BRIEFING

(661.1) Plastic Materials Of Construction, *USP 42* page 6819. The General Chapters—Packaging and Distribution Expert Committee is proposing the following revisions to clarify the intent of the chapter and to increase the ease in utilization. Listed below are the key changes being proposed:

1. The chapter has been reformatted so that all test methods and acceptance criteria are contained within each polymer section.
2. The implementation date is being changed from May 1, 2020 to December 1, 2025.
3. Text within the Introduction and Scope has been edited for simplification and clarification.
4. Table 1 and Table 2 have been merged to ensure consistency and clarity of requirements.
5. The requirement for extractable elements testing is being removed from this chapter. It is being left up to the material user 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. An example of an extractable elements testing strategy is provided in *Evaluation of Plastic Packaging Systems and Their Materials of Construction with Respect to Their User Safety Impact* (1661).
6. For the testing of Phenolic antioxidants under the Plastic Additives section for Cyclic Olefins and Polypropylene, the testing requirement for USP Plastic Additive 4 RS and USP Plastic Additive 5 RS for Test B is being removed. The testing of USP Plastic Additive 4 RS and USP Plastic Additive 5 RS can be found under Test C.
7. No other testing requirement is being added or removed beyond what is stated in the proposed changes above.

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

(GCPD: D. Hunt.)

Correspondence Number—C196751
PLASTIC MATERIALS OF CONSTRUCTION

Change to read:

(This chapter will become official on May 1, 2020 • 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 and must be met wherever this chapter or (661.2) is referenced in the USP-NF.) 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. (USP 1-Aug-2020)

Add the following:

INTRODUCTION

SCOPE

CYCLIC OLEFINS

POLYAMIDE 6

POLYCARBONATE

POLYETHYLENE
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, biocompatibility (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 requirement. An example of an extractable elements testing strategy is provided in Evaluation of Plastic Packaging Systems and Their Materials of Construction with Respect to Their User Safety Impact (1661). ▲ (USP 1-Aug-2020)

Change to read:

SCAPE

The purpose of this chapter is to provide test methods and specifications for determining suitability of plastic materials of construction used in packaging systems. Individual plastic materials of construction are considered to be well characterized and appropriate for use 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 specifications for the following materials: cyclic olefins; polyamide; 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 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 tested for biocompatibility, physicochemical properties, and plastic additives, and relevant extracted metals (see (1661)).

Specifications must be established for unaddressed materials, and such specifications should be consistent with the specifications for materials addressed in this chapter. For example, unaddressed materials whose aqueous extracts are tested for their total organic carbon (TOC) levels must have a specification for TOC that is consistent with the TOC specification for materials addressed in this chapter.

Alternatively, individual plastic materials of construction are deemed to be well characterized and appropriate for use if they are used in a packaging system that meets the requirements in (661.2). However, such materials are appropriate for use only in the packaging system
that meets the requirements of (661.2). The appropriateness for use of such materials in other packaging systems must be established for the other packaging systems via proper testing.\(^\text{▲}(\text{USP 1-Aug-2020})\)

**Table 1** provides the appropriate application of the chemical and biological tests for oral and topical dosage forms, which include oral tablets, oral hard and soft gelatin capsules, oral powders, solutions and suspensions, topical powders, and aqueous-based topical solutions and suspensions. **Table 2** provides guidance on the appropriate application of the chemical tests and biological reactivity tests for all other dosage forms as well as application of the chemical tests and biological reactivity tests for all other dosage forms. [NOTE—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 safety issues. If additional information is required, perform Extractable metals tests and tests as directed in **Table 2**.]

**Table 1. Guidelines for Application of Tests for Oral and Topical Dosage Forms**

<table>
<thead>
<tr>
<th>Biological Reactivity Tests</th>
<th>Chemical Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not required</td>
<td>• Identification, Physicochemical tests, and Extractable metals</td>
</tr>
<tr>
<td></td>
<td>• Provide appropriate reference to the Indirect Food Additive regulations in 21 CFR 174–186, specifically those</td>
</tr>
</tbody>
</table>
addressing the purity criteria and limitations pertaining to use

- Materials that do not meet these requirements are not suitable for packaging for these dosage forms unless the materials are established to be suitable by other means that have been approved by an appropriate regulatory authority.
### Table 2. Guidelines for Application of Tests for All-Other-Dosage Forms

<table>
<thead>
<tr>
<th>Biological Reactivity Tests</th>
<th>Chemical Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Biological Reactivity Tests, In Vitro (87)</td>
<td>- Identification, Physicochemical tests, Extractable metals, and Plastic Additives</td>
</tr>
<tr>
<td>- Biological Reactivity Tests, In Vivo (88), Classification of Plastics</td>
<td></td>
</tr>
<tr>
<td>- Materials that do not meet the requirements of the in vivo or in vitro tests are not suitable for containers for these dosage forms</td>
<td>- Materials that do not meet these requirements are not suitable for containers for these dosage forms unless the materials are established to be suitable by other means that have been approved by an appropriate regulatory authority</td>
</tr>
<tr>
<td>Test Parameter</td>
<td>Oral and Topical Dosage Forms&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>Identification</td>
<td>X</td>
</tr>
<tr>
<td>UV absorbance</td>
<td>X</td>
</tr>
<tr>
<td>Acidity/alkalinity</td>
<td>X</td>
</tr>
<tr>
<td>Total organic carbon (TOC)</td>
<td>X</td>
</tr>
<tr>
<td>Extractable elements</td>
<td>—&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Plastic additives</td>
<td>—&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Biological Reactivity</td>
<td></td>
</tr>
<tr>
<td>In vitro per Biological Reactivity Tests, In Vitro (87)</td>
<td>—</td>
</tr>
<tr>
<td>In vivo per Biological Reactivity Tests, In Vivo (88)</td>
<td>—</td>
</tr>
</tbody>
</table>

<sup>a</sup> This table provides the appropriate application of the chemical tests for oral and topical dosage forms. [NOTE—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 Additives tests as directed in this table.]
This table provides guidance on the appropriate application of the chemical tests and biological reactivity tests for all other dosage forms.

As deemed necessary and appropriate by end-user. See (1661) for additional information.

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.

Delete the following:

**SPECIFICATIONS**

Specifications are provided for absorbance and TOC. If the specification for absorbance or TOC is exceeded, then the material can still be deemed 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.

Delete the following:

**TEST METHODS**

**Identification**

The identification testing described in this chapter is required for all materials of construction used in packaging systems. The identification test should be accomplished by using the procedures specified in this
chapter (infrared spectrophotometry or thermal analysis). If neither of
these procedures are applicable for a particular material, then an
alternative procedure can be used. The alternate procedure must
establish the identity on the basis of obtaining substantially equivalent
results for the test article and its appropriate USP RS.

Specifications must be established for materials that are not specified in
this chapter, and such specifications should be consistent with the
specifications established for materials that are specified in this
chapter. For example, a DSC specification for a material that is not
currently listed in this chapter should be consistent, in language and in
rigor, with a DSC specification for a material that is listed in this
chapter (e.g., melting peak temperature agreement between sample
and reference material).

**Extractions**

Physicochemical testing of the plastic material requires that it be
extracted or dissolved. Different tests are facilitated by various
extraction methods. *Table 3* describes the extracts that are
generated and the tests that are performed on those extracts.
Subsequent discussions address methods for producing the
extracts. Note that these extracts may be used for tests other
than the physicochemical tests.
# Table 3. Extractions Performed for Various Chemical Tests

<table>
<thead>
<tr>
<th>Extraction Solution</th>
<th>Cyclic Olefin, Polyethylene, and Polypropylene</th>
<th>Polyamide-6</th>
<th>Polycarbonate</th>
<th>Polyethylene Terephthalate and Polyethylene Terephthalate G</th>
<th>Poly(ethylene-vinyl acetate)</th>
<th>Polyvinyl Chloride</th>
<th>Polyvinyl Chloride, Plasticized</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solution</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1 Water</td>
<td>Absorbance</td>
<td>Acidity/alkalinity</td>
<td>Absorbance</td>
<td>Absorbance</td>
<td>Absorbance</td>
<td>Absorbance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TOC</td>
<td></td>
<td>TOC</td>
<td></td>
<td>TOC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S2 Toluene</td>
<td>Phenolic antioxidants, nonphenolic antioxidants, amides, and stearates&lt;sup&gt;a&lt;/sup&gt;</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Phenolic antioxidants, amides, and stearic acid&lt;sup&gt;b&lt;/sup&gt;</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>S3 Acid</td>
<td>Extractable metals: Al, As, Ba, Cd, Co, Hg, Ca, Cd, Co, Hg</td>
<td>Extractable</td>
<td>Extractable</td>
<td>Extractable</td>
<td>Extractable</td>
<td>Extractable</td>
<td>Extractable</td>
</tr>
</tbody>
</table>

<sup>a</sup> Phenolic antioxidants, nonphenolic antioxidants, amides, and stearates
<sup>b</sup> Phenolic antioxidants, amides, and stearic acid
## Tests Performed on Plastics Using the Specified Extracting Solution

<table>
<thead>
<tr>
<th>Extraction Solution</th>
<th>Cyclic-Olefin, Polyethylene, and Polypropylene</th>
<th>Polyamide-6</th>
<th>Polycarbonate</th>
<th>Polyethylene Terephthalate and Polyethylene Terephthalate</th>
<th>Poly(ethylene-vinyl-acetate)</th>
<th>Polyvinyl Chloride, Plasticized</th>
</tr>
</thead>
<tbody>
<tr>
<td>S4  Alkali</td>
<td>Ni, Pb, Ti, V, Mn, Ni, Pb, Ti, V, and-Zn</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>S5  Alcohol</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Absorbance</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>S6  Tetrahydrofuran</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Absorbance</td>
</tr>
<tr>
<td>S7  Phenol</td>
<td>N/A</td>
<td>Free base</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### Notes:
- Although this extract is suitable for use with these specific ingredient methods, such an extract could be useful for other tests designed to establish a material's composition.
- For polyethylene only.

- Not applicable for cyclic olefins and polypropylene.

- For material used for containers for non-injectable aqueous solutions.
The extractable metals testing described in this chapter is required for all plastic materials of construction used in packaging systems. Specifically, all materials must be tested for those extractable metals listed in Table 3.

Change to read:

CYCLIC OLEFINS

Identification

• A. INFRARED SPECTROPHOTOMETRY (INFRARED ABSORPTION (197F))

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.

B. Differential Scanning Calorimetry (DSC)

Given the amorphous nature of these polymers and their compounded variety, material-to-material variations in the melting peak temperature can be anticipated. This it is neither recommended nor required that DSC be performed.

Extractable Metals

Aluminum:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Arsenic, cadmium, lead, mercury, cobalt, nickel, and vanadium:

Report the measured value in Solution S3 at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm), corresponding to less than 0.025 µg/g.

Titanium:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Zinc:
Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Test results for additional relevant extractable metals are similarly reported.

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 0.2 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 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. (USP 1-Aug-2020)

**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); octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (USP Plastic Additive 4 RS); tris(2,4-di-tert-butylphenyl) phosphite (USP Plastic Additive 5 RS); 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-s-triazine-2,4,6(1H,3H,5H)-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 (pentaerythritol 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-triy)(trimethylene)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 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 (197F)**

  *Refer to (854)* *(USP 1-Aug-2020)*

**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 \( \text{cm}^{-1} \) to 650 \( \text{cm}^{-1} \) (2.6–15 \( \mu \text{m} \)).

**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.

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**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\(^{\circ}\) at a heating rate of about 20\(^{\circ}\)/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; 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 0.2 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.

**Extractable metals**

*Arsenic, lead, cadmium, mercury, cobalt, nickel, and vanadium:*

Report the measured value in Solution S3 at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm), corresponding to less than 0.025 µg/g. Additional acceptance criteria for certain metals are provided as follows. Test results for additional relevant extractable metals are similarly reported.\(^{▲}(USP~1\text{-Aug-2020})\)

**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 (USP 1-Aug-2020) × 30-m×0.25-µm; (USP 1-Aug-2020) phase G25

Temperatures

Injection port:
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 3 times into the chromatographic system.
**System suitability:**

Inject *Reference solution WS4* 5 times into the chromatographic system. The % 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 ((197A))**

  *Refer to (854).\(^\text{▲}\) (USP 1-Aug-2020)*

**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).

**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 $-20^\circ$ to $300^\circ$ at a heating rate of about $10^\circ$/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 $8.0^\circ$. 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 0.2 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.

**Extractable Metals**

Arsenic, lead, cadmium, mercury, cobalt, nickel, and vanadium:

Report the measured value in Solution S3 at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm), corresponding to less than 0.025 µg/g. Additional acceptance criteria for certain metals are provided as follows.

Test results for additional relevant extractable metals are similarly reported.▲ (USP 1-Aug-2020)

**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

Column:

Stainless steel, 30-m×0.32-mm (USP 1-Aug-2020) × 0.32-mm×30-m, (USP 1-Aug-2020) 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%.

**Rinsing:**

Inject the *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 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.

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

**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:**
Detector:

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.

System suitability:
Inject *Reference solution WS3* 5 times into the chromatographic system. The % 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 \(\mu g/g\).

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

**Acceptance criteria:**

NMT 100 \(\mu g/g\)

Change to read:

**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 \(\langle 197F\rangle\)**

*Refer to \(854\)\(^\text{\(\uparrow\)}\) (USP 1-Aug-2020)
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°.

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 0.2 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.

**Extractable Metals**

**Aluminum:**

*Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

**Arsenic, cadmium, lead, mercury, cobalt, and nickel:**

Report the measured value in *Solution S3* at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm), corresponding to less than 0.025 µg/g.

**Chromium:**

*Solution S3* contains NMT 0.02 mg/L (ppm), corresponding to 0.05 µg/g.

**Titanium:**

*Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.
Vanadium:

Solution S3 contains NMT 0.04 mg/L (ppm), corresponding to 0.1 µg/g.

Zinc:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Zirconium:

Solution S3 contains NMT 0.04 mg/L (ppm), corresponding to 0.1 µg/g.

Test results for additional relevant extractable metals are similarly reported.

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. (USP 1-Aug-2020)

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*, 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(1H,3H,5H)-trione (USP Plastic Additive 6 RS), then carry out Test B.  ▲ (USP 1-Aug-2020)

**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. ▲ (USP 1-Aug-2020)

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 S8\*S9 (USP 1-Aug-2020) 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.

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:**
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* \(\text{\footnotesize (197F)}\)

\[\text{\footnotesize Refer to (854).}^\wedge\text{\footnotesize (USP 1-Aug-2020)}\]

**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 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 0.2 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.

**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.

Extractable Metals

Aluminum:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Antimony:

Solution S4 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Arsenic, cadmium, lead, mercury, cobalt, nickel, and vanadium:

Report the measured value in Solution S3 at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm), corresponding to less than 0.025 µg/g.
Barium:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Germanium:

Solution S4 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Manganese:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Titanium:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Zinc:

Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Test results for additional relevant extractable metals are similarly reported. ▲

Change to read:

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). *(USP 1-Aug-2020)*

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 \(\text{〈891〉}\).

**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 $-50^\circ$ to $120^\circ$ 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 0.2 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 1.0 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.

**Extractable Metals**

**All-metals:**

Report the measured value in *Solution S3* at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm).
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. (USP 1-Aug-2020)

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

**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<sub>254</sub>

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:

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

**Acceptance criteria:**

NMT 25% by weight

**For tubing:**

NMT 30% by weight

POLYPROPYLENE

**Identification**

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

- *A. Infrared Spectrophotometry* \(\text{〈(197F)〉}\)

  *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 0.2 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.

**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.

**Extractable Metals**

**Aluminum:**

*Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

**Arsenic, cadmium, lead, mercury, cobalt, nickel, and vanadium:**

Report the measured value in *Solution S3* at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm), corresponding to less than 0.025 µg/g.

**Chromium:**

*Solution S3* contains NMT 0.02 mg/L (ppm), corresponding to 0.05 µg/g.

**Titanium:**

*Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

**Zinc:**

*Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

Test results for additional relevant extractable metals are similarly reported.

▲ (USP 1-Aug-2020)
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.* (USP 1-Aug-2020)

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); octadeeyl-3-
(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (USP Plastic Additive 4 RS), tris(2,4-di-tert-butylphenyl) phosphite (USP Plastic Additive 5 RS), 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-s-triazine-2,4,6(1H,3H,5H)-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 tetrais[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.▲ (USP 1-Aug-2020)

**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 S8*S9▲ (USP 1-Aug-2020) 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<sub>254</sub>

- **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<sub>f</sub> 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.

Change to read:

POLYVINYL CHLORIDE

Identification

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

•A. INFRARED SPECTROPHOTOMETRY (197F)

*Refer to (854). (USP 1-Aug-2020)

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**.

**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 \textit{Solution S5}. Use \textit{Solution S5} within 4 h of preparation.\footnote{\textsuperscript{\textregistered} USP 1-Aug-2020}

**Absorbance**

Refer to (857).

**Procedures**

**Solution S1:**

Evaporate 100 mL of \textit{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 \textit{Solution S6} (1 in 10) with ethanol prior to measurement. In all other situations, analyze \textit{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 \textit{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 (USP 1-Aug-2020) **Additives and Stabilizers:**

The supplier of the material must be able to provide sufficient compositional information to establish whether the material meets the specifications 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 (benzoylstearoylemethane):
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 Solution S6 ▲[Reference solution U](USP 1-Aug-2020) 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 ▲[Reference solution U](USP 1-Aug-2020) through the same procedure as the 0.1 mL of Solution S6 ▲[Reference solution U](USP 1-Aug-2020).

**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 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*. The color in the *Sample solution* should not be as intense as the color in the *Standard solution*.▲ (USP 1-Aug-2020)

**Acceptance criteria:**

▲NMT 25 µg/g (ppm).▲ (USP 1-Aug-2020) The color in the *Sample solution* should not be as intense as the color in the *Standard solution*. Non-tin-stabilized materials, NMT 25 µg/g (ppm).▲ (USP 1-Aug-2020)

**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 blank from the volume of titrant used in the *Preparation*. Each milliliter of titrant volume is equal to 6.25 mg of polyvinyl chloride. The chlorine content, in weight %, is calculated as follows:
Chlorine content (weight %) = \{(\text{titrant volume (in mL) × 6.25 mg/mL})/\text{weight of sample (mg)}\} \times 100\%

Acceptance criteria:

NLT 80% by weight, expressed as polyvinyl chloride

Change to read:

POLYVINYL CHLORIDE, PLASTICIZED

Identification

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

\textbf{A. INFRARED SPECTROPHOTOMETRY (Infrared Absorption〈197F〉)}

\textbf{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.

\textbf{Sample preparation}

\textbf{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.

\textbf{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.

**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 0.2 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.

**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.

Extractable Metals

Arsenic, cadmium, lead, mercury, cobalt, nickel, and vanadium:

Report the measured value in Solution S3 at values above 0.01 mg/L (ppm), corresponding to 0.025 µg/g. If the measured values are below these values, report the result as less than 0.01 mg/L (ppm), corresponding to less than 0.025 µg/g.

Barium:

Solution S3 contains NMT 0.25 mg/L (ppm), corresponding to 5 µg/g.

Calcium:

Solution S3 contains NMT 35 mg/L (ppm), corresponding to 0.07 weight %.

Tin:

Solution S3 contains NMT 1 mg/L (ppm), corresponding to 20 µg/g.

Zinc:

Solution S3 contains NMT 100 mg/L (ppm), corresponding to 0.2 weight %.

Test results for additional relevant extractable metals are similarly reported.  ▲

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 \( \times \) 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. 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 dimethylstearylamine 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-32509-66-3].

USP Plastic Additive 2 RS
Pentaerythrityl tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate].
[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-1709-70-2].

USP Plastic Additive 4 RS
Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate.
[CAS-2082-79-3].

USP Plastic Additive 5 RS
Tris(2,4-di-tert-butylphenyl) phosphite.
[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(1H,3H,5H)-trione.
[CAS-27676-62-6].

USP Plastic Additive 8 RS
Dioctadecyl disulfide. [CAS-2500-88-1].

Didodecyl 3,3′-thiodipropionate. [CAS-123-28-4].

Diocatatrol 3,3′-thiodipropionate. [CAS-693-36-7].

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

Oleamide. [CAS-301-02-0].

Erucamide. [CAS-112-84-5].

Di(2-ethylhexyl) phthalate. [CAS-117-81-7].

Epoxidized soya oil. [CAS-8013-07-8].

Epoxidized linseed oil. [CAS-8016-11-3].

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

Related substances standards

USP Bisphenol A RS [CAS-80-05-07].

USP Butylated Hydroxytoluene RS [CAS-128-37-0].

USP Caprolactam RS [CAS-105-60-2].
USP Stearic Acid RS [CAS-57-11-4].