and place the assembly in the specimen beam of the infrared spectrophotometer. For internal reflectance, adjust the specimen position and mirrors within the accessory to permit maximum light transmission of the unattenuated reference beam. (For a double-beam instrument, attenuate the reference beam after completing the adjustment in the accessory to permit full-scale deflection during the scanning of the specimen.) Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 µm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Cyclic Olefin Polymer RS or USP Cyclic Olefin Copolymer RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

Physicochemical Tests

Water extraction, Solution S1: Place 25 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 500 mL of *Purified Water*, and boil under reflux conditions for 5 h. Allow to cool, and pass the extracting solution through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric flask and dilute with *Purified Water* to volume; the diluted solution is designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

Absorbance

Refer to *Ultraviolet-Visible Spectroscopy* ⟨857⟩.

Procedure: Determine the spectrum between 220 and 340 nm in *Solution S1*.

Acceptance criteria: NMT 0.2. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Procedure: To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*. Determine the titration volume of 0.01 N sodium hydroxide required to change the color of the indicator to blue. To a separate, 100-mL portion of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01 N hydrochloric acid required to reach the beginning of the color change of the indicator from yellow to orange.

Acceptance criteria: NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is required to reach the beginning of the color change of the indicator from yellow to orange.

Total organic carbon

Procedure: The total organic carbon (TOC) content of *Solution S1* is measured according to the general methodologies outlined in *Total Organic Carbon* ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with

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low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Plastic Additives

Phenolic antioxidants

Solvent mixture: Acetonitrile and tetrahydrofuran (50:50, v/v)

Toluene extraction, Solution S2: Place 2.0 g of the test material in a 250-mL borosilicate glass flask with a ground-glass neck. Add 80 mL of toluene and boil under a reflux condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add, with continued stirring, 120 mL of methanol. Pass the resulting solution through a sintered-glass filter. Rinse the flask and the filter with 25 mL of a mixture of 40 mL of toluene and 60 mL of methanol, add the rinsings to the filtrate, and dilute with the same mixture of solvents to 250 mL to produce *Solution S2*. Prepare a blank solution.

Sample solution S8: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 5.0 mL of the *Solvent mixture* to produce *Sample solution S8.* Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Sample solution S9: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the residue with 5.0 mL of methylene chloride to produce *Sample solution S9*. Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Reference solutions: Of the following reference solutions, prepare only those that are necessary for the analysis of the phenolic antioxidants stated in the composition of the substance to be examined.

Reference solution A: 0.1 mg/mL of USP Butylated Hydroxytoluene RS and 0.24 mg/mL of USP Plastic Additive 1 RS prepared in the *Solvent mixture*

Reference solution B: 0.24 mg/mL of USP Plastic Additive 2 RS and 0.24 mg/mL of USP Plastic Additive 3 RS prepared in the *Solvent mixture*

Reference solution C: 0.24 mg/mL of USP Plastic Additive 4 RS and 0.24 mg/mL of USP Plastic Additive 5 RS prepared in methylene chloride

Reference solution D: 0.1 mg/mL of USP Butylated Hydroxytoluene RS prepared in the *Solvent mixture*

Reference solution E: 0.24 mg/mL of USP Plastic Additive 1 RS prepared in the *Solvent mixture*

Reference solution F: 0.24 mg/mL of USP Plastic Additive 6 RS prepared in the *Solvent mixture*

Reference solution G: 0.24 mg/mL of USP Plastic Additive 2 RS prepared in the *Solvent mixture*

Reference solution H: 0.24 mg/mL of USP Plastic Additive 3 RS prepared in the *Solvent mixture*

Reference solution I: 0.24 mg/mL of USP Plastic Additive 4 RS prepared in methylene chloride

Reference solution J: 0.24 mg/mL of USP Plastic Additive 5 RS prepared in methylene chloride

- **Test A:** If the substance to be examined contains additive butylated hydroxytoluene and/or additive ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate] (USP Plastic Additive 1 RS), then carry out *Test A*.

Mobile phase: Acetonitrile and *Purified Water* (70:30, v/v)

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Liquid Chromatography*.)

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: 30 min

System suitability

Resolution: Minimum 5.0 between the additive USP Butylated Hydroxytoluene RS and USP Plastic Additive 1 RS (ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate]) peaks, *Reference solution A*

Sample solution S8 shows only peaks caused by antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis

Samples: *Sample solution S8*, corresponding blank solution, *Reference solution A*, and *Reference solution D*, *Reference solution E*, or both.

Acceptance criteria: The peak areas of *Sample solution S8*, are less than the corresponding peak areas of *Reference solution D* or *Reference solution E*.

- **Test B:** If the substance to be examined contains one or more of the following antioxidants: pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate] (USP Plastic Additive 2 RS); 2,2′,2″,6,6′,6″-hexa-*tert*-butyl-4,4′,4″-[(2,4,6-trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol (USP Plastic Additive 3 RS); 1,3,5-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-*s*-triazine-2,4,6(1*H*,3*H*,5*H*)-trione (USP Plastic Additive 6 RS), then carry out *Test B*.

Mobile phase: Acetonitrile, tetrahydrofuran, and *Purified Water* (60:30:10, v/v/v)

Chromatographic system: Carry out the test as described in *Test A* with the following modifications.

Detector: UV 280 nm

Flow rate: 1.5 mL/min

Injection volume: 20 µL

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System suitability

Resolution: Minimum 2.0 between USP Plastic Additive 2 RS (pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate]) and USP Plastic Additive 3 RS (2,2′,2″,6,6′,6″-hexa-*tert*-butyl-4,4′,4″-[(2,4,6-trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol peaks), *Reference solution B*

Sample solution S8 shows only peaks caused by antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis

Samples: *Sample solution S8*, corresponding blank solution, *Reference solution B*, and any *Reference solutions* of the antioxidants listed above that are stated in the composition

Acceptance criteria: The peak areas of *Sample solution S8* are less than the corresponding areas of the *Reference solutions* of the antioxidants that are listed above and that are stated in the composition.

- **Test C:** If the substance to be examined contains USP Plastic Additive 4 RS (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate) and/or USP Plastic Additive 5 RS (tris(2,4-di-*tert*-butylphenyl) phosphite), then carry out *Test C*.

Mobile phase: Methanol, 2-propanol, and *Purified Water* (50:45:5, v/v/v)

Chromatographic system: Carry out the test as described in *Test A* with the following modifications.

Detector: UV 280 nm

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Resolution: Minimum 2.0 between USP Plastic Additive 4 RS (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl) propionate) and USP Plastic Additive 5 RS (tris(2,4-di-*tert*-butylphenyl) phosphite) peaks, *Reference solution C*

Sample solution S9 shows only peaks due to antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis

Samples: *Sample solution S9*, corresponding blank solution, *Reference solution C*, and either *Reference solution I* or *Reference solution J*

Acceptance criteria: The peak areas of *Sample solution S9* are less than the corresponding peak areas of *Reference solution I* or *Reference solution J*.

Nonphenolic antioxidants

Methylene chloride, acidified: To 100 mL of methylene chloride add 10 mL of hydrochloric acid, shake, allow to stand, and separate the two layers. Use the lower layer.

Iodine in ethanol detection solution: Dissolve 10 g of iodine in 100 mL of alcohol absolute. Store protected from light.

Sample solution S10: Evaporate 100 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 2 mL of *Methylene chloride, acidified*.

Reference solution M: 6.0 mg/mL of USP Plastic Additive 8 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Reference solution N: 6.0 mg/mL of USP Plastic Additive 9 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Reference solution O: 6.0 mg/mL of USP Plastic Additive 10 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Reference solution P: 6.0 mg/mL of USP Plastic Additive 10 RS, and 6.0 mg/mL of USP Plastic Additive 9 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Mobile phase A: Hexane

Mobile phase B: Methylene chloride

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Thin-Layer Chromatography*.)

Detector: UV 254 nm. Spray with *Iodine in ethanol detection solution* and examine after 10–15 min.

Plate: TLC silica gel GF_{254}

Application volume: 20 µL

Development A: Over a path of 18 cm with *Mobile phase A*; dry in air

Development B: Over a path of 17 cm with *Mobile phase B*; dry in air

System suitability

Resolution: The chromatogram shows two clearly separated spots, *Reference solution P*.

Analysis

Samples: *Sample solution S10* and the reference solutions corresponding to all of the phenolic and nonphenolic antioxidants expected to be present in the test material

Acceptance criteria: Any spots in the chromatogram of *Sample solution S10* are not more intense than the spots in the same positions in the chromatograms of the *Reference solutions*.

Copolymer of dimethyl succinate and (4-hydroxy-2,2,6,6-tetramethylpiperidin-1-yl)ethanol

Solvent mixture: Hexane and anhydrous ethanol (89:11, v/v)

Sample solution S11: Evaporate 25 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the residue with 10 mL of toluene and 10 mL of a 10-g/L solution of tetrabutylammonium hydroxide in a mixture of 35 volumes of toluene and 65 volumes of anhydrous ethanol. Boil under a reflux condenser for 3 h. Allow to cool, and filter if necessary, to produce *Sample solution S11*.

Reference solution Q: 0.6 mg/mL of USP Plastic Additive 11 RS prepared in toluene. Add 1 mL of this solution to 25 mL of the blank solution corresponding to *Solution S2*, and evaporate to dryness under vacuum at 45°. Prepare a blank solution from the blank solution corresponding to *Solution S2*. Dissolve the residue with 10 mL of toluene and

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10 mL of a 10-g/L solution of tetrabutylammonium hydroxide in a mixture of 35 volumes of toluene and 65 volumes of anhydrous ethanol. Boil under a reflux condenser for 3 h. Allow to cool, and filter if necessary.

Mobile phase: Hexane and anhydrous ethanol (89:11, v/v)

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Liquid Chromatography*.)

Detector: UV 227 nm

Column: 4.6-mm × 25-cm; 5-µm packing L8

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Resolution: Minimum of 7 between the peaks of the diol component and the diluents of *Reference solution Q*

Analysis

Samples: *Sample solution S11*, the corresponding blank solution, and *Reference solution Q*

Acceptance criteria: The peak area of the diol component in *Sample solution S11* is less than the corresponding peak areas of *Reference solution Q*.

Amides and stearates

Sample solution: Use *Sample solution S10* described in *Nonphenolic antioxidants*.

Reference solution R: 2.0 mg/mL of USP Stearic Acid RS prepared in methylene chloride

Reference solution S: 2.0 mg/mL of USP Plastic Additive 12 RS prepared in methylene chloride

Reference solution T: 2.0 mg/mL of USP Plastic Additive 13 RS prepared in methylene chloride

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Thin-Layer Chromatography*.)

Plate: TLC silica gel GF_{254}

• **TEST A**

Mobile phase: 2,2,4-trimethylpentane and anhydrous ethanol (75:25, v/v)

Application volume: 10 µL

Development: Over a path of 10 cm with *Mobile phase*; dry in air

Detector: Spray with a 2-g/L solution of 2,6-dichlorophenol-indophenol sodium in dehydrated alcohol and heat in an oven at 120° for a few minutes to intensify the spots.

Analysis

Samples: *Sample solution S10* and *Reference solution R*

Acceptance criteria: Any spot corresponding to additive stearic acid in *Sample solution S10* is identical in position (R_F about 0.5) but is not more intense than the spot in the same position in *Reference solution R*.

• **TEST B**

Mobile phase A: Hexane

Mobile phase B: Methylene chloride and methanol (95:5, v/v)

Application volume: 10 µL

Development A: Over a path of 13 cm with *Mobile phase A*; dry in air

Development B: Over a path of 10 cm with *Mobile phase B*; dry in air

Detector: Spray with a 40-g/L solution of phosphomolybdic acid in alcohol, dehydrated, and heat in an oven at 120° until spots appear.

Analysis

Samples: *Sample solution S10*, *Reference solution S*, and *Reference solution T*

Acceptance criteria: Any spots corresponding to additives oleamide or erucamide in *Sample solution S10* are identical in position (*RF* about 0.2) but are not more intense than the corresponding spots in *Reference solution S* and *Reference solution T*.

POLYAMIDE 6

Identification

[NOTE—The identification of polyamide 6 needs compliance with only one test procedure to be established.]

• **A. INFRARED SPECTROPHOTOMETRY**

Refer to ⟨854⟩.

Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.

Sample preparation

Transmission mode: Prepare a specimen of appropriate thickness without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Procedure: Place the mounted specimen sections in the sample compartment of the infrared spectrophotometer or the internal reflectance accessory, and place the assembly in the specimen beam of the infrared spectrophotometer. For internal reflectance, adjust the specimen position and mirrors within the accessory to permit maximum light transmission of the unattenuated reference beam. (For a double-beam instrument, attenuate the reference beam after

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completing the adjustment in the accessory to permit full-scale deflection during the scanning of the specimen.) Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 µm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Polyamide 6 RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

- **B. Thermal Analysis**

Refer to *Thermal Analysis* ⟨891⟩.

Sample preparation: Place an appropriately sized sample in the test specimen pan. [Note—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]

Procedure: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from room temperature to 500° at a heating rate of about 20°/min. Quickly cool the specimen to room temperature.

Acceptance criteria: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Polyamide 6 RS, and the melting peak temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 8.0°. Note that the results of the DSC analysis are strongly dependent on the amount of plasticizer in the test article.

Physicochemical Tests

Water extraction, Solution S1: Place 25.0 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 500 mL of *Purified Water* and boil under a reflux condenser for 5 h. Allow the solution to cool to ambient temperature, decant and pass the solution through a sintered glass filter. ▲Collect the filtrate in a 500-mL volumetric flask and dilute with *Purified Water* to volume;▲ (RB 1-Mar-2021) the filtered solution is designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

Absorbance

Refer to ⟨857⟩.

Procedure: Determine the spectrum between 220 and 340 nm in *Solution S1*.

Acceptance criteria: NMT 0.25. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Procedure: To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*. Determine the titration volume of 0.01 N sodium hydroxide required to change the color of the indicator to blue. To a separate, 100-mL portion of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01 N hydrochloric acid required to reach the beginning of the color change of the indicator from yellow to orange.

Acceptance criteria: NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to blue. NMT 4.0 mL of 0.01 N hydrochloric acid is required to reach the beginning of the color change of the indicator from yellow to orange.

Total organic carbon

Procedure: The TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Free base functions

Titrant (perchloric acid in phenol): Dissolve approximately 0.72 g (target 0.710–0.7250 g) of perchloric acid in 50 mL of phenol (procured as a viscous liquid).

Phenol extraction, Solution S7: Dissolve 1.0 g of the test material in 50 mL of phenol (procured as a viscous liquid) by heating at 50° for 4 h with constant stirring. This process produces *Solution S7*. Prepare a blank solution.

Procedure: Potentiometrically titrate 50 mL of *Solution S7* with *Titrant*, determining the point of equivalence. Similarly titrate 50 mL of phenol (procured as a viscous liquid) as a blank. The difference in the amount of titrant used is the amount of titrant used for *Solution S7* minus the amount of titrant used for the blank.

Acceptance criteria: The difference between the titration volumes, extract versus extraction blank, is NMT 0.4 mL.

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Related Substances

Caprolactam

Sample solution: Weigh approximately 1.0 g of the test material and place it in a 10-mL volumetric flask, dissolve by adding anhydrous formic acid. Dilute with anhydrous formic acid to volume.

Caprolactam primary solution: Place 125 mg of USP Caprolactam RS in a 50-mL volumetric flask, dissolve by adding anhydrous formic acid. Dilute with anhydrous formic acid to volume. The caprolactam concentration of this primary solution is approximately 2500 mg/L.

Reference solutions: Pipet 0, 2, 4, 6, 8, and 10 mL of the *Caprolactam primary solution* into six 20-mL volumetric flasks. Dilute with anhydrous formic acid to volume. The 6 reference solutions thus obtained (*Reference solution blank* and *Reference solution WS1* through *WS5*) contain, respectively, 0, 250, 500, 750, 1000, and 1250 mg/L of caprolactam.

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Gas Chromatography*.)

Column: 30-m × 0.25-mm; 0.25-µm phase G25

Temperatures

Injection port: 250°

Column: Hold at 160° for 2 min, ramped to 210° at 5°/min, and hold at 210° for 10 min

Detector: Flame ionization detector (FID) 250°

Carrier gas: Helium

Flow rate: 1 mL/min

Injection volume: 1 µL

Injection type: Split ratio, 3:1

Analysis

Conditioning: Inject the *Reference solution blank* into the chromatographic system 3 times.

System suitability: Inject *Reference solution WS4* into the chromatographic system 5 times. The percent relative standard deviation of the peak areas obtained for these injections must be NMT 5%. The symmetry factor for the caprolactam peak obtained for the third injection must be between 0.8 and 1.3.

Rinsing: Inject *Reference solution blank* once.

Calibration, front of bracket: Inject each of the 5 *Reference solutions* once. Construct a linear calibration curve of the peak areas obtained for the *Reference solutions* versus their caprolactam concentrations. The correlation coefficient (*r*) obtained for the best-fit linear regression line must be NLT 0.99.

Rinsing: Inject the *Reference solution blank* once.

Sample: Inject *Sample solution* once. Inject NMT 6 *Sample solutions*.

Rinsing: Inject *Reference solution blank* once.

Calibration, back of bracket: Inject each of the 5 *Reference solutions* once.

Calculations: Construct a linear calibration curve of the peak areas obtained for the *Reference solutions* versus their caprolactam concentrations (both front and back of bracket). The correlation coefficient (*r*) obtained for the best-fit linear regression line must be NLT 0.99. Calculate the amount of caprolactam in the *Sample solution* by putting the peak area obtained for the *Sample solution* into the calibration curve. Calculate the amount of caprolactam in the test material by multiplying this result by a factor of 10 and dividing the product by the weight of the test material in grams, producing a result in weight %.

Acceptance criteria: NMT 1%

POLYCARBONATE

Identification

[NOTE—The identification of polycarbonate needs compliance with only one test procedure to be established.]

• **A. INFRARED SPECTROPHOTOMETRY**

Refer to ⟨854⟩.

Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.

Sample preparation

Transmission mode: Prepare a specimen of appropriate thickness without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Procedure: Prepare a hot-pressed film. Otherwise, dissolve 0.5 g of test material in 10 mL of methylene chloride by boiling under a reflux condenser for 15 min. Place a few drops of the resulting solution on a sodium chloride slide and evaporate the solvent in an oven at 80°. Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 µm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Polycarbonate RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

• **B. THERMAL ANALYSIS**

Refer to ⟨891⟩.

Do Not Official

Sample preparation: Place an appropriately sized sample in the test specimen pan. [NOTE—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]

Procedure: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from –20° to 300° at a heating rate of about 10°/min. Quickly cool the specimen to room temperature.

Acceptance criteria: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Polycarbonate RS, and the melting peak temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 8.0°. Note that the results of the DSC analysis are strongly dependent on the amount of plasticizer in the test article.

Physicochemical Tests

Water extraction, Solution S1: Place 25 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 500 mL of *Purified Water*, and boil under reflux conditions for 5 h. Allow to cool, and pass the extracting solution through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric flask and dilute with *Purified Water* to volume; the diluted solution is designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

Absorbance

Refer to ⟨857⟩.

Procedure: Determine the spectrum between 220 and 340 nm in *Solution S1*.

Acceptance criteria: NMT 0.20. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Total organic carbon

Procedure: The TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Related Substances

Residual solvents

Sample solution: Weigh approximately 1.0 g of the test material and place it in a 20-mL headspace vial. Add 10 mL of *N,N*′-dimethylformamide, cap the vial closed, and sonicate for 4 h. Cool to room temperature. Prepare a sample blank in a similar fashion.

Residual solvents primary solution: Accurately weigh 500 mg each of dichloromethane, toluene, and ethylbenzene and 1250 mg of chlorobenzene into a 50-mL volumetric flask; dissolve and adjust with *N,N*′-dimethylformamide to volume.

Residual solvents stock solution: Transfer 5 mL of the *Residual solvents primary solution* into a 100-mL volumetric flask; adjust with *N,N*′-dimethylformamide to volume. This solution has theoretical concentrations of 500 mg/L for dichloromethane, toluene, and ethylbenzene and 1250 mg/L for chlorobenzene.

Reference solutions: Pipet 0, 2, 3, 4, 5, and 6 mL of the *Residual solvents stock solution* into individual 100-mL volumetric flasks, dilute with *N-N*′-dimethylformamide to volume, and mix well. The 6 reference solutions thus obtained (*Reference solution blank* and *Reference solution WS1* through *WS5*) contain, respectively, 0, 10, 15, 20, 25, and 30 mg/L of dichloromethane, toluene, and ethylbenzene and 0, 25, 37.5, 50, 62.5, and 75 mg/L of chlorobenzene. Transfer 10 mL of the individual reference solution to 20-mL headspace vials and cap the vials closed.

Chromatographic system

(See *Chromatography* ⟨621⟩*, General Procedures, Gas Chromatography*.)

Headspace autosampler

Temperatures

Thermostating: 115°
Needle: 110°
Transfer: 120°

Times

Thermostating: 60 min
Pressurization: 0.5 min
Injection: 0.1 min
Withdrawal: 0.2 min

Carrier gas pressure: 20 psi

Not Official

Column: Stainless steel, 0.32-mm × 30-m, containing stationary phase (0.5 µm) coated with 100% bonded and cross-linked polyethylene glycol; phase G39

Temperatures

Injection port: 140°

Column: Start at 50°, hold for 20 min. Heat to 165° at 6°/min, hold for 20 min.

Detector: FID 250°

Carrier gas: Helium

Flow rate: Adequate to provide a constant pressure of 10 psi

Injection volume: 1 µL

Injection type: Split

Analysis

Conditioning: Inject the *Reference solution blank* 2 times into the chromatographic system.

System suitability: Inject *Reference solution WS3* 5 times into the chromatographic system. Note that one injection is done from each autosampler vial. The %relative standard deviation of the peak areas obtained for each analyte for these injections must be NMT 5%.

Calibration, front of bracket: Inject each of the 5 *Reference solutions* once. Construct a linear calibration curve of the peak areas obtained for the *Reference solutions* versus their analyte concentrations for each analyte. The correlation coefficient (*r*) obtained for the best-fit linear regression line must be NLT 0.99.

Rinsing: Inject the *Reference solution blank* once.

Sample: Inject *Sample solution* once, including the sample blank. Inject NMT 6 *Sample solutions*.

Rinsing: Inject *Reference solution blank* once.

Calibration, back of bracket: Inject each of the 5 *Reference solutions* once.

Calculations: Construct a linear calibration curve of the peak areas obtained for the *Reference solutions* versus their analyte concentrations (using the front and back of the bracket). The correlation coefficient (*r*) obtained for the best-fit linear regression line must be NLT 0.99. Calculate the amount of each analyte in the *Sample solution* by putting the peak area obtained for the *Sample solution* into the calibration curve.

Calculate the amount of each in the test material by multiplying this result by a factor of 10 and dividing the product by the weight of the test material in g, producing a result in µg/g.

$$\text{Analyte (µg/g)} = [\text{analyte in } \textit{Sample solution} \text{ (mg/L)} \times 10]/\text{weight of test material (g)}$$

Acceptance criteria

Methylene chloride: NMT 200 µg/g

Toluene: NMT 200 µg/g

Sum of toluene and ethylbenzene: NMT 200 µg/g

Chlorobenzene: NMT 500 µg/g

Bisphenol A

[NOTE—Bisphenol A is monitored although it is a residual monomer and not an additive.]

Sample solution: Weigh approximately 1.0 g of the test material and place it in a 250-mL round-bottom flask. Add 50 mL of methylene chloride and slightly heat at approximately 35° for 1 h under a reflux condenser to dissolve the test material. Cool the solution to room temperature and slowly add 75 mL of methanol to the room-temperature solution, stirring continuously. Place in a refrigerator for 2 h to cool the resulting solution. Pass the cooled solution through a sintered-glass filter. Wash the round-bottom flask and the filter twice with 15 mL of methanol. Evaporate the filtrate to dryness under vacuum at 45°. Dissolve the residue in 5 mL of methylene chloride. Add 0.5 mL of this solution and 0.5 mL of *N,O*-bis(trimethylsilyl)trifluoroacetamide to a 1.5-mL vial and close the vial immediately. Heat the closed vial at 40° for 2 h and then cool to room temperature. Prepare a sample blank in a similar fashion.

Bisphenol A primary solution: Accurately weigh 20 mg of USP Bisphenol A RS in a 200-mL volumetric flask; dissolve and dilute with methylene chloride to volume. The bisphenol A concentration of this primary solution is approximately 100 mg/L.

Reference solutions: Pipet 0, 5, 10, 20, 30, and 40 mL of the *Bisphenol A primary solution* into six 100-mL volumetric flasks. Dilute with methylene chloride to volume and mix well. The 6 reference solutions thus obtained (*Reference solution blank* and *Reference solution WS1* through *WS5*) contain, respectively, 0, 5, 10, 20, 30, and 40 mg/L of bisphenol A.

Add 0.5 mL each of the *Reference solutions* and 0.5 mL of *N,O*-bis(trimethylsilyl)trifluoroacetamide to separate 1.5-mL vials and close the vials immediately. Heat the closed vials at 40° for 2 h and then cool to room temperature.

Chromatographic system

(See *Chromatography* ⟨621⟩*, General Procedures, Gas Chromatography*.)

Column: Stainless steel, 25-m × 0.25-mm; stationary phase (0.25 µm) coated with 100% dimethylpolysiloxane, phase G38

Temperatures

Injection port: 300°

Column: 250°

Detector: FID 300°

Carrier gas: Helium

Flow rate: Adequate to provide a constant pressure of 13 psi

Injection volume: 2 µL

Injection type: Split

Analysis

Conditioning: Inject the *Reference solution blank* 3 times into the chromatographic system.

Not Official

System suitability: Inject *Reference solution WS3* 5 times into the chromatographic system. The percent relative standard deviation of the peak areas obtained for these injections must be NMT 5%.
Rinsing: Inject the *Reference solution blank* twice.
Calibration, front of bracket: Inject each of the 5 *Reference solutions* once. Construct a linear calibration curve of the peak areas obtained for the *Reference solutions* versus their bisphenol A concentrations. The correlation coefficient (*r*) obtained for the best-fit linear regression line must be NLT 0.98.
Rinsing: Inject the *Reference solution blank* once.
Sample: Inject *Sample solution* once, including the sample blank. Inject NMT 6 *Sample solutions*.
Rinsing: Inject the *Reference solution blank* once.
Calibration, back of bracket: Inject each of the 5 *Reference solutions* once.
Calculations: Construct a linear calibration curve of the peak areas obtained for the *Reference solutions* versus their bisphenol A concentrations (front and back of bracket). The correlation coefficient (*r*) obtained for the best-fit linear regression line must be NLT 0.99. Calculate the amount of bisphenol A in the *Sample solution* by putting the peak area obtained for the *Sample solution* into the calibration curve.
Calculate the amount of bisphenol A in the test material by multiplying this result by a factor of 5 and dividing the product by the weight of the test material in g, producing a result in µg/g.

$$\text{Bisphenol A (µg/g)} = [\text{bisphenol A in } \textit{Sample solution} \text{ (mg/L)} \times 5]/\text{weight of test material (g)}$$

Acceptance criteria: NMT 100 µg/g

POLYETHYLENE

Identification

[NOTE—The identification of low-density polyethylene and high-density polyethylene needs compliance with only one test procedure to be established.]

- **A. INFRARED SPECTROPHOTOMETRY**

Refer to ⟨854⟩.
Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.
Sample preparation
Transmission mode: Prepare a specimen of appropriate thickness (about 250 µm) without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.
Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.
Procedure: Place the mounted specimen sections in the sample compartment of the infrared spectrophotometer or the internal reflectance accessory, and place the assembly in the specimen beam of the infrared spectrophotometer. For internal reflectance, adjust the specimen position and mirrors within the accessory to permit maximum light transmission of the unattenuated reference beam. (For a double-beam instrument, attenuate the reference beam after completing the adjustment in the accessory to permit full-scale deflection during the scanning of the specimen.) Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 µm).
Acceptance criteria
Low-density polyethylene: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Low-Density Polyethylene RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.
High-density polyethylene: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP High-Density Polyethylene RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

- **B. THERMAL ANALYSIS**

Refer to ⟨891⟩.
Sample preparation: Place an appropriately sized sample in the test specimen pan. [NOTE—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]
Procedure: Determine the thermal analysis curve under nitrogen at temperatures between 40° and 200° at a heating rate between 2° and 10°/min, followed by cooling at a rate between 2° and 10°/min, to 40°. Using equipment capable of performing the determinations as described in ⟨891⟩.
Acceptance criteria
Low-density polyethylene: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Low-Density Polyethylene RS, and the melting peak temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 8.0°.

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High-density polyethylene: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP High-Density Polyethylene RS, and the melting peak temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 6.0°.

Physicochemical Tests

Water extraction, Solution S1: Place 25 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 500 mL of *Purified Water*, and boil under reflux conditions for 5 h. Allow to cool, and pass the extracting solution through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric flask and dilute with *Purified Water* to volume; the diluted solution is designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

Absorbance

Refer to ⟨857⟩.

Procedure: Determine the spectrum between 220 and 340 nm in *Solution S1*.

Acceptance criteria: NMT 0.2. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Procedure: To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*. Determine the titration volume of 0.01 N sodium hydroxide required to change the color of the indicator to blue. To a separate, 100-mL portion of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01 N hydrochloric acid required to reach the beginning of the color change of the indicator from yellow to orange.

Acceptance criteria: NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is required to reach the beginning of the color change of the indicator from yellow to orange.

Total organic carbon

Procedure: The TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Plastic Additives

The test results from these analyses are reported.

Phenolic antioxidants

Solvent mixture: Acetonitrile and tetrahydrofuran (50:50, v/v)

Toluene extraction, Solution S2: Place 2.0 g of the test material in a 250-mL borosilicate glass flask with a ground-glass neck. Add 80 mL of toluene and boil under a reflux condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add, with continued stirring, 120 mL of methanol. Pass the resulting solution through a sintered-glass filter. Rinse the flask and the filter with 25 mL of a mixture of 40 mL of toluene and 60 mL of methanol, add the rinsings to the filtrate, and dilute with the same mixture of solvents to 250 mL to produce *Solution S2*. Prepare a blank solution.

Sample solution S8: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 5.0 mL of the *Solvent mixture* to produce *Sample solution S8*. Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Sample solution S9: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the residue with 5.0 mL of methylene chloride to produce *Sample solution S9*. Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Reference solutions: Of the following reference solutions, prepare only those that are necessary for the analysis of the phenolic antioxidants stated in the composition of the substance to be examined.

Reference solution A: 0.1 mg/mL of USP Butylated Hydroxytoluene RS and 0.24 mg/mL of USP Plastic Additive 1 RS prepared in the *Solvent mixture*

Reference solution B: 0.24 mg/mL of USP Plastic Additive 2 RS and 0.24 mg/mL of USP Plastic Additive 3 RS prepared in the *Solvent mixture*

Reference solution C: 0.24 mg/mL of USP Plastic Additive 4 RS and 0.24 mg/mL of USP Plastic Additive 5 RS prepared in methylene chloride

Reference solution D: 0.1 mg/mL of USP Butylated Hydroxytoluene RS prepared in the *Solvent mixture*

Reference solution E: 0.24 mg/mL of USP Plastic Additive 1 RS prepared in the *Solvent mixture*

Reference solution F: 0.24 mg/mL of USP Plastic Additive 6 RS prepared in the *Solvent mixture*

Reference solution G: 0.24 mg/mL of USP Plastic Additive 2 RS prepared in the *Solvent mixture*

Reference solution H: 0.24 mg/mL of USP Plastic Additive 3 RS prepared in the *Solvent mixture*

Do Not Official

Reference solution I: 0.24 mg/mL of USP Plastic Additive 4 RS prepared in methylene chloride
Reference solution J: 0.24 mg/mL of USP Plastic Additive 5 RS prepared in methylene chloride

- **TEST A:** If the substance to be examined contains additive butylated hydroxytoluene and/or additive ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate] (USP Plastic Additive 1 RS), then carry out *Test A*.

Chromatographic system
(See *Chromatography* ⟨621⟩*, General Procedures, Liquid Chromatography*.)
Mobile phase: Acetonitrile and *Purified Water* (70:30, v/v)
Detector: UV 280 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 2 mL/min
Injection volume: 20 µL
Run time: 30 min

System suitability
Resolution: Minimum 5.0 between the additive USP Butylated Hydroxytoluene RS and USP Plastic Additive 1 RS (ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate]) peaks, *Reference solution A*
Sample solution S8 shows only peaks caused by antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis
Samples: *Sample solution S8*, corresponding blank solution, *Reference solution A*, *Reference solution D*, *Reference solution E*, or both

Acceptance criteria: The peak areas of *Sample solution S8* are less than the corresponding peak areas of *Reference solution D* or *Reference solution E*.

- **TEST B:** If the substance to be examined contains one or more of the following antioxidants: pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate (USP Plastic Additive 2 RS); 2,2′,2″,6,6′,6″-hexa-*tert*-butyl-4,4′,4″-[(2,4,6-trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol (USP Plastic Additive 3 RS); 1,3,5-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-*s*-triazine-2,4,6(1*H*,3*H*,5*H*)-trione (USP Plastic Additive 6 RS), then carry out *Test B*.

Mobile phase: Acetonitrile, tetrahydrofuran, and *Purified Water* (60:30:10, v/v/v)
Chromatographic system: Carry out the test as described in *Test A* with the following modifications.
Detector: UV 280 nm
Flow rate: 1.5 mL/min
Injection volume: 20 µL

System suitability
Resolution: Minimum 2.0 between USP Plastic Additive 2 RS (pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate]) and USP Plastic Additive 3 RS (2,2′,2″,6,6′,6″-hexa-*tert*-butyl-4,4′,4″-[(2,4,6-trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol peaks), *Reference solution B*
Sample solution S8 shows only peaks caused by antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis
Samples: *Sample solution S8*, corresponding blank solution, *Reference solution B*, and any *Reference solutions* of the antioxidants listed above that are stated in the composition.

Acceptance criteria: The peak areas of *Sample solution S8* are less than the corresponding areas of the *Reference solutions* of the antioxidants that are listed above and that are stated in the composition.

- **TEST C:** If the substance to be examined contains USP Plastic Additive 4 RS (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate) and/or USP Plastic Additive 5 RS (tris(2,4-di-*tert*-butylphenyl) phosphite), then carry out *Test C*.

Mobile phase: Methanol, 2-propanol, and *Purified Water* (50:45:5, v/v/v)
Chromatographic system: Carry out the test as described in *Test A* with the following modifications.
Detector: UV 280 nm
Flow rate: 1.5 mL/min
Injection volume: 20 µL

System suitability
Resolution: Minimum 2.0 between USP Plastic Additive 4 RS (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl) propionate) and USP Plastic Additive 5 RS (tris(2,4-di-*tert*-butylphenyl) phosphite) peaks, *Reference solution C*
Sample solution S9 shows only peaks caused by antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis
Samples: *Sample solution S9* corresponding blank solution, *Reference solution C*, and either *Reference solution I* or *Reference solution J*

Acceptance criteria: The peak areas of *Sample solution S9* are less than the corresponding peak areas of *Reference solution I* or *Reference solution J*.

Nonphenolic antioxidants
Methylene chloride, acidified: To 100 mL of methylene chloride add 10 mL of hydrochloric acid, shake, allow to stand, and separate the two layers. Use the lower layer.
Iodine in ethanol detection solution: Dissolve 10 g of iodine in 100 mL of alcohol absolute. Store protected from light.
Sample solution S10: Evaporate 100 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 2 mL of *Methylene chloride, acidified*.

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Reference solution M: 6.0 mg/mL of USP Plastic Additive 8 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.
Reference solution N: 6.0 mg/mL of USP Plastic Additive 9 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.
Reference solution O: 6.0 mg/mL of USP Plastic Additive 10 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.
Reference solution P: 6.0 mg/mL of USP Plastic Additive 10 RS, and 6.0 mg/mL of USP Plastic Additive 9 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.
Mobile phase A: Hexane
Mobile phase B: Methylene chloride
Chromatographic system
(See *Chromatography* ⟨621⟩, *General Procedures, Thin-Layer Chromatography*.)
Plate: TLC silica gel GF_{254}
Application volume: 20 µL
Development A: Over a path of 18 cm with *Mobile phase A*; dry in air
Development B: Over a path of 17 cm with *Mobile phase B*; dry in air
Detector: UV 254 nm; spray with *Iodine in ethanol detection solution* and examine after 10–15 min
System suitability
Resolution: The chromatogram shows two clearly separated spots, *Reference solution P*.
Analysis
Samples: *Sample solution S10* and the reference solutions corresponding to all of the phenolic and nonphenolic antioxidants expected to be present in the test material
Acceptance criteria: Any spots in the chromatogram of *Sample solution S10* are not more intense than the spots in the same positions in the chromatograms of the *Reference solutions*.

Amides and stearates
Sample solution: Use *Sample solution S10* described in *Nonphenolic antioxidants*.
Reference solution R: 2.0 mg/mL of USP Stearic Acid RS prepared in methylene chloride
Reference solution S: 2.0 mg/mL of USP Plastic Additive 12 RS prepared in methylene chloride
Reference solution T: 2.0 mg/mL of USP Plastic Additive 13 RS prepared in methylene chloride
Chromatographic system
(See *Chromatography* ⟨621⟩, *General Procedures, Thin-Layer Chromatography*.)
Plate: TLC silica gel GF_{254}

• **TEST A**
Mobile phase: 2,2,4-trimethylpentane and anhydrous ethanol (75:25, v/v)
Application volume: 10 µL
Development: Over a path of 10 cm with *Mobile phase*; dry in air
Detector: Spray with a 2-g/L solution of 2,6-dichlorophenol-indophenol sodium in dehydrated alcohol and heat in an oven at 120° for a few min to intensify the spots.
Analysis
Samples: *Sample solution S10* and *Reference solution R*
Acceptance criteria: Any spot corresponding to additive stearic acid in *Sample solution S10* is identical in position (R_F about 0.5) but is not more intense than the spot in the same position in *Reference solution R*.

• **TEST B**
Mobile phase A: Hexane
Mobile phase B: Methylene chloride and methanol (95:5, v/v)
Application volume: 10 µL
Development A: Over a path of 13 cm with *Mobile phase A*; dry in air
Development B: Over a path of 10 cm with *Mobile phase B*; dry in air
Detector: Spray with a 40-g/L solution of phosphomolybdic acid in alcohol, dehydrated, and heat in an oven at 120° until spots appear.
Analysis
Samples: *Sample solution S10*, *Reference solution S*, and *Reference solution T*
Acceptance criteria: Any spots corresponding to additives oleamide or erucamide in *Sample solution S10* are identical in position (R_F about 0.2) but are not more intense than the corresponding spots in *Reference solution S* and *Reference solution T*.

POLYETHYLENE TEREPHTHALATE AND POLYETHYLENE TEREPHTHALATE G

Identification
[NOTE—The identification of polyethylene terephthalate and polyethylene terephthalate G needs compliance with only one test procedure to be established.]

• **A. INFRARED SPECTROPHOTOMETRY**
Refer to ⟨854⟩.
Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.
Sample preparation
Transmission mode: Prepare a specimen of appropriate thickness without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest

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temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Procedure: Place the mounted specimen sections in the sample compartment of the infrared spectrophotometer or the internal reflectance accessory, and place the assembly in the specimen beam of the infrared spectrophotometer. For internal reflectance, adjust the specimen position and mirrors within the accessory to permit maximum light transmission of the unattenuated reference beam. (For a double-beam instrument, attenuate the reference beam after completing the adjustment in the accessory to permit full-scale deflection during the scanning of the specimen.) Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 µm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Polyethylene Terephthalate RS or USP Polyethylene Terephthalate G RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

• **B. Thermal Analysis**

Refer to ⟨891⟩.

Sample preparation: Place an appropriately sized sample in the test specimen pan. [Note—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]

Procedures

Polyethylene terephthalate: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from room temperature to 280° at a heating rate of about 20°/min. Hold the specimen at 280° for 1 min. Quickly cool the specimen to room temperature and reheat it to 280° at a heating rate of 5°/min.

Polyethylene terephthalate G: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from room temperature to 120° at a heating rate of about 20°/min. Hold the specimen at 120° for 1 min. Quickly cool the specimen to room temperature and reheat it to 120° at a heating rate of 10°/min.

Acceptance criteria

Polyethylene terephthalate: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Polyethylene Terephthalate RS and the melting peak temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 4.0°.

Polyethylene terephthalate G: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Polyethylene Terephthalate G RS. The melting peak temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 6.0°.

Physicochemical Tests

Water extraction, Solution S1: Place 10 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 200 mL of *Purified Water*, and heat at 50° for 5 h. Allow to cool, decant the solution into a 200-mL volumetric flask, and dilute with *Purified Water* to volume; the diluted sample is designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

Alcohol extraction, Solution S5: Place 10 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 100 mL of alcohol, absolute, and heat at 50° for 5 h. Allow to cool and the solids to settle, then decant the solution, producing *Solution S5*. Use *Solution S5* within 4 h of preparation.

Absorbance

Refer to ⟨857⟩.

Procedure: Determine the spectrum between 220 and 340 nm in *Solution S1*. For colored polyethylene terephthalate, determine the spectrum between 400 and 800 nm in *Solution S1*. For colored and noncolored polyethylene terephthalate, determine the spectrum between 400 and 800 nm in *Solution S5*.

Acceptance criteria: NMT 0.2 for *Solution S1* and 0.05 for *Solution S5*. In addition, for colored polyethylene terephthalate, maximum absorbance between 400 and 800 nm is 0.05 for *Solution S1*. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Procedure: To 50 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*. Determine the titration volume of 0.01 N sodium hydroxide required to change the color of the indicator to blue. To a separate, 50-mL portion of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01 N hydrochloric acid required to reach the beginning of the color change of the indicator from yellow to orange.

Acceptance criteria: NMT 0.5 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to blue. NMT 0.5 mL of 0.01 N hydrochloric acid is required to reach the beginning of the color change of the indicator from yellow to orange.

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Total organic carbon

Procedure: The TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

POLY(ETHYLENE-VINYL ACETATE)

Identification

[NOTE—The identification of poly(ethylene-vinyl acetate) needs compliance with only one test procedure to be established.]

• **A. INFRARED SPECTROPHOTOMETRY**

Refer to ⟨854⟩.

Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.

Sample preparation

Transmission mode: Prepare a specimen of appropriate thickness without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Procedure: Place the mounted specimen sections in the sample compartment of the infrared spectrophotometer or the internal reflectance accessory, and place the assembly in the specimen beam of the infrared spectrophotometer. For internal reflectance, adjust the specimen position and mirrors within the accessory to permit maximum light transmission of the unattenuated reference beam. (For a double-beam instrument, attenuate the reference beam after completing the adjustment in the accessory to permit full-scale deflection during the scanning of the specimen.) Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 μm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Poly(ethylene-vinyl acetate) RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

• **B. THERMAL ANALYSIS**

Refer to ⟨891⟩.

Sample preparation: Place an appropriately sized sample in the test specimen pan. [NOTE—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]

Procedure: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from –50° to 120° at a heating rate of about 10°/min. Quickly cool the specimen to room temperature.

Acceptance criteria: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Poly(ethylene-vinyl acetate) RS, and the melting point temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 6.0°.

Physicochemical Tests

Water extraction, Solution S1: Place 25 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 500 mL of *Purified Water*, and boil under reflux conditions for 5 h. Allow to cool, and pass the extracting solution through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric flask and dilute with *Purified Water* to volume; the diluted solution is designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

Absorbance

Refer to ⟨857⟩.

Procedure: Determine the spectrum between 220 and 340 nm in *Solution S1*.

Acceptance criteria: NMT 0.2. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

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Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Procedure: To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*. Determine the titration volume of 0.01 N sodium hydroxide required to change the color of the indicator to blue. To a separate, 100-mL portion of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01 N hydrochloric acid required to reach the beginning of the color change of the indicator from yellow to orange.

Acceptance criteria: NMT 1.0 mL of 0.01 N hydrochloric acid is required to reach the beginning of the color change of the indicator from yellow to orange.

Total organic carbon

Procedure: The TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis

Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Plastic Additives

The test results from these analyses are reported.

Phenolic antioxidants

Solvent mixture: Acetonitrile and tetrahydrofuran (50:50, v/v)

Toluene extraction, Solution S2: Place 2.0 g of the test material in a 250-mL borosilicate glass flask with a ground-glass neck. Add 80 mL of toluene and boil under a reflux condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add, with continued stirring, 120 mL of methanol. Pass the resulting solution through a sintered-glass filter. Rinse the flask and the filter with 25 mL of a mixture of 40 mL of toluene and 60 mL of methanol, add the rinsings to the filtrate, and dilute to 250 mL with the same mixture of solvents to produce *Solution S2*. Prepare a blank solution.

Sample solution S12: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 5.0 mL of the *Solvent mixture* to produce *Sample solution S12*. Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Sample solution S13: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the residue with 5.0 mL of methylene chloride to produce *Sample solution S13*. Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Reference solutions

Of the following reference solutions, prepare only those that are necessary for the analysis of the phenolic antioxidants stated in the composition of the substance to be examined.

Reference solution K: 0.1 mg/mL of USP Butylated Hydroxytoluene RS, 0.16 mg/mL of USP Plastic Additive 2 RS, 0.16 mg/mL of USP Plastic Additive 3 RS, and 0.16 mg/mL of USP Plastic Additive 4 RS prepared in the *Solvent mixture*

Reference solution L: 0.16 mg/mL of USP Plastic Additive 4 RS and 0.16 mg/mL of USP Plastic Additive 5 RS prepared in methylene chloride

• **TEST A**

Mobile phase: Tetrahydrofuran, acetonitrile, and *Purified Water* (30:60:10, v/v)

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Liquid Chromatography*.)

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: 30 min

System suitability

Resolution: Minimum 2.0 between USP Plastic Additive 2 RS and USP Plastic Additive 3 RS, *Reference solution K*

Column efficiency: Minimum 2500 theoretical plates, calculated for USP Butylated Hydroxytoluene RS, *Reference solution K*

Analysis

Samples: *Sample solution S12*, corresponding blank solution, and *Reference solution K*

Acceptance criteria: *Sample solution S12* shows only peaks caused by antioxidants in *Reference solution K* and minor peaks that also correspond to the blank solution. The peak areas of *Sample solution S12* are less than the corresponding peak areas of *Reference solution K*.

• **TEST B:** If the chromatogram obtained via *Test A* for *Sample solution S12* shows a peak with the same retention time as the last antioxidant eluted from *Reference solution K*, then carry out *Test B*.

Mobile phase: 2-propanol, methanol, and *Purified Water* (45:50:5, v/v/v)

Chromatographic system: Carry out the test as described in *Test A* with the following modifications.

Detector: UV 280 nm

Flow rate: 1.5 mL/min

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Injection volume: 20 µL

System suitability

Resolution: Minimum of 2.0 between USP Plastic Additive 4 RS and USP Plastic Additive 5 RS, *Reference solution L*

Analysis

Samples: *Sample solution S13*, corresponding blank solution, and *Reference solution L*.

Acceptance criteria: *Sample solution S13* shows only peaks caused by antioxidants in *Reference solution L* and minor peaks that also correspond to the blank solution. The peak areas of *Sample solution S13* are less than the corresponding peak areas of *Reference solution L*.

Amides and stearic acid

Sample solution S14: Evaporate 100 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 2 mL of acidified methylene chloride to produce *Sample solution S14*.

Reference solution R: 2.0 mg/mL of USP Stearic Acid RS prepared in methylene chloride

Reference solution S: 0.8 mg/mL of USP Plastic Additive 12 RS prepared in methylene chloride

Reference solution T: 0.8 mg/mL of USP Plastic Additive 13 RS prepared in methylene chloride

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Plate: TLC silica gel GF_{254}

• **TEST A**

Mobile phase: Anhydrous ethanol and trimethylpentane (25:75, v/v)

Application volume: 10 µL

Development: Over a path of 10 cm with *Mobile phase*; dry in air

Detector: Spray with a 2-g/L solution of 2,6-dichlorophenol-indophenol sodium in dehydrated alcohol and heat in an oven at 120° for a few minutes to intensify the spots.

Analysis

Samples: *Sample solution S14* and *Reference solution R*

Acceptance criteria: Any spot corresponding to additive stearic acid in *Sample solution S14* is identical in position and is not more intense than the spot in the same position in *Reference solution R*.

• **TEST B**

Chromatographic system: (See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Plate: TLC silica gel GF_{254}

Mobile phase A: Hexane

Mobile phase B: Methylene chloride and methanol (95:5, v/v)

Application: 10 µL

Development A: Over a path of 13 cm with *Mobile phase A*; dry in air

Development B: Over a path of 10 cm with *Mobile phase B*; dry in air

Detector: Spray with a 40-g/L solution of phosphomolybdic acid in alcohol, dehydrated, and heat in an oven at 120° until spots appear.

Analysis

Samples: *Sample solution S14*, *Reference solution S*, and *Reference solution T*.

Acceptance criteria: Any spots corresponding to additives oleamide or erucamide in *Sample solution S14* are identical in position but are not more intense than the corresponding spots in *Reference solution S* and *Reference solution T*.

Related Substances

Content of vinyl acetate

Alcoholic potassium hydroxide: Dissolve 6.6 g of potassium hydroxide in 50 mL of *Purified Water* and dilute with alcohol, dehydrated to 1000 mL.

Sample solution: Place 0.25–1.0 g of the test material into a 300-mL conical flask containing a magnetic stirrer. Prepare an extraction blank starting with an otherwise empty 300-mL conical flask. Add 40 mL of xylene and boil under a reflux condenser with stirring for 4 h. After heating, continue stirring, allowing the solution to cool to the point that precipitation starts. Slowly add 25 mL of alcoholic potassium hydroxide. Boil again under a reflux condenser for 3 h with continued stirring. While stirring, allow the solution to cool, rinse the condenser with 50 mL of water, and add 30 mL of 0.05 M sulfuric acid to the flask. Transfer the contents of the flask to a 400-mL beaker, rinsing the flask with the following:

- 2 quantities, 50 mL each, of a 200-g/L solution of anhydrous sodium sulfate
- 3 quantities, 20 mL each, of water

Add the rinsings to the beaker.

Procedure: Titrate the excess sulfuric acid in *Sample solution* with 0.1 M sodium hydroxide, determining the endpoint potentiometrically. Carry out a titration of the extraction blank.

Calculation: Determine the amount of titrant (mL) required by subtracting the titrant volume used for the extraction blank (mL) from the titrant volume used for the extract (mL). Determine the amount of vinyl acetate by multiplying the volume of titrant required by the quantity (8.609 mg/mL). The content of vinyl acetate is calculated as:

$$\text{Content of vinyl acetate (weight \%)} = [\text{amount of vinyl acetate (mg)}/\text{weight of material extracted (g)}]/10$$

Acceptance criteria: NMT 25% by weight

POLYPROPYLENE

Identification

[NOTE—The identification of polypropylene needs compliance with only one test procedure to be established.]

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- **A. Infrared Spectrophotometry**

Refer to ⟨854⟩.

Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.

Sample preparation

Transmission mode: Prepare a specimen of appropriate thickness (about 100 µm) without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Procedure: Place the mounted specimen sections in the sample compartment of the infrared spectrophotometer or the internal reflectance accessory, and place the assembly in the specimen beam of the infrared spectrophotometer. For internal reflectance, adjust the specimen position and mirrors within the accessory to permit maximum light transmission of the unattenuated reference beam. (For a double-beam instrument, attenuate the reference beam after completing the adjustment in the accessory to permit full-scale deflection during the scanning of the specimen.) Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 µm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of the USP Homopolymer Polypropylene RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

- **B. Thermal Analysis**

Refer to ⟨891⟩.

Sample preparation: Place an appropriately sized sample in the test specimen pan. [Note—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]]

Procedure: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from ambient to 30° above the melting point. Maintain the temperature for 10 min, then cool to 50° below the peak crystallization temperature at a rate of 10°–20°/min.

Acceptance criteria: The melting peak temperature in the thermal analysis curve does not differ from that of USP Homopolymer Polypropylene RS by more than 12.0°.

Physicochemical Tests

Water extraction, Solution S1: Place 25 g of the test material in a borosilicate glass flask with a ground-glass neck. Add 500 mL of *Purified Water*, and boil under reflux conditions for 5 h. Allow to cool, and pass the extracting solution through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric flask and dilute with *Purified Water* to volume; the diluted solution is designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

Absorbance

Refer to ⟨857⟩.

Procedure: Determine the spectrum between 220 and 340 nm in *Solution S1*.

Acceptance criteria: NMT 0.2. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Procedure: To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*. Determine the titration volume of 0.01 N sodium hydroxide required to change the color of the indicator to blue. To a separate, 100-mL portion of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01 N hydrochloric acid required to reach the beginning of the color change of the indicator from yellow to orange.

Acceptance criteria: NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is required to reach the beginning of the color change of the indicator from yellow to orange.

Total organic carbon

Procedure: The total organic carbon TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

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Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Plastic Additives

The test results from these analyses are reported.

Phenolic antioxidants

Solvent mixture: Acetonitrile and tetrahydrofuran (50:50, v/v)

Toluene extraction, Solution S2: Place 2.0 g of the test material in a 250-mL borosilicate glass flask with a ground-glass neck. Add 80 mL of toluene and boil under a reflux condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add, with continued stirring, 120 mL of methanol. Pass the resulting solution through a sintered-glass filter. Rinse the flask and the filter with 25 mL of a mixture of 40 mL of toluene and 60 mL of methanol, add the rinsings to the filtrate, and dilute with the same mixture of solvents to 250 mL to produce *Solution S2*. Prepare a blank solution.

Sample solution S8: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 5.0 mL of the *Solvent mixture* to produce *Sample solution S8.* Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Sample solution S9: Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the residue with 5.0 mL of methylene chloride to produce *Sample solution S9.* Prepare a blank solution from the blank solution corresponding to *Solution S2*.

Reference solutions: Of the following reference solutions, prepare only those that are necessary for the analysis of the phenolic antioxidants stated in the composition of the substance to be examined.

Reference solution A: 0.1 mg/mL of USP Butylated Hydroxytoluene RS and 0.24 mg/mL of USP Plastic Additive 1 RS prepared in the *Solvent mixture*

Reference solution B: 0.24 mg/mL of USP Plastic Additive 2 RS and 0.24 mg/mL of USP Plastic Additive 3 RS prepared in the *Solvent mixture*

Reference solution C: 0.24 mg/mL of USP Plastic Additive 4 RS and 0.24 mg/mL of USP Plastic Additive 5 RS prepared in methylene chloride

Reference solution D: 0.1 mg/mL of USP Butylated Hydroxytoluene RS prepared in the *Solvent mixture*

Reference solution E: 0.24 mg/mL of USP Plastic Additive 1 RS prepared in the *Solvent mixture*

Reference solution F: 0.24 mg/mL of USP Plastic Additive 6 RS prepared in the *Solvent mixture*

Reference solution G: 0.24 mg/mL of USP Plastic Additive 2 RS prepared in the *Solvent mixture*

Reference solution H: 0.24 mg/mL of USP Plastic Additive 3 RS prepared in the *Solvent mixture*

Reference solution I: 0.24 mg/mL of USP Plastic Additive 4 RS prepared in methylene chloride

Reference solution J: 0.24 mg/mL of USP Plastic Additive 5 RS prepared in methylene chloride

- **Test A:** If the substance to be examined contains additive butylated hydroxytoluene and/or additive ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate] (USP Plastic Additive 1 RS),then carry out *Test A*.

Mobile phase: Acetonitrile and *Purified Water* (70:30, v/v)

Chromatographic system

(See *Chromatography* ⟨621⟩*, General Procedures, Liquid Chromatography*.)

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: 30 min

System suitability

Resolution: Minimum 5.0 between the additive butylated hydroxytoluene and USP Plastic Additive 1 RS (ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate]) peaks, *Reference solution A*

Sample solution S8 shows only peaks caused by antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis

Samples: *Sample solution S8*, corresponding blank solution, *Reference solution A*, and *Reference solution D*, *Reference solution E*, or both

Acceptance criteria: The peak areas of *Sample solution S8* are less than the corresponding peak areas of *Reference solution D* or *Reference solution E*.

- **Test B:** If the substance to be examined contains one or more of the following antioxidants: pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate] (USP Plastic Additive 2 RS); 2,2′,2″,6,6′,6″-hexa-*tert*-butyl-4,4′,4″-[(2,4,6-trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol (USP Plastic Additive 3 RS); 1,3,5-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-*s*-triazine-2,4,6(1*H*,3*H*,5*H*)-trione (USP Plastic Additive 6 RS), then carry out *Test B*.

Mobile phase: Acetonitrile, tetrahydrofuran, and *Purified Water* (60:30:10, v/v/v)

Chromatographic system: Carry out the test as described in *Test A* with the following modifications.

Detector: UV 280 nm

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Resolution: Minimum 2.0 between USP Plastic Additive 2 RS (pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate]) and USP Plastic Additive 3 RS (2,2′,2″,6,6′,6″-hexa-*tert*-butyl-4,4′,4″-[(2,4,6-trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol peaks), *Reference solution B*

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Sample solution S8 shows only peaks caused by antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis

Samples: *Sample solution S8*, corresponding blank solution, *Reference solution B*, and any *Reference solutions* of the antioxidants listed above that are stated in the composition

Acceptance criteria: The peak areas of *Sample solution S8* are less than the corresponding areas of the *Reference solutions* of the antioxidants that are listed above and that are stated in the composition.

- **TEST C:** If the substance to be examined contains USP Plastic Additive 4 RS (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate) and/or USP Plastic Additive 5 RS (tris(2,4-di-*tert*-butylphenyl) phosphite), then carry out *Test C*.

Mobile phase: Methanol, 2-propanol, and *Purified Water* (50:45:5, v/v/v)

Chromatographic system: Carry out the test as described in *Test A* with the following modifications.

Detector: UV 280 nm

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Resolution: Minimum 2.0 between USP Plastic Additive 4 RS (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl) propionate) and USP Plastic Additive 5 RS (tris(2,4-di-*tert*-butylphenyl) phosphite) peaks, *Reference solution C*

Sample solution S9 shows only peaks due to antioxidants stated in the composition and minor peaks that also correspond to the blank solution.

Analysis

Samples: *Sample solution S9*, corresponding blank solution, *Reference solution C*, and either *Reference solution I* or *Reference solution J*

Acceptance criteria: The peak areas of *Sample solution S9* are less than the corresponding peak areas of *Reference solution I* or *Reference solution J*.

Nonphenolic antioxidants

Methylene chloride, acidified: To 100 mL of methylene chloride add 10 mL of hydrochloric acid, shake, allow to stand, and separate the two layers. Use the lower layer.

Iodine in ethanol detection solution: Dissolve 10 g of iodine in 100 mL of alcohol absolute. Store protected from light.

Sample solution S10: Evaporate 100 mL of *Solution S2* to dryness under vacuum at 45°. Dissolve the resulting residue with 2 mL of *Methylene chloride, acidified*.

Reference solution M: 6.0 mg/mL of USP Plastic Additive 8 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Reference solution N: 6.0 mg/mL of USP Plastic Additive 9 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Reference solution O: 6.0 mg/mL of USP Plastic Additive 10 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Reference solution P: 6.0 mg/mL of USP Plastic Additive 10 RS, and 6.0 mg/mL of USP Plastic Additive 9 RS prepared in methylene chloride. Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Thin-Layer Chromatography*.)

Plate: TLC silica gel GF_{254}

Mobile phase A: Hexane

Mobile phase B: Methylene chloride

Application volume: 20 µL

Development A: Over a path of 18 cm with *Mobile phase A*; dry in air

Development B: Over a path of 17 cm with *Mobile phase B*; dry in air

Detector: UV 254 nm. Spray with *Iodine in ethanol detection solution* and examine after 10–15 min.

System suitability

Resolution: The chromatogram shows two clearly separated spots, *Reference solution P*.

Analysis

Samples: *Sample solution S10* and the reference solutions corresponding to all of the phenolic and nonphenolic antioxidants expected to be present in the test material

Acceptance criteria: Any spots in the chromatogram of *Sample solution S10* are not more intense than the spots in the same positions in the chromatograms of the *Reference solutions*.

Amides and stearates

Sample solution: Use *Sample solution S10* described in *Nonphenolic antioxidants*.

Reference solution R: 2.0 mg/mL of USP Stearic Acid RS prepared in methylene chloride

Reference solution S: 2.0 mg/mL of USP Plastic Additive 12 RS prepared in methylene chloride

Reference solution T: 2.0 mg/mL of USP Plastic Additive 13 RS prepared in methylene chloride

Chromatographic system

(See *Chromatography* ⟨621⟩, *General Procedures, Thin-Layer Chromatography*.)

Plate: TLC silica gel GF_{254}

- **TEST A**

Mobile phase: 2,2,4-trimethylpentane and anhydrous ethanol (75:25, v/v)

Application volume: 10 µL

Development: Over a path of 10 cm with *Mobile phase*; dry in air

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Detector: Spray with a 2-g/L solution of 2,6-dichlorophenol-indophenol sodium in dehydrated alcohol and heat in an oven at 120° for a few minutes to intensify the spots.

Analysis

Samples: *Sample solution S10* and *Reference solution R*

Acceptance criteria: Any spot corresponding to additive stearic acid in *Sample solution S10* is identical in position (R_F about 0.5) but is not more intense than the spot in the same position in *Reference solution R*.

• **TEST B**

Mobile phase A: Hexane

Mobile phase B: Methylene chloride and methanol (95:5, v/v)

Application volume: 10 µL

Development A: Over a path of 13 cm with *Mobile phase A*; dry in air

Development B: Over a path of 10 cm with *Mobile phase B*; dry in air

Detector: Spray with a 40-g/L solution of phosphomolybdic acid in alcohol, dehydrated, and heat in an oven at 120° until spots appear.

Analysis

Samples: *Sample solution S10*, *Reference solution S*, and *Reference solution T*

Acceptance criteria: Any spots corresponding to additives oleamide or erucamide in *Sample solution S10* are identical in position (R_F about 0.2) but are not more intense than the corresponding spots in *Reference solution S* and *Reference solution T*.

POLYVINYL CHLORIDE

Identification

[NOTE—The identification of polyvinyl chloride needs compliance with only one test procedure to be established]

• **A. INFRARED SPECTROPHOTOMETRY**

Refer to ⟨854⟩.

Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.

Sample preparation

Transmission mode: Prepare a specimen of appropriate thickness without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Tetrahydrofuran extraction, Solution S6: Dissolve 5.0 g of the test material in 80 mL of tetrahydrofuran and dilute to a volume of 100 mL with the same solvent. Filter if necessary; the solution may remain opaque. Slowly and dropwise add 70 mL of ethanol to 20 mL of this solution. Cool the mixture in ice for 1 h. Filter or centrifuge the mixture, collecting residue A. Wash residue A with ethanol. Collect the washings and add them to the solution remaining after filtration or centrifugation. Transfer the solution to a 100-mL volumetric flask and dilute with ethanol to volume. This process produces *Solution S6*. Prepare a blank solution.

Procedure: Dissolve residue A from *Solution S6* in 5 mL of tetrahydrofuran. Apply a few drops of this solution to a sodium chloride plate and evaporate to dryness in an oven at 100°–105°. Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 µm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Polyvinyl Chloride RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

• **B. THERMAL ANALYSIS**

Refer to ⟨891⟩.

Sample preparation: Place an appropriately sized sample in the test specimen pan. [NOTE—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]

Procedure: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from –20° to 120° at a heating rate of about 10°/min. Quickly cool the specimen to room temperature.

Acceptance criteria: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Polyvinyl Chloride RS, and the melting peak temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS by more than 8.0°. Note that the results of the DSC analysis are strongly dependent on the amount of plasticizer in the test article.

Physicochemical Tests

Water extraction, Solution S1: Place 25 g of the test material into a borosilicate glass flask. Add 500 mL of *Purified Water*, cover the flask's neck with aluminum foil or a borosilicate beaker, and heat in an autoclave at 121 ± 2° for 20 min. Allow the solution to cool and the solids to settle, decant the solution into a 500-mL volumetric flask, and dilute with *Purified Water* to volume; the diluted solution is designated *Solution S1*. ▲Use *Solution S1* within 4 h of preparation.▲ (RB 1-Mar-2021)

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Absorbance

Refer to ⟨857⟩.

Procedures

Solution S1: Evaporate 100 mL of *Solution S1* to dryness. Dissolve the residue in 5 mL of hexane. If necessary, pass through a filter that has been previously rinsed with hexane. Determine the spectrum between 250 and 330 nm in the dissolved residue.

Solution S6: If the polyvinyl chloride contains 1-phenyleicosane-1,3-dione and is used as a container for dry dosage forms for oral administration, dilute *Solution S6* (1 in 10) with ethanol prior to measurement. In all other situations, analyze *Solution S6* with no further preparation. Determine the spectrum between 250 and 330 nm in the dissolved residue.

Acceptance criteria

Solution S1: NMT 0.25 for containers for non-injectable aqueous solutions. NMT 0.30 for containers for dry dosage forms for oral administration.

Solution S6: NMT 0.2 for tin-stabilized materials used as containers for non-injectable aqueous solutions. NMT 0.4 for other materials used as containers for non-injectable aqueous solutions. NMT 1.0 for materials that do not contain 1-phenyleicosane-1,3-dione used as containers for dry dosage forms for oral administration. NMT 0.4 for materials containing 1-phenyleicosane-1,3-dione used as containers for dry dosage forms for oral administration.

Total organic carbon

Procedure: The TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

Acceptance criteria: NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Plastic Additives and Stabilizers: The supplier of the material must be able to provide sufficient compositional information to establish whether the material meets the acceptance criteria for additives and stabilizers.

Plastic additives

Epoxidized soya oil of which the oxiran oxygen content is 6%–8% and the iodine value is NMT 6: For tin-stabilized materials, NMT 2%. For non-tin-stabilized materials, NMT 3%.

Calcium, magnesium, or zinc salts for aliphatic fatty acids with more than seven carbon atoms: NMT 1.5% of one salt or NMT 1.5% of a mixture of salts

Lubricants: For individual lubricants: waxes, NMT 4%; liquid paraffin, NMT 1.5%; hydrogenated oils or esters of aliphatic fatty acids, NMT 2%. Total lubricants: NMT 4%.

Macrogol esters: NMT 1.5%

Sorbitol: NMT 1.5%

2,4-Dinonylphenyl phosphite or di(4-nonylphenyl) phosphite or tris(nonylphenyl) phosphite: NMT 1%

Calcium carbonate: For materials used for containers for dry dosage forms for oral administration, NMT 1%

Silica: For materials used for containers for dry dosage forms for oral administration, NMT 1%

Colorants: May contain a colorant or pigment or may be opacified by titanium dioxide

Stabilizers

They may contain one of the following groups of stabilizers (where isooctyl is, for example, 2-ethylhexyl).

Tin as di(isooctyl) 2,2′-[(dioctylstannylene)bis(thio)]-diacetate containing about 27% of tri(isooctyl)2,2′,2″-[(monooctylstannylidyne)tris(thio) triacetate: NMT 0.25%

Tin as a mixture containing NMT 76% of di(isooctyl) 2,2′-[(dioctylstannylene)bis(thio)]-diacetate and NMT 85% of tri(isooctyl)2,2′,2″-[(monooctylstannylidyne)tris(thio) triacetate: NMT 0.25%

1-Phenyleicosane-1,3-dione (benzoylstearoylmethane): NMT 1%

Tin in tin-stabilized materials

Reference solution U: 0.81 mg/mL of USP Plastic Additive 18 RS prepared in tetrahydrofuran is diluted from 20 to 100 mL with ethanol.

Standard solution: Add 0.1 mL of *Reference solution U* to a test tube. Add 0.05 mL of 1 M hydrochloric acid, 0.5 mL of potassium iodide solution, and 5 mL of ethanol to the test tube. Mix thoroughly and wait for 5 min. Add 9 mL of water and 0.1 mL of a 5-g/L solution of sodium sulfite and mix thoroughly. Add 1.5 mL of dithizone solution freshly diluted 100-fold with methylene chloride, shake for 15 s, and allow to stand for 2 min.

Sample solution: Take 0.1 mL of *Solution S6* through the same procedure as the 0.1 mL of *Reference solution U*.

Analysis

Samples: *Standard solution* and *Sample solution* Compare the violet color in the lower layer of the *Sample solution* to the violet color in the lower layer of the *Standard solution*.

Acceptance criteria: NMT 0.25 weight %. The color in the *Sample solution* should not be as intense as the color in the *Standard solution*.

Tin in non-tin-stabilized materials

Standard solution: Take 0.05 mL of *Reference solution U* through the same procedure as the 0.1 mL of *Solution S6*.

Sample solution: Add 5 mL of *Solution S6* to a test tube. Add 0.05 mL of 1 M hydrochloric acid, 0.5 mL of potassium iodide solution, and 5 mL of ethanol to the test tube. Mix thoroughly and wait for 5 min. Add 9 mL of water and 0.1 mL of a 5-g/L solution of sodium sulfite and mix thoroughly. If the solution is not colorless, add the sodium

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sulfite in 0.05-mL fractions. Add 1.5 mL of dithizone solution freshly diluted 100-fold with methylene chloride, shake for 15 s and allow to stand for 2 min.

Analysis

Samples: *Standard solution* and *Sample solution*

Compare the violet color in the lower layer of the *Sample solution* to the violet color in the lower layer of the *Standard solution*.

Acceptance criteria: NMT 25 µg/g (ppm). The color in the *Sample solution* should not be as intense as the color in the *Standard solution*.

Related Substances

Vinyl chloride

Internal standard solution: Using a microsyringe, inject 10 µL of ethyl ether into 20.0 mL of *N,N*-dimethylacetamide, immersing the tip of the needle in the solvent. Immediately before use, dilute the solution with *N,N*-dimethylacetamide to 1000 times its volume.

Sample solution: Place 1.0 g of the test material in a 50-mL vial, and add 10.0 mL of the *Internal standard solution*. Close the vial, and secure with a stopper. Shake, avoiding contact between the stopper and the liquid. Place the vial in a water bath at 60 ± 1° for 2 h.

Vinyl chloride primary solution: [NOTE—Prepare under a ventilated hood.] Place 50.0 mL of *N,N*-dimethylacetamide in a 50-mL vial, stopper the vial, secure the stopper, and weigh to the nearest 0.1 mg. Fill a 50-mL polyethylene or polypropylene syringe with gaseous vinyl chloride, allow the gas to remain in contact with the syringe for about 3 min, empty the syringe, and fill again with 50 mL of gaseous vinyl chloride. Fit a hypodermic needle to the syringe, and reduce the volume of gas in the syringe from 50 to 25 mL. Inject the remaining 25 mL of vinyl chloride slowly into the vial, shaking gently and avoiding contact between the liquid and the needle. Weigh the vial again; the increase in mass is about 60 mg (1 µL of the solution obtained contains about 1.2 µg of vinyl chloride). Allow to stand for 2 h. Store the primary solution in a refrigerator.

Vinyl chloride standard solution: To 1 volume of the *Vinyl chloride primary solution* add 3 volumes of *N,N*-dimethylacetamide.

Reference solutions: Place 10.0 mL of the *Internal standard solution* in each of six 50-mL vials. Close the vials, and secure the stoppers. Inject 1, 2, 3, 5, and 10 µL, respectively, of the *Vinyl chloride standard solution* into 5 of the vials. The 6 solutions thus obtained contain, respectively, 0, 0.3, 0.6, 0.9, 1.5, and 3 µg of vinyl chloride. Shake, avoiding contact between the stopper and the liquid. Place the vials in a water bath at 60 ± 1° for 2 h.

Chromatographic system

(See *Chromatography* ⟨621⟩*, General Procedures, Gas Chromatography*.)

Column: Stainless steel 3-mm × 3-m packed with silanized diatomaceous earth for gas chromatography impregnated with 5% m/m of dimethylstearylamide and 5% m/m of polyethylene glycol 400

Temperatures

Injection port: 100°

Column: 45°

Detector: 150°

Carrier gas: Nitrogen

Flow rate: 30 mL/min

Analysis

Samples: *Sample solution* and *Reference solutions*

Inject 1 mL of the head space of each vial containing the *Sample solution* and the *Reference solutions*. Calculate the amount of vinyl chloride in the *Sample solution* by comparing the test result of the *Sample solution* with the test results of the *Reference solutions*. Calculate the amount of vinyl chloride in the test material by dividing the amount of vinyl chloride in the *Sample solution* by 1.0 g, producing a result in µg/g or ppm.

Acceptance criteria: NMT 1 ppm. Note that vinyl chloride is not an additive but is monitored as a residual monomer.

Chlorine content

Preparation: Prepare the sample using *Oxygen Flask Combustion* ⟨471⟩. Perform the combustion with 50.0 mg of the test material. Absorb the combustion products with 20 mL of 1 M sodium hydroxide.

Analysis: Add 2.5 mL of nitric acid, 10 mL of 0.1 M silver nitrate solution, 5 mL of ferric ammonium sulfate solution, and 1 mL of dibutyl phthalate to the *Preparation* solution. Titrate with 0.005 M ammonium thiocyanate solution until a reddish-yellow color is obtained. Carry out a blank titration.

Calculation: Calculate the titration volume by subtracting the volume of titrant used in the ▲*Preparation*▲ (RB 1-Mar-2021) from the volume of titrant used in the ▲blank.▲ (RB 1-Mar-2021) Each milliliter of titrant volume is equal to ▲0.3125▲ (RB 1-Mar-2021) mg of polyvinyl chloride. The chlorine content, in weight %, is calculated as follows:

$$\text{Chlorine content (weight \%)} = \{[{}^{\blacktriangle}(V_b - V_p)_{\blacktriangle\ (\text{RB 1-Mar-2021})} \times {}^{\blacktriangle}0.3125_{\blacktriangle\ (\text{RB 1-Mar-2021})}\ \text{mg/mL}]/\text{weight of sample (mg)}\} \times 100\%$$

${}^{\blacktriangle}V_b$ = volume of titrant used in the blank (mL)

V_p = volume of titrant used in the *Preparation* (mL)▲ (RB 1-Mar-2021)

Acceptance criteria: NLT 80% by weight, expressed as polyvinyl chloride

POLYVINYL CHLORIDE, PLASTICIZED

Identification

[NOTE—The identification of polyvinyl chloride, plasticized needs compliance with only one test procedure to be established.]

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- **A. Infrared Spectrophotometry**

Refer to ⟨854⟩.

Apparatus: Use an infrared spectrophotometer capable of correcting for the blank spectrum and able to measure in transmission mode or equipped with an internal reflectance accessory and an appropriate internal reflectance plate.

Sample preparation

Transmission mode: Prepare a specimen of appropriate thickness without visible defects (cracks or holes). The specimens can be compressed to form a thin, uniform film by exposure to elevated temperatures and pressures (2000 psi or more). The temperatures at which the thin films are generated represent a trade-off between producing a melt (which dictates the lowest temperature necessary) and degrading the sample (which dictates the highest temperature allowed). Ultimately, the temperatures that are used are appropriate if the film produced is conducive to the infrared analysis.

Internal reflectance mode: Prepare a flat section and trim it as necessary to obtain a segment that is convenient for mounting in the internal reflectance accessory. Taking care to avoid scratching the surfaces, wipe the specimen with dry paper or, if necessary, a soft cloth dampened with methanol, and permit the surfaces to dry. Then securely mount the specimen on the internal reflection plate, ensuring adequate surface contact.

Tetrahydrofuran extraction, Solution S6: Dissolve 5.0 g of the test material in 80 mL of tetrahydrofuran and dilute with the same solvent to a volume of 100 mL. Filter if necessary; the solution may remain opaque. Slowly and dropwise add 70 mL of ethanol to 20 mL of this solution. Cool the mixture in ice for 1 h. Filter or centrifuge the mixture, collecting residue A. Wash residue A with ethanol. Collect the washings and add them to the solution remaining after filtration or centrifugation. Transfer the solution to a 100-mL volumetric flask and dilute to volume with ethanol. This process produces *Solution S6*. Prepare a blank solution.

Procedure: Dissolve residue A from *Solution S6* in 5 mL of tetrahydrofuran. Apply a few drops of this solution to a sodium chloride plate and evaporate to dryness in an oven at 100°–105°. Determine the infrared spectrum from 3800 cm^{-1} to 650 cm^{-1} (2.6–15 mm).

Acceptance criteria: The specimen exhibits an absorption spectrum that is substantially equivalent to that of USP Polyvinyl Chloride, Plasticized RS. Substantial, as opposed to exact, equivalence allows for minor spectral differences arising from the natural compositional and/or physical variation among polymers of this class. Substantial equivalence is achieved when all differences between the sample and RS spectra can be explained in the context of such natural compositional and/or physical variations.

- **B. Thermal Analysis**

Refer to ⟨891⟩.

Sample preparation: Place an appropriately sized sample in the test specimen pan. [Note—Intimate contact between the pan and the thermocouple is essential for obtaining reproducible results.]]

Procedure: Determine the thermal analysis curve under nitrogen, using heating/cooling conditions specified for the polymer type and using equipment capable of performing the determinations as described in ⟨891⟩. Heat the specimen from –20° to 120° at a heating rate of about 10°/min. Quickly cool the specimen to room temperature.

Acceptance criteria: The thermal analysis curve of the specimen is similar to the thermal analysis curve of USP Polyvinyl Chloride, Plasticized RS, and the glass transition temperature obtained from the thermal analysis curve of the specimen does not differ from that of the RS. The nature of these polymers and compositional variety, material-to-material variations in the melting peak temperature can be anticipated. [Note—that the results of the DSC analysis are strongly dependent on the amount of plasticizer in the test article.]

Physicochemical Tests

Water extraction, Solution S1: Place 25 g of the test material into a borosilicate glass flask. Add 500 mL of *Purified Water*, cover the flask's neck with aluminum foil or a borosilicate beaker, and heat in an autoclave at 121 ± 2° for 20 min. Allow the solution to cool and the solids to settle, decant the solution into a 500-mL volumetric flask, and dilute with *Purified Water* to volume; the diluted solution is designated *Solution S1*. ▲Use *Solution S1* within 4 h of preparation.▲ (RB 1-Mar-2021)

Absorbance

Refer to ⟨857⟩.

Procedure: Evaporate 100 mL of *Solution S1* to dryness. Dissolve the resulting residue in 5 mL of hexane to produce the hexane sample. Pass the hexane sample, if necessary, through a filter previously rinsed with hexane. Determine the spectrum between 250 and 310 nm in the hexane sample.

Acceptance criteria: NMT 0.25. If the specification for absorbance is exceeded, then the material can still be considered compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Acidity or alkalinity

BRP indicator solution: 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 2.0 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

Methyl orange solution: Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of 1 N hydrochloric acid is required to change the color from yellow to red.

Procedure: To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*. Determine the titration volume of 0.01 N sodium hydroxide required to change the color of the indicator to blue. To 100 mL of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01 N hydrochloric acid required to reach the beginning of the color change of the indicator from yellow to orange.

Acceptance criteria: NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is required to reach the beginning of the color change of the indicator from yellow to orange.

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Total organic carbon

Procedure: The TOC content of *Solution S1* is measured according to the general methodologies outlined in ⟨643⟩. However, although ⟨643⟩ is designed for the testing of high-purity water with low TOC values, material extracts may have TOC values that are higher than those of *Purified Water* because of extracted organic substances. Thus, the method used to perform the TOC analyses should have a limit of detection of 0.2 mg/L (ppm) and should have a demonstrated linear dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit). A linear range with a higher upper concentration can be used if linearity is established. If sample extracts exceed this upper linear range, they must be diluted appropriately for analysis.

Acceptance criteria: The difference between the sample and blank TOC concentrations is NMT 5 mg/L. If the specification for TOC is exceeded, then the material can still be considered to be compliant with this chapter if the chemicals responsible for the test results can be established (identity and concentration) and the chemicals are characterized to establish that the probable risk posed by all the chemicals, considered individually, is within acceptable parameters.

Plastic Additives

Additives are di(2-ethylhexyl) phthalate, *N′N″*-diacylethylenediamines, epoxidized soya oil, and epoxidized linseed oil. Vinyl chloride monomer (VCM) is also monitored, although it is a residual monomer and not an additive.

Solution A1: Add 2.0 g of the test material to 200 mL of peroxide-free ether and heat under a reflux condenser for 8 h. Separate the resulting residue B and extraction solution A by filtration. Evaporate extraction solution A to dryness under reduced pressure in a water bath at 30°, producing residue C. Dissolve residue C in 10 mL of toluene to produce *Solution A1*.

Precipitate B2: Dissolve residue B in 60 mL of ethylene chloride heating on a water bath under a reflux condenser, producing solution D. Filter the resulting solution D. Add the filtered solution D dropwise and with vigorous shaking to 600 mL of heptanes heated almost to boiling. Separate by hot filtration the coagulum B1 and the organic solution E. Allow solution E to cool; separate the precipitate B2 that forms upon cooling, and pass through a tared sintered-glass filter (pore size of 16–40 µm).

Reference solutions U, V, W: 10.0-mg/mL solutions of USP Plastic Additive 14 RS, USP Plastic Additive 15 RS, and USP Plastic Additive 16 RS, respectively, in toluene

Chromatographic system

(See *Chromatography* ⟨621⟩*, General Procedures, Thin-Layer Chromatography*.)

Plate: TLC silica gel GF_{254} (1-mm thick)

Procedure: Apply 0.5 mL of *Solution A1* to the plate as a 30-mm × 3-mm band. Apply 5 µL each of *Reference solutions U*, *V*, and *W* to the plate. Develop the plate over a path of 15 cm using toluene. Dry the plate carefully.

Additive di(2-ethylhexyl) phthalate: UV 254 nm. Locate the zone corresponding to additive di(2-ethylhexyl) phthalate, USP Plastic Additive 14 RS (R_F about 0.4). Remove the area of silica gel corresponding to this zone, mix with 40 mL of ethyl ether, and shake for 1 min. Filter, rinse filter with two quantities each of 10 mL of ethyl ether, add the rinsings to the filtrate, and evaporate to dryness.

Additives epoxidized soya oil and epoxidized linseed oil: Expose the plate to iodine vapor for 5 min. Examine the chromatogram, and locate the band corresponding to additives epoxidized soya oil, USP Plastic Additive 15 RS, and epoxidized linseed oil, USP Plastic Additive 16 RS ($R_F = 0$). Remove the area of silica gel corresponding to this band. Similarly, remove a corresponding area of silica gel as a blank reference. Separately mix both samples with separate 40-mL portions of methanol, shaking for 15 min. Filter, rinse the filter with two quantities of 10 mL of methanol, add the rinsings to the filtrate, and evaporate to dryness.

Additive *N,N′*-diacylethylenediamines: Wash precipitate B2 with alcohol, absolute. Dry to constant mass over diphosphorus pentoxide, and weigh the filter.

Acceptance criteria

Di(2-ethylhexyl)phthalate: Residue is NMT 40 mg.

Epoxidized soya oil: The difference between the masses of both residues is NMT 10 mg.

Epoxidized linseed oil: The difference between the masses of both residues is NMT 10 mg.

***N′N″*-Diacylethylenediamines:** Residue is NMT 20 mg.

Related Substances

Vinyl chloride

Internal standard solution: Using a microsyringe, inject 10 µL of ethyl ether into 20.0 mL of *N,N*-dimethylacetamide, immersing the tip of the needle in the solvent. Immediately before use, dilute the solution with *N,N*-dimethylacetamide to 1000 times its volume.

Sample solution: Place 1.0 g of the test material in a 50-mL vial, and add 10.0 mL of the *Internal standard solution*. Close the vial, and secure with a stopper. Shake, avoiding contact between the stopper and the liquid. Place the vial in a water bath at 60 ± 1° for 2 h.

Vinyl chloride primary solution: [NOTE—Prepare under a ventilated hood.] Place 50.0 mL of *N,N*-dimethylacetamide in a 50-mL vial, stopper the vial, secure the stopper, and weigh to the nearest 0.1 mg. Fill a 50-mL polyethylene or polypropylene syringe with gaseous vinyl chloride, allow the gas to remain in contact with the syringe for about 3 min, empty the syringe, and fill again with 50 mL of gaseous vinyl chloride. Fit a hypodermic needle to the syringe, and reduce the volume of gas in the syringe from 50 to 25 mL. Inject the remaining 25 mL of vinyl chloride slowly into the vial, shaking gently and avoiding contact between the liquid and the needle. Weigh the vial again; the increase in mass is about 60 mg (1 µL of the solution obtained contains about 1.2 µg of vinyl chloride). Allow to stand for 2 h. Store the primary solution in a refrigerator.

Vinyl chloride standard solution: To 1 volume of the *Vinyl chloride primary solution* add 3 volumes of *N,N*-dimethylacetamide.

Reference solutions: Place 10.0 mL of the *Internal standard solution* in each of six 50-mL vials. Close the vials, and secure the stoppers. Inject 1, 2, 3, 5, and 10 µL, respectively, of the *Vinyl chloride standard solution* into 5 of the vials.

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The 6 solutions thus obtained contain, respectively, 0, 0.3, 0.6, 0.9, 1.5, and 3 µg of vinyl chloride. Shake, avoiding contact between the stopper and the liquid. Place the vials in a water bath at 60 ± 1° for 2 h.

Chromatographic system

(See *Chromatography* ⟨621⟩*, General Procedures, Gas Chromatography*.)

Column: Stainless steel 3-mm × 3-m packed with silanized diatomaceous earth for gas chromatography impregnated with 5% m/m of dimethylstearylamide and 5% m/m of polyethylene glycol 400

Temperatures

Injection port: 100°

Column: 45°

Detector: FID 150°

Carrier gas: Nitrogen

Flow rate: 30 mL/min

Analysis

Samples: *Sample solution* and *Reference solutions*

Inject 1 mL of the head space of each vial containing the *Sample solution* and the *Reference solutions*. Calculate the amount of vinyl chloride in the *Sample solution* by comparing the test result of the *Sample solution* with the test results of the *Reference solutions*. Calculate the amount of vinyl chloride in the test material by dividing the amount of vinyl chloride in the *Sample solution* by 1.0 g, producing a result in µg/g or ppm.

Acceptance criteria: NMT 1 ppm. Note that vinyl chloride is not an additive but is monitored as a residual monomer.

ADDITIONAL REQUIREMENTS

• **USP REFERENCE STANDARDS** ⟨11⟩

Polymer standards

USP Cyclic Olefin Copolymer RS
USP Cyclic Olefin Polymer RS
USP Polyamide 6 RS
USP Polycarbonate RS
USP High-Density Polyethylene RS
USP Homopolymer Polypropylene RS
USP Low-Density Polyethylene RS
USP Polyethylene Terephthalate RS
USP Polyethylene Terephthalate G RS
USP Poly(ethylene-vinyl acetate) RS
USP Polyvinyl Chloride RS
USP Polyvinyl Chloride, Plasticized RS

Plastic additive standards

USP Plastic Additive 1 RS

Ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate].
CAS RN®: CAS-32509-66-3
USP Plastic Additive 2 RS

Pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate].
CAS RN®: CAS-6683-19-8
USP Plastic Additive 3 RS

2,2′,2″,6,6′,6″-Hexa-*tert*-butyl-4,4′,4″-[(2,4,6-trimethyl-1,3,5-benzenetriyl)trismethylene]triphenol.
CAS RN®: CAS-1709-70-2
USP Plastic Additive 4 RS

Octadecyl 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate.
CAS RN®: CAS-2082-79-3
USP Plastic Additive 5 RS

Tris(2,4-di-*tert*-butylphenyl) phosphite.
CAS RN®: CAS-31570-04-4
USP Plastic Additive 6 RS

1,3,5-Tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-*s*-triazine-2,4,6(1*H*,3*H*,5*H*)-trione.
CAS RN®: CAS-27676-62-6
USP Plastic Additive 8 RS

Dioctadecyl disulfide.
CAS RN®: CAS-2500-88-1
USP Plastic Additive 9 RS

Didodecyl 3,3′-thiodipropionate.
CAS RN®: CAS-123-28-4
USP Plastic Additive 10 RS

Dioctadecyl 3,3′-thiodipropionate.
CAS RN®: CAS-693-36-7
USP Plastic Additive 11 RS

Copolymer of dimethyl succinate and (4-hydroxy-2,2,6,6-tetramethylpiperidin-1-yl)ethanol.
CAS RN®: CAS-65447-77-0

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USP Plastic Additive 12 RS

Oleamide.
CAS RN®: CAS-301-02-0
USP Plastic Additive 13 RS

Erucamide.
CAS RN®: CAS-112-84-5
USP Plastic Additive 14 RS

Di(2-ethylhexyl) phthalate.
CAS RN®: CAS-117-81-7
USP Plastic Additive 15 RS

Epoxidized soya oil.
CAS RN®: CAS-8013-07-8
USP Plastic Additive 16 RS

Epoxidized linseed oil.
CAS RN®: CAS-8016-11-3
USP Plastic Additive 18 RS

Mixture of Di(isooctyl) 2,2′-(dioctylstannylene)-bis(thio)diacetate and Tri(isooctyl) 2,2′,2″-[monooctylstannylidyne) tris(thio)]triacetate.
CAS RN®: CAS-26401-97-8; CAS-26401-86-5

Related substances standards

USP Bisphenol A RS
CAS RN®: CAS-80-05-07
USP Butylated Hydroxytoluene RS
CAS RN®: CAS-128-37-0
USP Caprolactam RS
CAS RN®: CAS-105-60-2
USP Stearic Acid RS
CAS RN®: CAS-57-11-4▲ (Official 1-Dec-2025)

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