

## 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

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1      **(661.1) PLASTIC MATERIALS OF CONSTRUCTION**

2      Change to read:

3      **(This chapter will become official on May 1, 2020~~December 1,~~**

4      **2025.)<sup>▲ (USP 1-Aug-2020)</sup> Early adoption of the requirements in this chapter**

5      **and its companion chapter *Plastic Packaging Systems for***

6      ***Pharmaceutical Use* (661.2) are permitted by USP. When early**

7      **adoption is not used, *Plastic Packaging Systems and Their***

8      ***Materials of Construction* (661) will apply. ~~and must be met~~**

9      **~~wherever this chapter or (661.2) is referenced in the USP-NF.~~)<sup>▲ If</sup>**

10     **<661.1> or <661.2> are referenced elsewhere in the USP-NF prior**

11     **to December 1, 2025, the standards in (661) will apply if early**

12     **adoption of <661.1> or <661.2> has not occurred.<sup>▲ (USP 1-Aug-2020)</sup>**

13     Add the following:

14     <sup>▲</sup>

15     **INTRODUCTION**

16     **SCOPE**

17     **CYCLIC OLEFINS**

18     **POLYAMIDE 6**

19     **POLYCARBONATE**

20     **POLYETHYLENE**

21 **POLYETHYLENE TEREPHTHALATE AND POLYETHYLENE TEREPHTHALATE**

22 **G**

23 **POLY(ETHYLENE-VINYL ACETATE)**

24 **POLYPROPYLENE**

25 **POLYVINYL CHLORIDE**

26 **POLYVINYL CHLORIDE, PLASTICIZED**

27 **ADDITIONAL REQUIREMENTS**

28 ▲ (USP 1-Aug-2020)

29 Change to read:

## 30 **INTRODUCTION**

31 The use of well-characterized materials to construct packaging systems  
32 is a primary means of ensuring that the packaging system is suited for  
33 its intended use. Materials are characterized so that their properties  
34 and characteristics can be matched to the performance requirements  
35 of the packaging system, thus facilitating the intentional selection of  
36 appropriate materials. For the purposes of this chapter, a plastic  
37 material of construction is considered to be well characterized for its  
38 intended use if the following characteristics have been adequately  
39 established: its identity, biocompatibility (biological reactivity), general  
40 physicochemical properties, and composition (i.e., additives likely to  
41 be present). Extractable elements may also be relevant to the

42 selection of a packaging system's materials of construction and  
43 therefore a relevant aspect of material characterization. Materials of  
44 construction can vary widely in terms of their intentionally and  
45 unintentionally added elements and their potential use. Because of  
46 this, it is challenging to provide universally effective and efficient tests  
47 methodologies, lists of target elements and reporting requirements. It  
48 is the material user's responsibility to evaluate the need for  
49 extractable elements testing and, if such testing is necessary, to  
50 establish and justify the means by which testing is accomplished,  
51 taking into account extraction conditions, target elements, and  
52 reporting requirement. An example of an extractable elements testing  
53 strategy is provided in *Evaluation of Plastic Packaging Systems and*  
54 *Their Materials of Construction with Respect to Their User Safety*  
55 *Impact* (1661).▲ (USP 1-Aug-2020)

56 Change to read:

## 57 SCOPE

58 The purpose of this chapter is to provide test methods and specifications  
59 for determining suitability of▲ (USP 1-Aug-2020) plastic materials of  
60 construction used in packaging systems. Individual plastic materials of  
61 construction are considered to be well characterized and appropriate  
62 for use▲ (USP 1-Aug-2020) if they meet the requirements in this chapter or are  
63 used in a packaging system that meets the requirements in *Plastic*  
64 *Packaging Systems for Pharmaceutical Use* (661.2). The testing and  
65 qualification of plastic packaging systems and components for  
66 pharmaceutical use are covered in (661.2).

67 This chapter contains tests, methods, and specifications<sup>▲ acceptance</sup>  
68 criteria<sup>▲ (USP 1-Aug-2020)</sup> for the following materials: cyclic olefins; polyamide  
69 6; polycarbonate; polyethylene; polyethylene terephthalate;  
70 polyethylene terephthalate G; poly(ethylene-vinyl acetate);  
71 polypropylene; polyvinyl chloride; and polyvinyl chloride, plasticized.

72 Plastic packaging systems could be constructed from materials that are  
73 not specifically addressed in this chapter; such materials of  
74 construction are termed "unaddressed materials". For an unaddressed  
75 material to be considered compliant with this chapter, it must be  
76 characterized<sup>▲ and acceptance criteria<sup>▲ (USP 1-Aug-2020)</sup></sup> established in ways  
77 that are comparable to those used for the materials specified in this  
78 chapter. Specifically, the unaddressed material of construction must be  
79 identified by appropriate methodology and tested for biocompatibility,  
80 physicochemical properties, and<sup>▲ plastic<sup>▲ (USP 1-Aug-2020)</sup></sup> additives<sup>,</sup> and  
81 relevant extracted metals<sup>▲ (see (1661)).<sup>▲ (USP 1-Aug-2020)</sup></sup>

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

88 Alternatively, individual plastic materials of construction are deemed to  
89 be well characterized and appropriate for use if they are used in a  
90 packaging system that meets the requirements in (661.2). However,  
91 such materials are appropriate for use only in the packaging system

92 that meets the requirements of (661.2). The appropriateness for use of  
93 such materials in other packaging systems must be established for the  
94 other packaging systems via proper testing. ▲ (USP 1-Aug-2020)

95 [Table 1](#) provides the appropriate application of the chemical ▲ and  
96 biological ▲ tests for oral and topical dosage forms, which  
97 include oral tablets, oral hard and soft gelatin capsules, oral powders,  
98 solutions and suspensions, topical powders, and aqueous-based topical  
99 solutions and suspensions. [Table 2](#) provides guidance on the  
100 appropriate application of the chemical tests and biological reactivity  
101 tests for all other dosage forms as well as application of the chemical  
102 tests and biological reactivity tests for all other dosage forms. [NOTE—  
103 For aqueous-based oral drug products that contain cosolvents (or if,  
104 for any reason, it may be expected to extract greater amounts of  
105 substances from plastic packaging components than water), additional  
106 extractables information may be needed to determine safety issues. If  
107 additional information is required, perform *Extractable metals tests*  
108 and tests as directed in [Table 2](#).]

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

<b>Biological Reactivity Tests</b>	<b>Chemical Tests</b>
Not required	<ul style="list-style-type: none"><li>• <i>Identification, Physicochemical tests, and Extractable metals</i></li><li>• Provide appropriate reference to the Indirect Food Additive regulations in 21 CFR 174–186, specifically those</li></ul>

	addressing the purity criteria and limitations pertaining to use	111 112
	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	

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**Table 2. Guidelines for Application of Tests for All Other Dosage Forms**

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<b>Biological Reactivity Tests</b>	<b>Chemical Tests</b>
<ul style="list-style-type: none"><li>• <i>Biological Reactivity Tests, In Vitro</i> (87)</li><li>• <i>Biological Reactivity Tests, In Vivo</i> (88), <i>Classification of Plastics</i></li><li>• Materials that do not meet the requirements of the in vivo or in vitro tests are not suitable for containers for these dosage forms</li></ul>	<ul style="list-style-type: none"><li>• <i>Identification, Physicochemical tests, Extractable metals, and Plastic Additives</i></li><li>• 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</li></ul>

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**Table 1. Application of Tests**

Test Parameter	Oral and Topical Dosage Forms <sup>a</sup>	All Other Dosage Forms <sup>b</sup>
Identification	X	X
<b>Physicochemical</b>		
UV absorbance	X	X
Acidity/alkalinity	X	X
Total organic carbon (TOC)	X	X
Extractable elements	— <sup>c</sup>	— <sup>c</sup>
Plastic additives	— <sup>d</sup>	X
<b>Biological Reactivity</b>		
In vitro per <i>Biological Reactivity Tests, In Vitro</i> (87)	—	X
In vivo per <i>Biological Reactivity Tests, In Vivo</i> (88)	—	Required as needed to obtain plastic classification

119

- 120      <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.]
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- 122
- 123
- 124
- 125
- 126

- 127      b This table provides guidance on the appropriate application of the chemical tests and  
128      biological reactivity tests for all other dosage forms.
- 129      c As deemed necessary and appropriate by end-user. See (1661) for additional information.
- 130      d Provide appropriate reference to the Indirect Food Additive regulations in 21 CFR 174–  
131      186, specifically those addressing the purity criteria and limitations pertaining to use.
- 132      ▲ (USP 1-Aug-2020)

133      Delete the following:

## 134      **SPECIFICATIONS**

135      ~~Specifications are provided for absorbance and TOC. If the specification~~  
136      ~~for absorbance or TOC is exceeded, then the material can still be~~  
137      ~~deemed to be compliant with this chapter if the chemicals responsible~~  
138      ~~for the test results can be established (identity and concentration) and~~  
139      ~~the chemicals are characterized to establish that the probable risk~~  
140      ~~posed by all the chemicals, considered individually, is within~~  
141      ~~acceptable parameters.~~▲ (USP 1-Aug-2020)

142      Delete the following:

## 143      **TEST METHODS**

### 144      **Identification**

145      ~~The identification testing described in this chapter is required for all~~  
146      ~~materials of construction used in packaging systems. The identification~~  
147      ~~test should be accomplished by using the procedures specified in this~~

148 chapter (infrared spectrophotometry or thermal analysis). If neither of  
149 these procedures are applicable for a particular material, then an  
150 alternative procedure can be used. The alternate procedure must  
151 establish the identity on the basis of obtaining substantially equivalent  
152 results for the test article and its appropriate USP RS.

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

161 **Extractions**

162 Physicochemical testing of the plastic material requires that it be  
163 extracted or dissolved. Different tests are facilitated by various  
164 extraction methods. [Table 3](#) describes the extracts that are  
165 generated and the tests that are performed on those extracts.  
166 Subsequent discussions address methods for producing the  
167 extracts. Note that these extracts may be used for tests other  
168 than the physicochemical tests.

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**Table 3. Extractions Performed for Various Chemical Tests**

		Tests Performed on Plastics Using the Specified Extracting Solution							
Extraction	Extracting Solution	Cyclic Olefin, Polyethylene, and Polypropylene	Polyamide-6	Polycarbonate	Polyethylene Terephthalate and Polyethylene Terephthalate (G)	Poly(ethylene vinyl acetate)	Polyvinyl Chloride, Chloride	Polyvinyl Chloride, Plasticized	
S1	Water	Absorbance Acidity/alkalinity TOC	Absorbance Acidity/alkalinity TOC	Absorbance <sup>a</sup> Acidity/alkalinity TOC	Absorbance Acidity/alkalinity TOC	Absorbance Acidity/alkalinity TOC	Absorbance Acidity/alkalinity TOC	Absorbance Acidity/alkalinity TOC	
S2	Toluene	Phenolic antioxidants, nonphenolic antioxidants, amides, and stearates <sup>a</sup>	N/A	N/A	N/A	Phenolic antioxidants, amides, and stearic acid <sup>a</sup>	N/A	N/A	
S3	Acid	Extractable metals: Al, As, Cd, Co, Cr, Hg, Ba, Cd, Co, Hg,	Extractable metals: Al, As, Ba, Cd, Co, Hg,	Extractable metals: As, Ba, Ca, Cd, Co, Hg,	Extractable metals: Al, As, Ba, Cd, Co, Hg,	Extractable metals: Al, As, Cd, Co, Hg, Ni, Ba, Cd, Co, Hg,	Extractable metals: Al, As, Ba, Cd, Co, Hg,	Extractable metals: As, Ba, Ca, Cd, Co, Hg,	

		Tests Performed on Plastics Using the Specified Extracting Solution							
Extraction	Extracting Solution	Cyclic Olefin, Polyethylene, and Polypropylene	Polyamide-6	Polycarbonate	Polyethylene Terephthalate and Polyethylene Terephthalate	Poly(ethylene-vinyl acetate)	Polyvinyl Chloride	Polyvinyl Chloride, Plasticized	
		Ni, Pb, Ti, V, Zn, and Zr <sup>a</sup>	Mn, Ni, Pb, Ti, V, and Zn	Ni, Pb, Sn, V, and Zn	Mn, Ni, Pb, Ti, V, and Zn	Pb, V, and Zn	Ni, Pb, Ti, V, and Zn	Ni, Pb, Sn, V, and Zn	
S4	Alkali	N/A	Ge	N/A	Extractable metals: Sb and Ge	N/A	N/A	N/A	
S5	Alcohol	N/A	N/A	N/A	Absorbance	N/A	N/A	N/A	
S6	Tetrahydrofuran	N/A	N/A	N/A	N/A	N/A	Absorbance	N/A	
S7	Phenol	N/A	Free-base function	N/A	N/A	N/A	N/A	N/A	

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<sup>a</sup> 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.

174

175

b For polyethylene only.

176

c Not applicable for cyclic olefins and polypropylene.

177

d For material used for containers for non-injectable aqueous solutions.



179

## Extractable Metals

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The extractable metals testing described in this chapter is required for all

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plastic materials of construction used in packaging systems.

182

Specifically, all materials must be tested for those extractable metals

183

listed in [Table 3](#).<sup>▲ (USP 1-Aug-2020)</sup>

184

Change to read:

185

## CYCLIC OLEFINS

186

## Identification

187

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

188

▲Refer to *Mid-Infrared Spectroscopy (854)*.<sup>▲ (USP 1-Aug-2020)</sup>

189

## Apparatus:

190

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.

194

## Sample preparation

195

## Transmission mode:

196

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

199 (2000 psi or more). The temperatures at which the thin films are  
200 generated represent a trade-off between producing a melt (which  
201 dictates the lowest temperature necessary) and degrading the sample  
202 (which dictates the highest temperature allowed). Ultimately, the  
203 temperatures that are used are appropriate if the film produced is  
204 conducive to the infrared analysis.

205 **Internal reflectance mode:**

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

212 **Procedure:**

213 Place the mounted specimen sections in the sample compartment of the  
214 infrared spectrophotometer or the internal reflectance accessory, and  
215 place the assembly in the specimen beam of the infrared  
216 spectrophotometer. For internal reflectance, adjust the specimen  
217 position and mirrors within the accessory to permit maximum light  
218 transmission of the unattenuated reference beam. (For a double-beam  
219 instrument, attenuate the reference beam after completing the  
220 adjustment in the accessory to permit full-scale deflection during the  
221 scanning of the specimen.) Determine the infrared spectrum from 3800  
222  $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$  (2.6–15  $\mu\text{m}$ ).

223 **Acceptance criteria:**

224 The specimen exhibits an absorption spectrum that is substantially  
225 equivalent to that of [USP Cyclic Olefin Polymer RS](#) or [USP Cyclic Olefin](#)

226      Copolymer RS. Substantial, as opposed to exact, equivalence allows for  
227      minor spectral differences arising from the natural compositional and/or  
228      physical variation among polymers of this class. Substantial equivalence  
229      is achieved when all differences between the sample and RS spectra can  
230      be explained in the context of such natural compositional and/or physical  
231      variations.

232      •**Differential Scanning Calorimetry (DSC)**

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

237      **Extractable Metals**

238      **Aluminum:**

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

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

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

245      **Titanium:**

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

247      **Zinc:**

248 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.  
249 ~~Test results for additional relevant extractable metals are similarly~~  
250 ~~reported.~~ ▲ (USP 1-Aug-2020)

251 **Physicochemical Tests**

252 **Water extraction, Solution S1:**

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

259 **Absorbance**

260 Refer to *Ultraviolet-Visible Spectroscopy* (857).

261 **Procedure:**

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

263 **Acceptance criteria:**

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

270      **Acidity or alkalinity**

271      **BRP indicator solution:**

272      1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
273      mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

274      **Methyl orange solution:**

275      Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
276      with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
277      *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
278      1 N hydrochloric acid is required to change the color from yellow to red.

279      **Procedure:**

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

286      **Acceptance criteria:**

287      NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color  
288      of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is  
289      required to reach the beginning of the color change of the indicator from  
290      yellow to orange.

291      **Total organic carbon**

292      **Procedure:**

293 The total organic carbon (TOC) content of *Solution S1* is measured  
294 according to the general methodologies outlined in *Total Organic Carbon*  
295 <643>. However, although <643> is designed for the testing of high-purity  
296 water with low TOC values, material extracts may have TOC values that  
297 are higher than those of *Purified Water* because of extracted organic  
298 substances. Thus, the method used to perform the TOC analyses should  
299 have a limit of detection of 0.2 mg/L (ppm) and should have a  
300 demonstrated linear dynamic range from 0.2 to 20 mg/L (which  
301 encompasses the TOC limit). A linear range with a higher upper  
302 concentration can be used if linearity is established. If sample extracts  
303 exceed this upper linear range, they must be diluted appropriately for  
304 analysis.

305 **Acceptance criteria:**

306 The difference between the sample and blank TOC concentrations is NMT  
307 5 mg/L. If the specification for TOC is exceeded, then the material can  
308 still be considered compliant with this chapter if the chemicals  
309 responsible for the test results can be established (identity and  
310 concentration) and the chemicals are characterized to establish that the  
311 probable risk posed by all the chemicals, considered individually, is  
312 within acceptable parameters.

313 **Plastic Additives**

314 **Phenolic antioxidants**

315 **Solvent mixture:**

316 Acetonitrile and tetrahydrofuran (50:50, v/v)

317 **Toluene extraction, Solution S2:**

318 Place 2.0 g of the test material in a 250-mL borosilicate glass flask with  
319 a ground-glass neck. Add 80 mL of toluene and boil under a reflux  
320 condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add,  
321 with continued stirring, 120 mL of methanol. Pass the resulting solution  
322 through a sintered-glass filter. Rinse the flask and the filter with 25 mL  
323 of a mixture of 40 mL of toluene and 60 mL of methanol, add the  
324 rinsings to the filtrate, and dilute with the same mixture of solvents to  
325 250 mL to produce *Solution S2*. Prepare a blank solution.

326 **Sample solution S8:**

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

331 **Sample solution S9:**

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

336 **Reference solutions:**

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

340 **Reference solution A:**

341 0.1 mg/mL of [USP Butylated Hydroxytoluene RS](#) and 0.24 mg/mL of [USP](#)  
342 [Plastic Additive 1 RS](#) prepared in the *Solvent mixture*

343      **Reference solution B:**

344      0.24 mg/mL of [USP Plastic Additive 2 RS](#) and 0.24 mg/mL of [USP Plastic](#)  
345      [Additive 3 RS](#) prepared in the *Solvent mixture*

346      **Reference solution C:**

347      0.24 mg/mL of [USP Plastic Additive 4 RS](#) and 0.24 mg/mL of [USP Plastic](#)  
348      [Additive 5 RS](#) prepared in methylene chloride

349      **Reference solution D:**

350      0.1 mg/mL of [USP Butylated Hydroxytoluene RS](#) prepared in the *Solvent*  
351      *mixture*

352      **Reference solution E:**

353      0.24 mg/mL of [USP Plastic Additive 1 RS](#) prepared in the *Solvent*  
354      *mixture*

355      **Reference solution F:**

356      0.24 mg/mL of [USP Plastic Additive 6 RS](#) prepared in the *Solvent*  
357      *mixture*

358      **Reference solution G:**

359      0.24 mg/mL of [USP Plastic Additive 2 RS](#) prepared in the *Solvent*  
360      *mixture*

361      **Reference solution H:**

362      0.24 mg/mL of [USP Plastic Additive 3 RS](#) prepared in the *Solvent*  
363      *mixture*

364      **Reference solution I:**

365      0.24 mg/mL of [USP Plastic Additive 4 RS](#) prepared in methylene chloride

366      **Reference solution J:**

367      0.24 mg/mL of [USP Plastic Additive 5 RS](#) prepared in methylene chloride

368      •**TEST A:**

369      If the substance to be examined contains additive butylated  
370      hydroxytoluene and/or additive ethylene bis[3,3-bis[3-(1,1-  
371      dimethylethyl)-4-hydroxyphenyl]butanoate]([USP Plastic Additive 1 RS](#)),  
372      ▲then carry out *Test A.* ▲ (USP 1-Aug-2020)

373      **Mobile phase:**

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

375      **Chromatographic system**

376      (See *Chromatography* (621), *General Procedures, Liquid*  
377      *Chromatography*.)

378      **Detector:**

379      UV 280 nm

380      **Column:**

381        4.6-mm × 25-cm; 5-μm packing L1

382        **Flow rate:**

383        2 mL/min

384        **Injection volume:**

385        20 μL

386        **Run time:**

387        30 min

388        **System suitability**

389        **Resolution:**

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

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

397        **Analysis**

398        **Samples:**

399        *Sample solution S8*, corresponding blank solution, *Reference solution A*,  
400        and *Reference solution D*, *Reference solution E*, or both.

401 **Acceptance criteria:**

402 The peak areas of *Sample solution S8*, are less than the corresponding  
403 peak areas of *Reference solution D* or *Reference solution E*.

404 •**TEST B:**

405 If the substance to be examined contains one or more of the following  
406 antioxidants: pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-  
407 hydroxyphenyl)propionate] ([USP Plastic Additive 2 RS](#)); 2,2',2'',6,6',6''-  
408 hexa-*tert*-butyl-4,4',4''-[(2,4,6-trimethyl-1,3,5-benzene-  
409 triyl)trismethylene]triphenol ([USP Plastic Additive 3 RS](#)); octadecyl 3-  
410 (3,5-di *tert* butyl 4-hydroxyphenyl)propionate ([USP Plastic Additive 4](#)  
411 [RS](#)); tris(2,4-di *tert* butylphenyl) phosphite ([USP Plastic Additive 5](#)  
412 [RS](#));<sup>▲ (USP 1-Aug-2020)</sup> 1,3,5-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-s-triazine-  
413 2,4,6(1H,3H,5H)-trione ([USP Plastic Additive 6 RS](#)),<sup>▲</sup> then carry out *Test*  
414 **B.**<sup>▲ (USP 1-Aug-2020)</sup>

415 **Mobile phase:**

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

417 **Chromatographic system:**

418 Carry out the test as described in *Test A* with the following modifications.

419 **Detector:**

420 UV 280 nm

421 **Flow rate:**

422 1.5 mL/min

423      **Injection volume:**

424      20 µL

425      **System suitability**

426      **Resolution:**

427      Minimum 2.0 between [USP Plastic Additive 2 RS](#) (pentaerythrityl  
428      tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate]) and [USP](#)  
429      [Plastic Additive 3 RS](#) (2,2',2'',6,6',6''-hexa-*tert*-butyl-4,4',4''-[(2,4,6-  
430      trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol peaks), Reference  
431      solution B

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

435      **Analysis**

436      **Samples:**

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

440      **Acceptance criteria:**

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

444      •**TEST C:**

445 If the substance to be examined contains [USP Plastic Additive 4 RS](#)  
446 (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate) and/or [USP](#)  
447 [Plastic Additive 5 RS](#) (tris(2,4-di-*tert*-butylphenyl) phosphite), **then**  
448 carry out *Test C.* ▲ (USP 1-Aug-2020)

449 **Mobile phase:**

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

451 **Chromatographic system:**

452 Carry out the test as described in *Test A* with the following modifications.

453 **Detector:**

454 UV 280 nm

455 **Flow rate:**

456 1.5 mL/min

457 **Injection volume:**

458 20 µL

459 **System suitability**

460 **Resolution:**

461 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](#)  
462 (tris(2,4-di-*tert*-butylphenyl) phosphite) peaks, *Reference solution C*  
463

464      *Sample solution S8<sup>▲</sup>S9<sup>▲</sup>* (USP 1-Aug-2020) shows only peaks due to antioxidants  
465      stated in the composition and minor peaks that also correspond to the  
466      blank solution.

467      **Analysis**

468      **Samples:**

469      *Sample solution S9*, corresponding blank solution, *Reference solution C*,  
470      and either *Reference solution I* or *Reference solution J*

471      **Acceptance criteria:**

472      The peak areas of *Sample solution S9* are less than the corresponding  
473      peak areas of *Reference solution I* or *Reference solution J*.

474      **Nonphenolic antioxidants**

475      **Methylene chloride, acidified:**

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

478      **Iodine in ethanol detection solution:**

479      Dissolve 10 g of iodine in 100 mL of alcohol absolute. Store protected  
480      from light.

481      **Sample solution S10:**

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

484      **Reference solution M:**

485      6.0 mg/mL of [USP Plastic Additive 8 RS](#) prepared in methylene chloride.  
486      Dilute 2 mL of the solution with *Methylene chloride*, *acidified* to 10 mL.

487      **Reference solution N:**

488      6.0 mg/mL of [USP Plastic Additive 9 RS](#) prepared in methylene chloride.  
489      Dilute 2 mL of the solution with *Methylene chloride*, *acidified* to 10 mL.

490      **Reference solution O:**

491      6.0 mg/mL of [USP Plastic Additive 10 RS](#) prepared in methylene chloride.  
492      Dilute 2 mL of the solution with *Methylene chloride*, *acidified* to 10 mL.

493      **Reference solution P:**

494      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.

497      **Mobile phase A:**

498      Hexane

499      **Mobile phase B:**

500      Methylene chloride ▲ (USP 1-Aug-2020)

501      **Chromatographic system**

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

504      **Detector:**

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

507      **Plate:**

508      TLC silica gel GF<sub>254</sub>

509      **Application volume:**

510      20 µL

511      **Development A:**

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

513      **Development B:**

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

515      **System suitability**

516      **Resolution:**

517      The chromatogram shows two clearly separated spots, *Reference*  
518      *solution P*.

519      **Analysis**

520      **Samples:**

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

524      **Acceptance criteria:**

525      Any spots in the chromatogram of *Sample solution S10* are not more  
526      intense than the spots in the same positions in the chromatograms of  
527      the *Reference solutions*

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

530      **Solvent mixture:**

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

532      **Sample solution S11:**

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

539      **Reference solution Q:**

540      0.6 mg/mL of [USP Plastic Additive 11 RS](#) prepared in toluene. Add 1 mL  
541      of this solution to 25 mL of the blank solution corresponding to *Solution*  
542      *S2*, and evaporate to dryness under vacuum at 45°. Prepare a blank  
543      solution from the blank solution corresponding to *Solution S2*. Dissolve  
544      the residue with 10 mL of toluene and 10 mL of a 10-g/L solution of

545 tetrabutylammonium hydroxide in a mixture of 35 volumes of toluene  
546 and 65 volumes of anhydrous ethanol. Boil under a reflux condenser for  
547 3 h. Allow to cool, and filter if necessary.

548 **Mobile phase:**

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

550 **Chromatographic system**

551 (See *Chromatography* (621), *General Procedures, Liquid*  
552 *Chromatography*.)

553 **Detector:**

554 UV 227 nm

555 **Column:**

556 4.6-mm × 25-cm; 5-μm packing L8

557 **Flow rate:**

558 2 mL/min

559 **Injection volume:**

560 20 μL

561 **System suitability**

562 **Resolution:**

563 Minimum of 7 between the peaks of the diol component and the diluents  
564 of *Reference solution Q*

565 **Analysis**

566 **Samples:**

567 *Sample solution S11*, the corresponding blank solution, and *Reference*  
568 *solution Q*

569 **Acceptance criteria:**

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

572 **Amides and stearates**

573 **Sample solution:**

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

575 **Reference solution R:**

576 2.0 mg/mL of [USP Stearic Acid RS](#) prepared in methylene chloride

577 **Reference solution S:**

578 2.0 mg/mL of [USP Plastic Additive 12 RS](#) prepared in methylene chloride

579 **Reference solution T:**

580 2.0 mg/mL of [USP Plastic Additive 13 RS](#) prepared in methylene chloride

581      **Chromatographic system**

582      (See *Chromatography* {621}, *General Procedures, Thin-Layer*  
583      *Chromatography*.)

584      **Plate:**

585      TLC silica gel GF<sub>254</sub>

586      •**TEST A**

587      **Mobile phase:**

588      2,2,4-trimethylpentane and anhydrous ethanol (75:25, v/v)

589      **Application volume:**

590      10 µL

591      **Development:**

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

593      **Detector:**

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

597      **Analysis**

598      **Samples:**

599      *Sample solution S10 and Reference solution R*

600      **Acceptance criteria:**

601      Any spot corresponding to additive stearic acid in *Sample solution S10* is  
602      identical in position ( $R_f$  about 0.5) but is not more intense than the spot  
603      in the same position in *Reference solution R*.

604      •**TEST B**

605      **Mobile phase A:**

606      Hexane

607      **Mobile phase B:**

608      Methylene chloride and methanol (95:5, v/v)

609      **Application volume:**

610      10 µL

611      **Development A:**

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

613      **Development B:**

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

615      **Detector:**

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

618      **Analysis**

619      **Samples:**

620      *Sample solution S10, Reference solution S, and Reference solution T*

621      **Acceptance criteria:**

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

626      Change to read:

627      **POLYAMIDE 6**

628      **Identification**

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

631      **•A. INFRARED SPECTROPHOTOMETRY (197F)**

632      Refer to (854). ▲ (USP 1-Aug-2020)

633      **Apparatus:**

634      Use an infrared spectrophotometer capable of correcting for the blank  
635      spectrum and able to measure in transmission mode or equipped with an

636 internal reflectance accessory and an appropriate internal reflectance  
637 plate.

638 **Sample preparation**

639 **Transmission mode:**

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

649 **Internal reflectance mode:**

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

656 **Procedure:**

657 Place the mounted specimen sections in the sample compartment of the  
658 infrared spectrophotometer or the internal reflectance accessory, and  
659 place the assembly in the specimen beam of the infrared  
660 spectrophotometer. For internal reflectance, adjust the specimen  
661 position and mirrors within the accessory to permit maximum light  
662 transmission of the unattenuated reference beam. (For a double-beam

663 instrument, attenuate the reference beam after completing the  
664 adjustment in the accessory to permit full-scale deflection during the  
665 scanning of the specimen.) Determine the infrared spectrum from 3800  
666  $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$  (2.6–15  $\mu\text{m}$ ).

667 **Acceptance criteria:**

668 The specimen exhibits an absorption spectrum that is substantially  
669 equivalent to that of [USP Polyamide 6 RS](#). Substantial, as opposed to  
670 exact, equivalence allows for minor spectral differences arising from the  
671 natural compositional and/or physical variation among polymers of this  
672 class. Substantial equivalence is achieved when all differences between  
673 the sample and RS spectra can be explained in the context of such  
674 natural compositional and/or physical variations.

675 **•B. THERMAL ANALYSIS**

676 Refer to *Thermal Analysis* (891).

677 **Sample preparation:**

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

681 **Procedure:**

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

687 **Acceptance criteria:**

688 The thermal analysis curve of the specimen is similar to the thermal  
689 analysis curve of [USP Polyamide 6 RS](#), and the melting peak  
690 temperature obtained from the thermal analysis curve of the specimen  
691 does not differ from that of the RS by more than 8.0°. Note that the  
692 results of the DSC analysis are strongly dependent on the amount of  
693 plasticizer in the test article.

694 **Physicochemical Tests**

695 **Water extraction, Solution S1:**

696 Place 25.0 g of the test material in a borosilicate glass flask with a  
697 ground-glass neck. Add 500 mL of *Purified Water* and boil under a reflux  
698 condenser for 5 h. Allow the solution to cool to ambient temperature,  
699 decant and pass the solution through a sintered glass filter; the filtered  
700 solution is designated *Solution S1*. Use *Solution S1* within 4 h of  
701 preparation.

702 **Absorbance**

703 Refer to {857}.

704 **Procedure:**

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

706 **Acceptance criteria:**

707 NMT 0.25. If the specification for absorbance is exceeded, then the  
708 material can still be considered compliant with this chapter if the  
709 chemicals responsible for the test results can be established (identity  
710 and concentration) and the chemicals are characterized to establish that

711 the probable risk posed by all the chemicals, considered individually, is  
712 within acceptable parameters.

713 **Acidity or alkalinity**

714 **BRP indicator solution:**

715 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
716 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

717 **Methyl orange solution:**

718 Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
719 with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
720 *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
721 1 N hydrochloric acid is required to change the color from yellow to red.

722 **Procedure:**

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

729 **Acceptance criteria:**

730 NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color  
731 of the indicator to blue. NMT 4.0 mL of 0.01 N hydrochloric acid is  
732 required to reach the beginning of the color change of the indicator from  
733 yellow to orange.

734 **Total organic carbon**

735      **Procedure:**

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

747      **Acceptance criteria:**

748      The difference between the sample and blank TOC concentrations is NMT  
749      5 mg/L. If the specification for TOC is exceeded, then the material can  
750      still be considered compliant with this chapter if the chemicals  
751      responsible for the test results can be established (identity and  
752      concentration) and the chemicals are characterized to establish that the  
753      probable risk posed by all the chemicals, considered individually, is  
754      within acceptable parameters.

755      **Free base functions**

756      **Titrant (perchloric acid in phenol):**

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

759      **Phenol extraction, Solution S7:**

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

763 **Procedure:**

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

769 **Acceptance criteria:**

770 The difference between the titration volumes, extract versus extraction  
771 blank, is NMT 0.4 mL.

772 **Extractable metals**

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

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

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

781 **Related Substances**

782 **Caprolactam**

783      **Sample solution:**

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

787      **Caprolactam primary solution:**

788      Place 125 mg of [USP Caprolactam RS](#) in a 50-mL volumetric flask,  
789      dissolve by adding anhydrous formic acid. Dilute with anhydrous formic  
790      acid to volume. The caprolactam concentration of this primary solution is  
791      approximately 2500 mg/L.

792      **Reference solutions:**

793      Pipet 0, 2, 4, 6, 8, and 10 mL of the *Caprolactam primary solution* into  
794      six 20-mL volumetric flasks. Dilute with anhydrous formic acid to  
795      volume. The 6 reference solutions thus obtained (*Reference solution*  
796      *blank* and *Reference solution WS1* through *WS5*) contain, respectively,  
797      0, 250, 500, 750, 1000, and 1250 mg/L of caprolactam.

798      **Chromatographic system**

799      (See *Chromatography* (621), *General Procedures, Gas Chromatography.*)

800      **Column:**

801      30-m<sup>▲</sup>0.25-mm<sup>▲</sup> (USP 1-Aug-2020) × 30-m<sup>▲</sup>0.25-μm<sup>▲</sup> (USP 1-Aug-2020) phase G25

802      **Temperatures**

803      **Injection port:**

804        250°

805        **Column:**

806        Hold at 160° for 2 min, ramped to 210° at 5°/min, and hold at 210° for  
807        10 min

808        **Detector:**

809        Flame ionization detector (FID) 250°

810        **Carrier gas:**

811        Helium

812        **Flow rate:**

813        1 mL/min

814        **Injection volume:**

815        1 µL

816        **Injection type:**

817        Split ratio, 3:1

818        **Analysis**

819        **Conditioning:**

820        Inject the *Reference solution blank* 3 times into the chromatographic  
821        system.

822     **System suitability:**

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

827     **Rinsing:**

828       Inject *Reference solution blank* once.

829     **Calibration, front of bracket:**

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

834     **Rinsing:**

835       Inject the *Reference solution blank* once.

836     **Sample:**

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

838     **Rinsing:**

839       Inject *Reference solution blank* once.

840     **Calibration, back of bracket:**

841       Inject each of the 5 *Reference solutions* once.

842     **Calculations:**

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

852 **Acceptance criteria:**

853 NMT 1%

854 Change to read:

855 **POLYCARBONATE**

856 **Identification**

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

859 **•A. INFRARED SPECTROPHOTOMETRY {~~(197A)~~}**

860 Refer to {~~(854)~~}.<sup>▲</sup> (USP 1-Aug-2020)

861 **Apparatus:**

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

866      **Sample preparation**

867      **Transmission mode:**

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

877      **Internal reflectance mode:**

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

884      **Procedure:**

885      Prepare a hot-pressed film. Otherwise, dissolve 0.5 g of test material in  
886      10 mL of methylene chloride by boiling under a reflux condenser for 15  
887      min. Place a few drops of the resulting solution on a sodium chloride  
888      slide and evaporate the solvent in an oven at 80°. Determine the  
889      infrared spectrum from 3800 cm<sup>-1</sup> to 650 cm<sup>-1</sup> (2.6–15 µm).

890      **Acceptance criteria:**

891 The specimen exhibits an absorption spectrum that is substantially  
892 equivalent to that of [USP Polycarbonate RS](#). Substantial, as opposed to  
893 exact, equivalence allows for minor spectral differences arising from the  
894 natural compositional and/or physical variation among polymers of this  
895 class. Substantial equivalence is achieved when all differences between  
896 the sample and RS spectra can be explained in the context of such  
897 natural compositional and/or physical variations.

898 **•B. THERMAL ANALYSIS**

899 Refer to [\(891\)](#).

900 **Sample preparation:**

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

904 **Procedure:**

905 Determine the thermal analysis curve under nitrogen, using  
906 heating/cooling conditions specified for the polymer type and using  
907 equipment capable of performing the determinations as described in  
908 [\(891\)](#). Heat the specimen from  $-20^{\circ}$  to  $300^{\circ}$  at a heating rate of about  
909  $10^{\circ}/\text{min}$ . Quickly cool the specimen to room temperature.

910 **Acceptance criteria:**

911 The thermal analysis curve of the specimen is similar to the thermal  
912 analysis curve of [USP Polycarbonate RS](#), and the melting peak  
913 temperature obtained from the thermal analysis curve of the specimen  
914 does not differ from that of the RS by more than  $8.0^{\circ}$ . Note that the  
915 results of the DSC analysis are strongly dependent on the amount of  
916 plasticizer in the test article.

917 **Physicochemical Tests**

918 **Water extraction, Solution S1:**

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

925 **Absorbance**

926 Refer to (857).

927 **Procedure:**

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

929 **Acceptance criteria:**

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

936 **Acidity or alkalinity**

937 **BRP indicator solution:**

938        1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
939        mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

940        **Methyl orange solution:**

941        Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
942        with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
943        *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
944        1 N hydrochloric acid is required to change the color from yellow to red.

945        **Total organic carbon**

946        **Procedure:**

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

958        **Acceptance criteria:**

959        The difference between the sample and blank TOC concentrations is NMT  
960        5 mg/L. If the specification for TOC is exceeded, then the material can  
961        still be considered compliant with this chapter if the chemicals  
962        responsible for the test results can be established (identity and  
963        concentration) and the chemicals are characterized to establish that the

964       probable risk posed by all the chemicals, considered individually, is  
965       within acceptable parameters.

966       **Extractable Metals**

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

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

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

975       **Related Substances**

976       **Residual solvents**

977       **Sample solution:**

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

982       **Residual solvents primary solution:**

983       Accurately weigh 500 mg each of dichloromethane, toluene, and  
984       ethylbenzene and 1250 mg of chlorobenzene into a 50-mL volumetric  
985       flask; dissolve and adjust with *N,N'*-dimethylformamide to volume.

986     **Residual solvents stock solution:**

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

991     **Reference solutions:**

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

1000     **Chromatographic system**

1001     (See *Chromatography* (621), *General Procedures, Gas Chromatography.*)

1002     **Headspace autosampler**

1003     **Temperatures**

1004     **Thermostating:**

1005         115°

1006     **Needle:**

1007         110°

1008      **Transfer:**

1009      120°

1010      **Times**

1011      **Thermostating:**

1012      60 min

1013      **Pressurization:**

1014      0.5 min

1015      **Injection:**

1016      0.1 min

1017      **Withdrawal:**

1018      0.2 min

1019      **Carrier gas pressure:**

1020      20 psi

1021      **Column:**

1022      Stainless steel, 30-m<sup>▲</sup>0.32-mm<sup>▲</sup>(USP 1-Aug-2020) × 0.32-mm<sup>▲</sup>30-m<sup>▲</sup>(USP 1-Aug-2020)  
1023      containing stationary phase (0.5 µm) coated with 100% bonded and  
1024      cross-linked polyethylene glycol; phase G39

1025      **Temperatures**

- 1026     **Injection port:**
- 1027       140°
- 1028     **Column:**
- 1029       Start at 50°, hold for 20 min. Heat to 165° at 6°/min, hold for 20 min.
- 1030     **Detector:**
- 1031       FID 250°
- 1032     **Carrier gas:**
- 1033       Helium
- 1034     **Flow rate:**
- 1035       Adequate to provide a constant pressure of 10 psi
- 1036     **Injection volume:**
- 1037       1 µL
- 1038     **Injection type:**
- 1039       Split
- 1040     **Analysis**
- 1041     **Conditioning:**

1042     Inject the *Reference solution blank* 2 times into the chromatographic  
1043     system.

1044     **System suitability:**

1045     Inject *Reference solution WS3* 5 times into the chromatographic system.  
1046     Note that one injection is done from each autosampler vial. The  
1047     %relative standard deviation of the peak areas obtained for each analyte  
1048     for these injections must be NMT 5%.

1049     **Rinsing:**

1050     ~~Inject the *Reference solution blank* once.~~▲ (USP 1-Aug-2020)

1051     **Calibration, front of bracket:**

1052     Inject each of the 5*Reference solutions* once. Construct a linear  
1053     calibration curve of the peak areas obtained for the *Reference solutions*  
1054     versus their analyte concentrations for each analyte. The correlation  
1055     coefficient (*r*) obtained for the best-fit linear regression line must be NLT  
1056     0.99.

1057     **Rinsing:**

1058     Inject the *Reference solution blank* once.

1059     **Sample:**

1060     Inject *Sample solution* once, including the sample blank. Inject NMT 6  
1061     *Sample solutions*.

1062     **Rinsing:**

1063 Inject Reference solution blank once.

## 1064 Calibration, back of bracket:

1065 Inject each of the 5 *Reference solutions* once.

## 1066 Calculations:

1067 Construct a linear calibration curve of the peak areas obtained for the  
1068 *Reference solutions* versus their analyte concentrations (using the front  
1069 and back of the bracket). The correlation coefficient (*r*) obtained for the  
1070 best-fit linear regression line must be NLT 0.99. Calculate the amount of  
1071 each analyte in the *Sample solution* by putting the peak area obtained  
1072 for the *Sample solution* into the calibration curve.

1073 Calculate the amount of each in the test material by multiplying this  
1074 result by a factor of 10 and dividing the product by the weight of the  
1075 test material in g, producing a result in  $\mu\text{g/g}$ .

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

## 1078 Acceptance criteria

## 1079 Methylene chloride:

1080 NMT 200 µg/g

1081 Toluene:

1082 NMT 200 µg/g

1083      **Sum of toluene and ethylbenzene:**

1084      NMT 200 µg/g

1085      **Chlorobenzene:**

1086      NMT 500 µg/g

1087      **Bisphenol A**

1088      [NOTE—Bisphenol A is monitored although it is a residual monomer and  
1089      not an additive.]

1090      **Sample solution:**

1091      Weigh approximately 1.0 g of the test material and place it in a 250-mL  
1092      round-bottom flask. Add 50 mL of methylene chloride and slightly heat  
1093      at approximately 35° for 1 h under a reflux condenser to dissolve the  
1094      test material. Cool the solution to room temperature and slowly add 75  
1095      mL of methanol to the room-temperature solution, stirring continuously.  
1096      Place in a refrigerator for 2 h to cool the resulting solution. Pass the  
1097      cooled solution through a sintered-glass filter. Wash the round-bottom  
1098      flask and the filter twice with 15 mL of methanol. Evaporate the filtrate  
1099      to dryness under vacuum at 45°. Dissolve the residue in 5 mL of  
1100      methylene chloride. Add 0.5 mL of this solution and 0.5 mL of *N,O*-  
1101      bis(trimethylsilyl)trifluoroacetamide to a 1.5-mL vial and close the vial  
1102      immediately. Heat the closed vial at 40° for 2 h and then cool to room  
1103      temperature. Prepare a sample blank in a similar fashion.

1104      **Bisphenol A primary solution:**

1105      Accurately weigh 20 mg of [USP Bisphenol A RS](#) in a 200-mL volumetric  
1106      flask; dissolve and dilute with methylene chloride to volume. The

1107 bisphenol A concentration of this primary solution is approximately 100  
1108 mg/L.

1109 **Reference solutions:**

1110 Pipet 0, 5, 10, 20, 30, and 40 mL of the *Bisphenol A primary solution*  
1111 into six 100-mL volumetric flasks. Dilute with methylene chloride to  
1112 volume and mix well. The 6 reference solutions thus obtained (*Reference*  
1113 *solution blank* and *Reference solution WS1* through *WS5*) contain,  
1114 respectively, 0, 5, 10, 20, 30, and 40 mg/L of bisphenol A.

1115 Add 0.5 mL each of the *Reference solutions* and 0.5 mL of *N,O-*  
1116 *bis(trimethylsilyl)trifluoroacetamide* to separate 1.5-mL vials and close  
1117 the vials immediately. Heat the closed vials at 40° for 2 h and then  
1118 cool to room temperature.

1119 **Chromatographic system**

1120 (See *Chromatography* (621), *General Procedures, Gas Chromatography.*)

1121 **Column:**

1122 Stainless steel, 25-m × 0.25-mm; stationary phase (0.25 µm) coated  
1123 with 100% dimethylpolysiloxane, phase G38

1124 **Temperatures**

1125 **Injection port:**

1126 300°

1127 **Column:**

1128      250°

1129      **Detector:**

1130      FID 300°

1131      **Carrier gas:**

1132      Helium

1133      **Flow rate:**

1134      Adequate to provide a constant pressure of 13 psi

1135      **Injection volume:**

1136      2 µL

1137      **Injection type:**

1138      Split

1139      **Analysis**

1140      **Conditioning:**

1141      Inject the *Reference solution blank* 3 times into the chromatographic  
1142      system.

1143      **System suitability:**

1144 Inject *Reference solution WS3* 5 times into the chromatographic system.  
1145 The % relative standard deviation of the peak areas obtained for these  
1146 injections must be NMT 5%.

1147 **Rinsing:**

1148 Inject the *Reference solution blank* twice.

1149 **Calibration, front of bracket:**

1150 Inject each of the 5 *Reference solutions* once. Construct a linear  
1151 calibration curve of the peak areas obtained for the *Reference solutions*  
1152 versus their bisphenol A concentrations. The correlation coefficient (*r*)  
1153 obtained for the best-fit linear regression line must be NLT 0.98.

1154 **Rinsing:**

1155 Inject the *Reference solution blank* once.

1156 **Sample:**

1157 Inject *Sample solution* once, including the sample blank. Inject NMT 6  
1158 *Sample solutions*.

1159 **Rinsing:**

1160 Inject the *Reference solution blank* once.

1161 **Calibration, back of bracket:**

1162 Inject each of the 5 *Reference solutions* once.

1163 **Calculations:**

1164 Construct a linear calibration curve of the peak areas obtained for the  
1165 *Reference solutions* versus their bisphenol A concentrations (front and  
1166 back of bracket). The correlation coefficient (*r*) obtained for the best-fit  
1167 linear regression line must be NLT 0.99. Calculate the amount of  
1168 bisphenol A in the *Sample solution* by putting the peak area obtained for  
1169 the *Sample solution* into the calibration curve.

1170 Calculate the amount of bisphenol A in the test material by multiplying  
1171 this result by a factor of 5 and dividing the product by the weight of  
1172 the test material in g, producing a result in µg/g.

1173 Bisphenol A (µg/g) = [bisphenol A in *Sample solution* (mg/L) ×  
1174 5]/weight of test material (g)

1175 **Acceptance criteria:**

1176 NMT 100 µg/g

1177 Change to read:

1178 **POLYETHYLENE**

1179 **Identification**

1180 [NOTE—The identification of low-density polyethylene and high-density  
1181 polyethylene needs compliance with only one test procedure to be  
1182 established.]

1183 **•A. INFRARED SPECTROPHOTOMETRY (197F)**

1184 Refer to [\(854\)](#). ▲ (USP 1-Aug-2020)

1185      **Apparatus:**

1186      Use an infrared spectrophotometer capable of correcting for the blank  
1187      spectrum and able to measure in transmission mode or equipped with an  
1188      internal reflectance accessory and an appropriate internal reflectance  
1189      plate.

1190      **Sample preparation**

1191      **Transmission mode:**

1192      Prepare a specimen of appropriate thickness (about 250 µm) without  
1193      visible defects (cracks or holes). The specimens can be compressed to  
1194      form a thin, uniform film by exposure to elevated temperatures and  
1195      pressures (2000 psi or more). The temperatures at which the thin films  
1196      are generated represent a trade-off between producing a melt (which  
1197      dictates the lowest temperature necessary) and degrading the sample  
1198      (which dictates the highest temperature allowed). Ultimately, the  
1199      temperatures that are used are appropriate if the film produced is  
1200      conducive to the infrared analysis.

1201      **Internal reflectance mode:**

1202      Prepare a flat section and trim it as necessary to obtain a segment that  
1203      is convenient for mounting in the internal reflectance accessory. Taking  
1204      care to avoid scratching the surfaces, wipe the specimen with dry paper  
1205      or, if necessary, a soft cloth dampened with methanol, and permit the  
1206      surfaces to dry. Then securely mount the specimen on the internal  
1207      reflection plate, ensuring adequate surface contact.

1208      **Procedure:**

1209      Place the mounted specimen sections in the sample compartment of the  
1210      infrared spectrophotometer or the internal reflectance accessory, and

1211 place the assembly in the specimen beam of the infrared  
1212 spectrophotometer. For internal reflectance, adjust the specimen  
1213 position and mirrors within the accessory to permit maximum light  
1214 transmission of the unattenuated reference beam. (For a double-beam  
1215 instrument, attenuate the reference beam after completing the  
1216 adjustment in the accessory to permit full-scale deflection during the  
1217 scanning of the specimen.) Determine the infrared spectrum from 3800  
1218  $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$  (2.6–15  $\mu\text{m}$ ).

1219 **Acceptance criteria**

1220 **Low-density polyethylene:**

1221 The specimen exhibits an absorption spectrum that is substantially  
1222 equivalent to that of [USP Low-Density Polyethylene RS](#). Substantial, as  
1223 opposed to exact, equivalence allows for minor spectral differences  
1224 arising from the natural compositional and/or physical variation among  
1225 polymers of this class. Substantial equivalence is achieved when all  
1226 differences between the sample and RS spectra can be explained in the  
1227 context of such natural compositional and/or physical variations.

1228 **High-density polyethylene:**

1229 The specimen exhibits an absorption spectrum that is substantially  
1230 equivalent to that of [USP High-Density Polyethylene RS](#). Substantial, as  
1231 opposed to exact, equivalence allows for minor spectral differences  
1232 arising from the natural compositional and/or physical variation among  
1233 polymers of this class. Substantial equivalence is achieved when all  
1234 differences between the sample and RS spectra can be explained in the  
1235 context of such natural compositional and/or physical variations.

1236 **•B. THERMAL ANALYSIS**

1237 Refer to (891).

1238     **Sample preparation:**

1239     Place an appropriately sized sample in the test specimen pan. [NOTE—  
1240     Intimate contact between the pan and the thermocouple is essential for  
1241     obtaining reproducible results.]

1242     **Procedure:**

1243     Determine the thermal analysis curve under nitrogen at temperatures  
1244     between 40° and 200° at a heating rate between 2° and 10°/min,  
1245     followed by cooling at a rate between 2° and 10°/min, to 40°. Using  
1246     equipment capable of performing the determinations as described in  
1247     <891>.

1248     **Acceptance criteria**

1249     **Low-density polyethylene:**

1250     The thermal analysis curve of the specimen is similar to the thermal  
1251     analysis curve of [USP Low-Density Polyethylene RS](#), and the melting  
1252     peak temperature obtained from the thermal analysis curve of the  
1253     specimen does not differ from that of the RS by more than 8.0°.

1254     **High-density polyethylene:**

1255     The thermal analysis curve of the specimen is similar to the thermal  
1256     analysis curve of [USP High-Density Polyethylene RS](#), and the melting  
1257     peak temperature obtained from the thermal analysis curve of the  
1258     specimen does not differ from that of the RS by more than 6.0°.

1259     **Physicochemical Tests**

1260     **Water extraction, Solution S1:**

1261 Place 25 g of the test material in a borosilicate glass flask with a ground-  
1262 glass neck. Add 500 mL of *Purified Water*, and boil under reflux  
1263 conditions for 5 h. Allow to cool, and pass the extracting solution  
1264 through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric  
1265 flask and dilute with *Purified Water* to volume; the diluted solution is  
1266 designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

1267 **Absorbance**

1268 Refer to *(857)*.

1269 **Procedure:**

1270 Determine the spectrum between 220 and 340 nm in *Solution S1*.

1271 **Acceptance criteria:**

1272 NMT 0.2. If the specification for absorbance is exceeded, then the  
1273 material can still be considered compliant with this chapter if the  
1274 chemicals responsible for the test results can be established (identity  
1275 and concentration) and the chemicals are characterized to establish that  
1276 the probable risk posed by all the chemicals, considered individually, is  
1277 within acceptable parameters.

1278 **Acidity or alkalinity**

1279 **BRP indicator solution:**

1280 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
1281 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

1282 **Methyl orange solution:**

1283 Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
1284 with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
1285 *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
1286 1 N hydrochloric acid is required to change the color from yellow to red.

1287 **Procedure:**

1288 To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*.  
1289 Determine the titration volume of 0.01 N sodium hydroxide required to  
1290 change the color of the indicator to blue. To a separate, 100-mL portion  
1291 of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the  
1292 titration volume of 0.01 N hydrochloric acid required to reach the  
1293 beginning of the color change of the indicator from yellow to orange.

1294 **Acceptance criteria:**

1295 NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color  
1296 of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is  
1297 required to reach the beginning of the color change of the indicator from  
1298 yellow to orange.

1299 **Total organic carbon**

1300 **Procedure:**

1301 The TOC content of *Solution S1* is measured according to the general  
1302 methodologies outlined in (643). However, although (643) is designed for  
1303 the testing of high-purity water with low TOC values, material extracts  
1304 may have TOC values that are higher than those of *Purified Water*  
1305 because of extracted organic substances. Thus, the method used to  
1306 perform the TOC analyses should have a limit of detection of 0.2 mg/L  
1307 (ppm) and should have a demonstrated linear dynamic range from 0.2  
1308 to 20 mg/L (which encompasses the TOC limit). A linear range with a  
1309 higher upper concentration can be used if linearity is established. If

1310 sample extracts exceed this upper linear range, they must be diluted  
1311 appropriately for analysis.

1312 **Acceptance criteria:**

1313 The difference between the sample and blank TOC concentrations is NMT  
1314 5 mg/L. If the specification for TOC is exceeded, then the material can  
1315 still be considered compliant with this chapter if the chemicals  
1316 responsible for the test results can be established (identity and  
1317 concentration) and the chemicals are characterized to establish that the  
1318 probable risk posed by all the chemicals, considered individually, is  
1319 within acceptable parameters.

1320 **Extractable Metals**

1321 **Aluminum:**

1322 ~~Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.~~

1323 **Arsenic, cadmium, lead, mercury, cobalt, and nickel:**

1324 Report the measured value in ~~Solution S3 at values above 0.01 mg/L~~  
1325 ~~(ppm), corresponding to 0.025 µg/g. If the measured values are below~~  
1326 ~~these values, report the result as less than 0.01 mg/L (ppm),~~  
1327 ~~corresponding to less than 0.025 µg/g.~~

1328 **Chromium:**

1329 ~~Solution S3 contains NMT 0.02 mg/L (ppm), corresponding to 0.05 µg/g.~~

1330 **Titanium:**

1331 ~~Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.~~

1332

### **Vanadium:**

1333

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

1334

### **Zinc:**

1335

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

1336

### **Zirconium:**

1337

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

1338

~~Test results for additional relevant extractable metals are similarly~~

1339

~~reported.~~▲ (USP 1-Aug-2020)

1340

## **Plastic Additives**

1341

The test results from these analyses are reported.

1342

## **Phenolic antioxidants**

1343

### **Solvent mixture:**

1344

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

1345

### **Toluene extraction, Solution S2:**

1346

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

1347

1348

1349

1350

1351 of a mixture of 40 mL of toluene and 60 mL of methanol, add the  
1352 rinsings to the filtrate, and dilute with the same mixture of solvents to  
1353 250 mL to produce *Solution S2*. Prepare a blank solution.

1354 **Sample solution S8:**

1355 Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°.  
1356 Dissolve the resulting residue with 5.0 mL of the *Solvent mixture* to  
1357 produce *Sample solution S8*. Prepare a blank solution from the blank  
1358 solution corresponding to *Solution S2*.

1359 **Sample solution S9:**

1360 Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°.  
1361 Dissolve the residue with 5.0 mL of methylene chloride to produce  
1362 *Sample solution S9*. Prepare a blank solution from the blank solution  
1363 corresponding to *Solution S2*.

1364 **Reference solutions:**

1365 Of the following reference solutions, prepare only those that are  
1366 necessary for the analysis of the phenolic antioxidants stated in the  
1367 composition of the substance to be examined.

1368 **Reference solution A:**

1369 0.1 mg/mL of [USP Butylated Hydroxytoluene RS](#) and 0.24 mg/mL of [USP](#)  
1370 [Plastic Additive 1 RS](#) prepared in the *Solvent mixture*

1371 **Reference solution B:**

1372 0.24 mg/mL of [USP Plastic Additive 2 RS](#) and 0.24 mg/mL of [USP Plastic](#)  
1373 [Additive 3 RS](#) prepared in the *Solvent mixture*

1374      **Reference solution C:**

1375      0.24 mg/mL of [USP Plastic Additive 4 RS](#) and 0.24 mg/mL of [USP Plastic](#)  
1376      [Additive 5 RS](#) prepared in methylene chloride

1377      **Reference solution D:**

1378      0.1 mg/mL of [USP Butylated Hydroxytoluene RS](#) prepared in the *Solvent*  
1379      *mixture*

1380      **Reference solution E:**

1381      0.24 mg/mL of [USP Plastic Additive 1 RS](#) prepared in the *Solvent*  
1382      *mixture*

1383      **Reference solution F:**

1384      0.24 mg/mL of [USP Plastic Additive 6 RS](#) prepared in the *Solvent*  
1385      *mixture*

1386      **Reference solution G:**

1387      0.24 mg/mL of [USP Plastic Additive 2 RS](#) prepared in the *Solvent*  
1388      *mixture*

1389      **Reference solution H:**

1390      0.24 mg/mL of [USP Plastic Additive 3 RS](#) prepared in the *Solvent*  
1391      *mixture*

1392      **Reference solution I:**

1393      0.24 mg/mL of [USP Plastic Additive 4 RS](#) prepared in methylene chloride

1394     **Reference solution J:**

1395     0.24 mg/mL of [USP Plastic Additive 5 RS](#) prepared in methylene chloride

1396     ●**TEST A:**

1397     If the substance to be examined contains additive butylated  
1398     hydroxytoluene and/or additive ethylene bis[3,3-bis[3-(1,1-  
1399     dimethylethyl)-4-hydroxyphenyl]butanoate] ([USP Plastic Additive 1 RS](#)),  
1400     ▲then carry out *Test A.* ▲ (USP 1-Aug-2020)

1401     **Chromatographic system**

1402     (See *Chromatography* (621), *General Procedures, Liquid*  
1403       *Chromatography.*)

1404     **Mobile phase:**

1405     Acetonitrile and *Purified Water* (70:30, v/v)

1406     **Detector:**

1407     UV 280 nm

1408     **Column:**

1409     4.6-mm × 25-cm; 5-μm packing L1

1410     **Flow rate:**

1411     2 mL/min

1412     **Injection volume:**

1413      20 µL

1414      **Run time:**

1415      30 min

1416      **System suitability**

1417      **Resolution:**

1418      Minimum 5.0 between the additive [USP Butylated Hydroxytoluene RS](#)  
1419      and [USP Plastic Additive 1 RS](#) (ethylene bis[3,3-bis[3-(1,1-  
1420      dimethylethyl)-4-hydroxyphenyl]butanoate]) peaks, *Reference solution*  
1421      A

1422      *Sample solution S8* shows only peaks caused by antioxidants stated in  
1423      the composition and minor peaks that also correspond to the blank  
1424      solution.

1425      **Analysis**

1426      **Samples:**

1427      *Sample solution S8*, corresponding blank solution, *Reference solution A*,  
1428      and *Reference solution D*, *Reference solution E*, or both

1429      **Acceptance criteria:**

1430      The peak areas of *Sample solution S8* are less than the corresponding  
1431      peak areas of *Reference solution D* or *Reference solution E*.

1432      •**TEST B:**

1433 If the substance to be examined contains one or more of the following  
1434 antioxidants: pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-  
1435 hydroxyphenyl)propionate ([USP Plastic Additive 2 RS](#)); 2,2',2'',6,6',6''-  
1436 hexa-*tert*-butyl-4,4',4''-[(2,4,6-trimethyl-1,3,5-benzene-  
1437 triyl)trismethylene]triphenol ([USP Plastic Additive 3 RS](#)); 1,3,5-tris(3,5-  
1438 di-*tert*-butyl-4-hydroxybenzyl)-s-triazine-2,4,6(1*H*,3*H*,5*H*)-trione ([USP](#)  
1439 [Plastic Additive 6 RS](#)), **then carry out Test B.** ▲ (USP 1-Aug-2020)

1440 **Mobile phase:**

1441 Acetonitrile, tetrahydrofuran, and *Purified Water* (60:30:10, v/v/v)

1442 **Chromatographic system:**

1443 Carry out the test as described in *Test A* with the following modifications.

1444 **Detector:**

1445 UV 280 nm

1446 **Flow rate:**

1447 1.5 mL/min

1448 **Injection volume:**

1449 20 µL

1450 **System suitability**

1451 **Resolution:**

1452 Minimum 2.0 between [USP Plastic Additive 2 RS](#) (pentaerythrityl  
1453 tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate]) and [USP](#)

1454      [Plastic Additive 3 RS](#) (2,2',2'',6,6',6''-hexa-*tert*-butyl-4,4',4''-[(2,4,6-  
1455      trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol peaks), *Reference*  
1456      *solution B*

1457      *Sample solution S8* shows only peaks caused by antioxidants stated in  
1458      the composition and minor peaks that also correspond to the blank  
1459      solution.

1460      **Analysis**

1461      **Samples:**

1462      *Sample solution S8*, corresponding blank solution, *Reference solution B*,  
1463      and any *Reference solutions* of the antioxidants listed above that are  
1464      stated in the composition.

1465      **Acceptance criteria:**

1466      The peak areas of *Sample solution S8* are less than the corresponding  
1467      areas of the *Reference solutions* of the antioxidants that are listed above  
1468      and that are stated in the composition.

1469      **•TEST C:**

1470      If the substance to be examined contains [USP Plastic Additive 4 RS](#)  
1471      (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate) and/or [USP](#)  
1472      [Plastic Additive 5 RS](#) (tris(2,4-di-*tert*-butylphenyl) phosphite), **▲then**  
1473      carry out *Test C.* ▲ (USP 1-Aug-2020)

1474      **Mobile phase:**

1475      Methanol, 2-propanol, and *Purified Water* (50:45:5, v/v/v)

1476     **Chromatographic system:**

1477     Carry out the test as described in *Test A* with the following modifications.

1478     **Detector:**

1479     UV 280 nm

1480     **Flow rate:**

1481     1.5 mL/min

1482     **Injection volume:**

1483     20 µL

1484     **System suitability**

1485     **Resolution:**

1486     Minimum 2.0 between [USP Plastic Additive 4 RS](#) (octadecyl-3-(3,5-di-  
1487     *tert*-butyl-4-hydroxyphenyl)propionate) and [USP Plastic Additive 5 RS](#)  
1488     (tris(2,4-di-*tert*-butylphenyl) phosphite) peaks, *Reference solution C*

1489     *Sample solution S8<sup>a</sup>S9<sup>a</sup> (USP 1-Aug-2020)* shows only peaks caused by  
1490     antioxidants stated in the composition and minor peaks that also  
1491     correspond to the blank solution.

1492     **Analysis**

1493     **Samples:**

1494     *Sample solution S9* corresponding blank solution, *Reference solution C*,  
1495     and either *Reference solution I* or *Reference solution J*

1496     **Acceptance criteria:**

1497     The peak areas of *Sample solution S9* are less than the corresponding  
1498     peak areas of *Reference solution I* or *Reference solution J*.

1499     **Nonphenolic antioxidants**

1500     **Methylene chloride, acidified:**

1501     To 100 mL of methylene chloride add 10 mL of hydrochloric acid, shake,  
1502     allow to stand, and separate the two layers. Use the lower layer.

1503     **Iodine in ethanol detection solution:**

1504     Dissolve 10 g of iodine in 100 mL of alcohol absolute. Store protected  
1505     from light.

1506     **Sample solution S10:**

1507     Evaporate 100 mL of *Solution S2* to dryness under vacuum at 45°.  
1508     Dissolve the resulting residue with 2 mL of *Methylene chloride, acidified*.

1509     **Reference solution M:**

1510     6.0 mg/mL of [USP Plastic Additive 8 RS](#) prepared in methylene chloride.  
1511     Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

1512     **Reference solution N:**

1513      6.0 mg/mL of [USP Plastic Additive 9 RS](#) prepared in methylene chloride.  
1514      Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

1515      **Reference solution O:**

1516      6.0 mg/mL of [USP Plastic Additive 10 RS](#) prepared in methylene chloride.  
1517      Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

1518      **Reference solution P:**

1519      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.

1522      **Mobile phase A:**

1523      Hexane

1524      **Mobile phase B:**

1525      Methylene chloride

1526      **Chromatographic system**

1527      (See *Chromatography* (621), *General Procedures, Thin-Layer Chromatography*.)  
1528

1529      **Plate:**

1530      TLC silica gel GF<sub>254</sub>

1531      **Application volume:**

1532      20 µL

1533      **Development A:**

1534      Over a path of 18 cm with *Mobile phase A*; dry in air

1535      **Development B:**

1536      Over a path of 17 cm with *Mobile phase B*; dry in air

1537      **Detector:**

1538      UV 254 nm; spray with *Iodine in ethanol detection solution* and examine  
1539      after 10–15 min

1540      **System suitability**

1541      **Resolution:**

1542      The chromatogram shows two clearly separated spots, *Reference*  
1543      *solution P*.

1544      **Analysis**

1545      **Samples:**

1546      *Sample solution S10* and the reference solutions corresponding to all of  
1547      the phenolic and nonphenolic antioxidants expected to be present in the  
1548      test material

1549      **Acceptance criteria:**

1550 Any spots in the chromatogram of *Sample solution S10* are not more  
1551 intense than the spots in the same positions in the chromatograms of  
1552 the *Reference solutions*.

1553 **Amides and stearates**

1554 **Sample solution:**

1555 Use *Sample solution S10* described in *Nonphenolic antioxidants*.

1556 **Reference solution R:**

1557 2.0 mg/mL of [USP Stearic Acid RS](#) prepared in methylene chloride

1558 **Reference solution S:**

1559 2.0 mg/mL of [USP Plastic Additive 12 RS](#) prepared in methylene chloride

1560 **Reference solution T:**

1561 2.0 mg/mL of [USP Plastic Additive 13 RS](#) prepared in methylene chloride

1562 **Chromatographic system**

1563 (See *Chromatography* (621), *General Procedures, Thin-Layer*  
1564 *Chromatography*.)

1565 **Plate:**

1566 TLC silica gel GF<sub>254</sub>

1567 **•TEST A**

- 1568     **Mobile phase:**
- 1569       2,2,4-trimethylpentane and anhydrous ethanol (75:25, v/v)
- 1570     **Application volume:**
- 1571       10 µL
- 1572     **Development:**
- 1573       Over a path of 10 cm with *Mobile phase*; dry in air
- 1574     **Detector:**
- 1575       Spray with a 2-g/L solution of 2,6-dichlorophenol-indophenol sodium in  
1576       dehydrated alcohol and heat in an oven at 120° for a few min to  
1577       intensify the spots.
- 1578     **Analysis**
- 1579     **Samples:**
- 1580       *Sample solution S10* and *Reference solution R*
- 1581     **Acceptance criteria:**
- 1582       Any spot corresponding to additive stearic acid in *Sample solution S10* is  
1583       identical in position ( $R_f$  about 0.5) but is not more intense than the spot  
1584       in the same position in *Reference solution R*.
- 1585     •**TEST B**
- 1586     **Mobile phase A:**

1587 Hexane

1588 **Mobile phase B:**

1589 Methylene chloride and methanol (95:5, v/v)

1590 **Application volume:**

1591 10 µL

1592 **Development A:**

1593 Over a path of 13 cm with *Mobile phase A*; dry in air

1594 **Development B:**

1595 Over a path of 10 cm with *Mobile phase B*; dry in air

1596 **Detector:**

1597 Spray with a 40-g/L solution of phosphomolybdic acid in alcohol,  
1598 dehydrated, and heat in an oven at 120° until spots appear.

1599 **Analysis**

1600 **Samples:**

1601 *Sample solution S10, Reference solution S, and Reference solution T*

1602 **Acceptance criteria:**

1603 Any spots corresponding to additives oleamide or erucamide in *Sample*  
1604 *solution S10* are identical in position ( $R_F$  about 0.2) but are not more

1605 intense than the corresponding spots in *Reference solution S* and  
1606 *Reference solution T*.

1607 Change to read:

1608 **POLYETHYLENE TEREPHTHALATE AND POLYETHYLENE**  
1609 **TEREPHTHALATE G**

1610 **Identification**

1611 [NOTE—The identification of polyethylene terephthalate and polyethylene  
1612 terephthalate G needs compliance with only one test procedure to be  
1613 established.]

1614 •**A. INFRARED SPECTROPHOTOMETRY {~~(197F)~~}**

1615 Refer to **(854)**. ▲ (USP 1-Aug-2020)

1616 **Apparatus:**

1617 Use an infrared spectrophotometer capable of correcting for the blank  
1618 spectrum and able to measure in transmission mode or equipped with an  
1619 internal reflectance accessory and an appropriate internal reflectance  
1620 plate.

1621 **Sample preparation**

1622 **Transmission mode:**

1623 Prepare a specimen of appropriate thickness without visible defects  
1624 (cracks or holes). The specimens can be compressed to form a thin,  
1625 uniform film by exposure to elevated temperatures and pressures (2000  
1626 psi or more). The temperatures at which the thin films are generated

1627 represent a trade-off between producing a melt (which dictates the  
1628 lowest temperature necessary) and degrading the sample (which  
1629 dictates the highest temperature allowed). Ultimately, the temperatures  
1630 that are used are appropriate if the film produced is conducive to the  
1631 infrared analysis.

1632 **Internal reflectance mode:**

1633 Prepare a flat section and trim it as necessary to obtain a segment that  
1634 is convenient for mounting in the internal reflectance accessory. Taking  
1635 care to avoid scratching the surfaces, wipe the specimen with dry paper  
1636 or, if necessary, a soft cloth dampened with methanol, and permit the  
1637 surfaces to dry. Then securely mount the specimen on the internal  
1638 reflection plate, ensuring adequate surface contact.

1639 **Procedure:**

1640 Place the mounted specimen sections in the sample compartment of the  
1641 infrared spectrophotometer or the internal reflectance accessory, and  
1642 place the assembly in the specimen beam of the infrared  
1643 spectrophotometer. For internal reflectance, adjust the specimen  
1644 position and mirrors within the accessory to permit maximum light  
1645 transmission of the unattenuated reference beam. (For a double-beam  
1646 instrument, attenuate the reference beam after completing the  
1647 adjustment in the accessory to permit full-scale deflection during the  
1648 scanning of the specimen.) Determine the infrared spectrum from 3800  
1649  $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$  (2.6–15  $\mu\text{m}$ ).

1650 **Acceptance criteria:**

1651 The specimen exhibits an absorption spectrum that is substantially  
1652 equivalent to that of [USP Polyethylene Terephthalate RS](#) or [USP](#)  
1653 [Polyethylene Terephthalate G RS](#). Substantial, as opposed to exact,  
1654 equivalence allows for minor spectral differences arising from the natural

1655 compositional and/or physical variation among polymers of this class.  
1656 Substantial equivalence is achieved when all differences between the  
1657 sample and RS spectra can be explained in the context of such natural  
1658 compositional and/or physical variations.

1659 **•B. THERMAL ANALYSIS**

1660 Refer to [\(891\)](#).

1661 **Sample preparation:**

1662 Place an appropriately sized sample in the test specimen pan. [NOTE—  
1663 Intimate contact between the pan and the thermocouple is essential for  
1664 obtaining reproducible results.]

1665 **Procedures**

1666 **Polyethylene terephthalate:**

1667 Determine the thermal analysis curve under nitrogen, using  
1668 heating/cooling conditions specified for the polymer type and using  
1669 equipment capable of performing the determinations as described in  
1670 [\(891\)](#). Heat the specimen from room temperature to 280° at a heating  
1671 rate of about 20°/min. Hold the specimen at 280° for 1 min. Quickly cool  
1672 the specimen to room temperature and reheat it to 280° at a heating  
1673 rate of 5°/min.

1674 **Polyethylene terephthalate G:**

1675 Determine the thermal analysis curve under nitrogen, using  
1676 heating/cooling conditions specified for the polymer type and using  
1677 equipment capable of performing the determinations as described in  
1678 [\(891\)](#). Heat the specimen from room temperature to 120° at a heating

1679 rate of about 20°/min. Hold the specimen at 120° for 1 min. Quickly cool  
1680 the specimen to room temperature and reheat it to 120° at a heating  
1681 rate of 10°/min.

1682 **Acceptance criteria**

1683 **Polyethylene terephthalate:**

1684 The thermal analysis curve of the specimen is similar to the thermal  
1685 analysis curve of [USP Polyethylene Terephthalate RS](#) and the melting  
1686 peak temperature obtained from the thermal analysis curve of the  
1687 specimen does not differ from that of the RS by more than 4.0°.

1688 **Polyethylene terephthalate G:**

1689 The thermal analysis curve of the specimen is similar to the thermal  
1690 analysis curve of [USP Polyethylene Terephthalate G RS](#). The melting  
1691 peak temperature obtained from the thermal analysis curve of the  
1692 specimen does not differ from that of the RS by more than 6.0°.

1693 **Physicochemical Tests**

1694 **Water extraction, Solution S1:**

1695 Place 10 g of the test material in a borosilicate glass flask with a ground-  
1696 glass neck. Add 200 mL of *Purified Water*, and heat at 50° for 5 h. Allow  
1697 to cool, decant the solution into a 200-mL volumetric flask, and dilute  
1698 with *Purified Water* to volume; the diluted sample is designated *Solution*  
1699 *S1*. Use *Solution S1* within 4 h of preparation.

1700 **Alcohol extraction, Solution S5:**

1701 Place 10 g of the test material in a borosilicate glass flask with a ground-  
1702 glass neck. Add 100 mL of alcohol, absolute, and heat at 50° for 5 h.  
1703 Allow to cool and the solids to settle, then decant the solution, producing  
1704 *Solution S5*. Use *Solution S5* within 4 h of preparation.

1705 **Absorbance**

1706 Refer to *<857>*.

1707 **Procedure:**

1708 Determine the spectrum between 220 and 340 nm in *Solution S1*. For  
1709 colored polyethylene terephthalate, determine the spectrum between  
1710 400 and 800 nm in *Solution S1*. For colored and noncolored polyethylene  
1711 terephthalate, determine the spectrum between 400 and 800 nm in  
1712 *Solution S5*.

1713 **Acceptance criteria:**

1714 NMT 0.2 for *Solution S1* and 0.05 for *Solution S5*. In addition, for  
1715 colored polyethylene terephthalate, maximum absorbance between 400  
1716 and 800 nm is 0.05 for *Solution S1*. If the specification for absorbance is  
1717 exceeded, then the material can still be considered compliant with this  
1718 chapter if the chemicals responsible for the test results can be  
1719 established (identity and concentration) and the chemicals are  
1720 characterized to establish that the probable risk posed by all the  
1721 chemicals, considered individually, is within acceptable parameters.

1722 **Acidity or alkalinity**

1723 **BRP indicator solution:**

1724      1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
1725      mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

1726      **Methyl orange solution:**

1727      Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
1728      with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
1729      *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
1730      1 N hydrochloric acid is required to change the color from yellow to red.

1731      **Procedure:**

1732      To 50 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*.  
1733      Determine the titration volume of 0.01 N sodium hydroxide required to  
1734      change the color of the indicator to blue. To a separate, 50-mL portion of  
1735      *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the  
1736      titration volume of 0.01 N hydrochloric acid required to reach the  
1737      beginning of the color change of the indicator from yellow to orange.

1738      **Acceptance criteria:**

1739      NMT 0.5 mL of 0.01 N sodium hydroxide is required to change the color  
1740      of the indicator to blue. NMT 0.5 mL of 0.01 N hydrochloric acid is  
1741      required to reach the beginning of the color change of the indicator from  
1742      yellow to orange.

1743      **Total organic carbon**

1744      **Procedure:**

1745      The TOC content of *Solution S1* is measured according to the general  
1746      methodologies outlined in (643). However, although (643) is designed for  
1747      the testing of high-purity water with low TOC values, material extracts  
1748      may have TOC values that are higher than those of *Purified Water*.

1749 because of extracted organic substances. Thus, the method used to  
1750 perform the TOC analyses should have a limit of detection of 0.2 mg/L  
1751 (ppm) and should have a demonstrated linear dynamic range from 0.2  
1752 to 20 mg/L (which encompasses the TOC limit). A linear range with a  
1753 higher upper concentration can be used if linearity is established. If  
1754 sample extracts exceed this upper linear range, they must be diluted  
1755 appropriately for analysis.

1756 **Acceptance criteria:**

1757 The difference between the sample and blank TOC concentrations is NMT  
1758 5 mg/L. If the specification for TOC is exceeded, then the material can  
1759 still be considered compliant with this chapter if the chemicals  
1760 responsible for the test results can be established (identity and  
1761 concentration) and the chemicals are characterized to establish that the  
1762 probable risk posed by all the chemicals, considered individually, is  
1763 within acceptable parameters.

1764 **Extractable Metals**

1765 **Aluminum:**

1766 *Solution S3 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.*

1767 **Antimony:**

1768 *Solution S4 contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.*

1769 **Arsenic, cadmium, lead, mercury, cobalt, nickel, and vanadium:**

1770 Report the measured value in *Solution S3* at values above 0.01 mg/L  
1771 (ppm), corresponding to 0.025 µg/g. If the measured values are below  
1772 these values, report the result as less than 0.01 mg/L (ppm),  
1773 corresponding to less than 0.025 µg/g.

1774 **Barium:**

1775 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

1776 **Germanium:**

1777 *Solution S4* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

1778 **Manganese:**

1779 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

1780 **Titanium:**

1781 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

1782 **Zinc:**

1783 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

1784 Test results for additional relevant extractable metals are similarly

1785 reported.▲ (USP 1-Aug-2020)

1786 Change to read:

## 1787 **POLY(ETHYLENE-VINYL ACETATE)**

### 1788 **Identification**

1789 ▲[NOTE—The identification of poly(ethylene-vinyl acetate) needs

1790 compliance with only one test procedure to be established.]▲ (USP 1-AUG-2020)

- 1791 •A. INFRARED SPECTROPHOTOMETRY (197F)
- 1792 ▲Refer to (854).▲ (USP 1-Aug-2020)
- 1793 **Apparatus:**
- 1794 Use an infrared spectrophotometer capable of correcting for the blank  
1795 spectrum and able to measure in transmission mode or equipped with an  
1796 internal reflectance accessory and an appropriate internal reflectance  
1797 plate.
- 1798 **Sample preparation**
- 1799 **Transmission mode:**
- 1800 Prepare a specimen of appropriate thickness without visible defects  
1801 (cracks or holes). The specimens can be compressed to form a thin,  
1802 uniform film by exposure to elevated temperatures and pressures (2000  
1803 psi or more). The temperatures at which the thin films are generated  
1804 represent a trade-off between producing a melt (which dictates the  
1805 lowest temperature necessary) and degrading the sample (which  
1806 dictates the highest temperature allowed). Ultimately, the temperatures  
1807 that are used are appropriate if the film produced is conducive to the  
1808 infrared analysis.
- 1809 **Internal reflectance mode:**
- 1810 Prepare a flat section and trim it as necessary to obtain a segment that  
1811 is convenient for mounting in the internal reflectance accessory. Taking  
1812 care to avoid scratching the surfaces, wipe the specimen with dry paper  
1813 or, if necessary, a soft cloth dampened with methanol, and permit the  
1814 surfaces to dry. Then securely mount the specimen on the internal  
1815 reflection plate, ensuring adequate surface contact.

1816      **Procedure:**

1817      Place the mounted specimen sections in the sample compartment of the  
1818      infrared spectrophotometer or the internal reflectance accessory, and  
1819      place the assembly in the specimen beam of the infrared  
1820      spectrophotometer. For internal reflectance, adjust the specimen  
1821      position and mirrors within the accessory to permit maximum light  
1822      transmission of the unattenuated reference beam. (For a double-beam  
1823      instrument, attenuate the reference beam after completing the  
1824      adjustment in the accessory to permit full-scale deflection during the  
1825      scanning of the specimen.) Determine the infrared spectrum from 3800  
1826       $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$  (2.6–15  $\mu\text{m}$ ).

1827      **Acceptance criteria:**

1828      The specimen exhibits an absorption spectrum that is substantially  
1829      equivalent to that of [USP Poly\(ethylene-vinyl acetate\) RS](#). Substantial,  
1830      as opposed to exact, equivalence allows for minor spectral differences  
1831      arising from the natural compositional and/or physical variation among  
1832      polymers of this class. Substantial equivalence is achieved when all  
1833      differences between the sample and RS spectra can be explained in the  
1834      context of such natural compositional and/or physical variations.

1835      **•B. THERMAL ANALYSIS**

1836      Refer to [\(891\)](#).

1837      **Sample preparation:**

1838      Place an appropriately sized sample in the test specimen pan. [NOTE—  
1839      Intimate contact between the pan and the thermocouple is essential for  
1840      obtaining reproducible results.]

1841      **Procedure:**

1842 Determine the thermal analysis curve under nitrogen, using  
1843 heating/cooling conditions specified for the polymer type and using  
1844 equipment capable of performing the determinations as described in  
1845 [\(891\)](#). Heat the specimen from  $-50^{\circ}$  to  $120^{\circ}$  at a heating rate of about  
1846  $10^{\circ}/\text{min}$ . Quickly cool the specimen to room temperature.

1847 **Acceptance criteria:**

1848 The thermal analysis curve of the specimen is similar to the thermal  
1849 analysis curve of [USP Poly\(ethylene-vinyl acetate\) RS](#), and the melting  
1850 point temperature obtained from the thermal analysis curve of the  
1851 specimen does not differ from that of the RS by more than  $6.0^{\circ}$ .

1852 **Physicochemical Tests**

1853 **Water extraction, Solution S1:**

1854 Place 25 g of the test material in a borosilicate glass flask with a ground-  
1855 glass neck. Add 500 mL of *Purified Water*, and boil under reflux  
1856 conditions for 5 h. Allow to cool, and pass the extracting solution  
1857 through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric  
1858 flask and dilute with *Purified Water* to volume; the diluted solution is  
1859 designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

1860 **Absorbance**

1861 Refer to [\(857\)](#).

1862 **Procedure:**

1863 Determine the spectrum between 220 and 340 nm in *Solution S1*.

1864 **Acceptance criteria:**

1865 NMT 0.2. If the specification for absorbance is exceeded, then the  
1866 material can still be considered compliant with this chapter if the  
1867 chemicals responsible for the test results can be established (identity  
1868 and concentration) and the chemicals are characterized to establish that  
1869 the probable risk posed by all the chemicals, considered individually, is  
1870 within acceptable parameters.

1871 **Acidity or alkalinity**

1872 **BRP indicator solution:**

1873 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
1874 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

1875 **Methyl orange solution:**

1876 Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
1877 with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
1878 *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
1879 1 N hydrochloric acid is required to change the color from yellow to red.

1880 **Procedure:**

1881 To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*.  
1882 Determine the titration volume of 0.01 N sodium hydroxide required to  
1883 change the color of the indicator to blue. To a separate, 100-mL portion  
1884 of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the  
1885 titration volume of 0.01 N hydrochloric acid required to reach the  
1886 beginning of the color change of the indicator from yellow to orange.

1887 **Acceptance criteria:**

1888 NMT 1.0 mL of 0.01 N hydrochloric acid is required to reach the  
1889 beginning of the color change of the indicator from yellow to orange.

1890      **Total organic carbon**

1891      **Procedure:**

1892      The TOC content of *Solution S1* is measured according to the general  
1893      methodologies outlined in (643). However, although (643) is designed for  
1894      the testing of high-purity water with low TOC values, material extracts  
1895      may have TOC values that are higher than those of *Purified Water*  
1896      because of extracted organic substances. Thus, the method used to  
1897      perform the TOC analyses should have a limit of detection of 0.2 mg/L  
1898      (ppm) and should have a demonstrated linear dynamic range from 0.2  
1899      to 20 mg/L (which encompasses the TOC limit). A linear range with a  
1900      higher upper concentration can be used if linearity is established. If  
1901      sample extracts exceed this upper linear range, they must be diluted  
1902      appropriately for analysis

1903      **Acceptance criteria:**

1904      The difference between the sample and blank TOC concentrations is NMT  
1905      5 mg/L. If the specification for TOC is exceeded, then the material can  
1906      still be considered compliant with this chapter if the chemicals  
1907      responsible for the test results can be established (identity and  
1908      concentration) and the chemicals are characterized to establish that the  
1909      probable risk posed by all the chemicals, considered individually, is  
1910      within acceptable parameters.

1911      **Extractable Metals**

1912      **All metals:**

1913      Report the measured value in *Solution S3* at values above 0.01 mg/L  
1914      (ppm), corresponding to 0.025 µg/g. If the measured values are below  
1915      these values, report the result as less than 0.01 mg/L (ppm),

1916 corresponding to less than 0.025 µg/g. Test results for additional relevant  
1917 extractable metals are similarly reported.

1918 ~~Test results for additional relevant extractable metals are similarly~~  
1919 ~~reported.~~ ▲ (USP 1-Aug-2020)

## 1920 **Plastic Additives**

1921 The test results from these analyses are reported.

## 1922 **Phenolic antioxidants**

### 1923 **Solvent mixture:**

1924 Acetonitrile and tetrahydrofuran (50:50, v/v)

### 1925 **Toluene extraction, Solution S2:**

1926 Place 2.0 g of the test material in a 250-mL borosilicate glass flask with  
1927 a ground-glass neck. Add 80 mL of toluene and boil under a reflux  
1928 condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add,  
1929 with continued stirring, 120 mL of methanol. Pass the resulting solution  
1930 through a sintered-glass filter. Rinse the flask and the filter with 25 mL  
1931 of a mixture of 40 mL of toluene and 60 mL of methanol, add the  
1932 rinsings to the filtrate, and dilute to 250 mL with the same mixture of  
1933 solvents to produce *Solution S2*. Prepare a blank solution.

### 1934 **Sample solution S12:**

1935 Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°.  
1936 Dissolve the resulting residue with 5.0 mL of the *Solvent mixture* to  
1937 produce *Sample solution S12*. Prepare a blank solution from the blank  
1938 solution corresponding to *Solution S2*.

1939     **Sample solution S13:**

1940     Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°.  
1941     Dissolve the residue with 5.0 mL of methylene chloride to produce  
1942     *Sample solution S13*. Prepare a blank solution from the blank solution  
1943     corresponding to *Solution S2*.

1944     **Reference solutions**

1945     Of the following reference solutions, prepare only those that are  
1946     necessary for the analysis of the phenolic antioxidants stated in the  
1947     composition of the substance to be examined.

1948     **Reference solution K:**

1949     0.1 mg/mL of [USP Butylated Hydroxytoluene RS](#), 0.16 mg/mL of [USP](#)  
1950     [Plastic Additive 2 RS](#), 0.16 mg/mL of [USP Plastic Additive 3 RS](#), and 0.16  
1951     mg/mL of [USP Plastic Additive 4 RS](#) prepared in the *Solvent mixture*.

1952     **Reference solution L:**

1953     0.16 mg/mL of [USP Plastic Additive 4 RS](#) and 0.16 mg/mL of [USP Plastic](#)  
1954     [Additive 5 RS](#) prepared in methylene chloride

1955     •**TEST A**

1956     **Mobile phase:**

1957     Tetrahydrofuran, acetonitrile, and *Purified Water* (30:60:10, v/v)

1958     **Chromatographic system**

1959       (See *Chromatography* (621), *General Procedures, Liquid Chromatography.*)  
1960

1961       **Detector:**

1962       UV 280 nm

1963       **Column:**

1964       4.6-mm × 25-cm; 5-μm packing L1

1965       **Flow rate:**

1966       1.5 mL/min

1967       **Injection volume:**

1968       20 μL

1969       **Run time:**

1970       30 min

1971       **System suitability**

1972       **Resolution:**

1973       Minimum 2.0 between [USP Plastic Additive 2 RS](#) and [USP Plastic Additive 3 RS](#), *Reference solution K*  
1974

1975       **Column efficiency:**

1976 Minimum 2500 theoretical plates, calculated for [USP Butylated](#)  
1977 [Hydroxytoluene RS, Reference solution K](#)

1978 **Analysis**

1979 **Samples:**

1980 *Sample solution S12*, corresponding blank solution, and *Reference*  
1981 *solution K*

1982 **Acceptance criteria:**

1983 *Sample solution S12* shows only peaks caused by antioxidants in  
1984 *Reference solution K* and minor peaks that also correspond to the blank  
1985 solution. The peak areas of *Sample solution S12* are less than the  
1986 corresponding peak areas of *Reference solution K*.

1987 **•TEST B:**

1988 If the chromatogram obtained via *Test A* for *Sample solution S12* shows  
1989 a peak with the same retention time as the last antioxidant eluted from  
1990 *Reference solution K*, **then carry out Test B.**▲ (USP 1-Aug-2020)

1991 **Mobile phase:**

1992 2-propanol, methanol, and *Purified Water* (45:50:5, v/v/v)

1993 **Chromatographic system:**

1994 Carry out the test as described in *Test A* with the following modifications.

1995 **Detector:**

- 1996      UV 280 nm
- 1997      **Flow rate:**
- 1998      1.5 mL/min
- 1999      **Injection volume:**
- 2000      20 µL
- 2001      **System suitability**
- 2002      **Resolution:**
- 2003      Minimum of 2.0 between [USP Plastic Additive 4 RS](#) and [USP Plastic Additive 5 RS](#), *Reference solution L*
- 2004
- 2005      **Analysis**
- 2006      **Samples:**
- 2007      *Sample solution S13, corresponding blank solution, and Reference solution L.*
- 2008
- 2009      **Acceptance criteria:**
- 2010      *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.*
- 2011
- 2012
- 2013
- 2014      **Amides and stearic acid**

- 2015    **Sample solution S14:**
- 2016    Evaporate 100 mL of *Solution S2* to dryness under vacuum at 45°.
- 2017    Dissolve the resulting residue with 2 mL of acidified methylene chloride
- 2018    to produce *Sample solution S14*.
- 2019    **Reference solution R:**
- 2020    2.0 mg/mL of [USP Stearic Acid RS](#) prepared in methylene chloride
- 2021    **Reference solution S:**
- 2022    0.8 mg/mL of [USP Plastic Additive 12 RS](#) prepared in methylene chloride
- 2023    **Reference solution T:**
- 2024    0.8 mg/mL of [USP Plastic Additive 13 RS](#) prepared in methylene chloride
- 2025    **Chromatographic system**
- 2026    (See *Chromatography* (621), *General Procedures, Thin-Layer Chromatography*.)
- 2027
- 2028    **Plate:**
- 2029    TLC silica gel GF<sub>254</sub>
- 2030    •**TEST A**
- 2031    **Mobile phase:**
- 2032    Anhydrous ethanol and trimethylpentane (25:75, v/v)

- 2033    **Application volume:**
- 2034    10 µL
- 2035    **Development:**
- 2036    Over a path of 10 cm with *Mobile phase*; dry in air
- 2037    **Detector:**
- 2038    Spray with a 2-g/L solution of 2,6-dichlorophenol-indophenol sodium in  
2039    dehydrated alcohol and heat in an oven at 120° for a few minutes to  
2040    intensify the spots.
- 2041    **Analysis**
- 2042    **Samples:**
- 2043    *Sample solution S14* and *Reference solution R*
- 2044    **Acceptance criteria:**
- 2045    Any spot corresponding to additive stearic acid in *Sample solution S14* is  
2046    identical in position and is not more intense than the spot in the same  
2047    position in *Reference solution R*.
- 2048    •**TEST B**
- 2049    **Chromatographic system:**
- 2050    (See *Chromatography (621)*, *General Procedures*, *Thin-Layer*  
2051    *Chromatography*.)

- 2052     **Plate:**
- 2053     TLC silica gel GF<sub>254</sub>
- 2054     **Mobile phase A:**
- 2055     Hexane
- 2056     **Mobile phase B:**
- 2057     Methylene chloride and methanol (95:5, v/v)
- 2058     **Application:**
- 2059     10 µL
- 2060     **Development A:**
- 2061     Over a path of 13 cm with *Mobile phase A*; dry in air
- 2062     **Development B:**
- 2063     Over a path of 10 cm with *Mobile phase B*; dry in air
- 2064     **Detector:**
- 2065     Spray with a 40-g/L solution of phosphomolybdic acid in alcohol,
- 2066     dehydrated, and heat in an oven at 120° until spots appear.
- 2067     **Analysis**
- 2068     **Samples:**
- 2069     *Sample solution S14, Reference solution S, and Reference solution T.*

2070     **Acceptance criteria:**

2071     Any spots corresponding to additives oleamide or erucamide in *Sample*  
2072     *solution S14* are identical in position but are not more intense than the  
2073     corresponding spots in *Reference solution S* and *Reference solution T*.

2074     **Related Substances**

2075     **Content of vinyl acetate**

2076     **Alcoholic potassium hydroxide:**

2077     Dissolve 6.6 g of potassium hydroxide in 50 mL of *Purified Water* and  
2078     dilute with alcohol, dehydrated to 1000 mL.

2079     **Sample solution:**

2080     Place 0.25–1.0 g of the test material into a 300-mL conical flask  
2081     containing a magnetic stirrer. Prepare an extraction blank starting with  
2082     an otherwise empty 300-mL conical flask. Add 40 mL of xylene and boil  
2083     under a reflux condenser with stirring for 4 h. After heating, continue  
2084     stirring, allowing the solution to cool to the point that precipitation  
2085     starts. Slowly add 25 mL of alcoholic potassium hydroxide. Boil again  
2086     under a reflux condenser for 3 h with continued stirring. While stirring,  
2087     allow the solution to cool, rinse the condenser with 50 mL of water and  
2088     add 30 mL of 0.05 M sulfuric acid to the flask. Transfer the contents of  
2089     the flask to a 400-mL beaker, rinsing the flask with the following:

- 2090         • 2 quantities, 50 mL each, of a 200-g/L solution of anhydrous  
2091             sodium sulfate  
2092         • 3 quantities, 20 mL each, of water

2093 Add the rinsings to the beaker.

2094 **Procedure:**

2095 Titrate the excess sulfuric acid in *Sample solution* with 0.1 M sodium  
2096 hydroxide, determining the endpoint potentiometrically. Carry out a  
2097 titration of the extraction blank.

2098 **Calculation:**

2099 Determine the amount of titrant (mL) required by subtracting the titrant  
2100 volume used for the extraction blank (mL) from the titrant volume used  
2101 for the extract (mL). Determine the amount of vinyl acetate by  
2102 multiplying the volume of titrant required by the quantity (8.609  
2103 mg/mL). The content of vinyl acetate is calculated as:

2104 Content of vinyl acetate (weight %) = [amount of vinyl acetate  
2105 (mg)/weight of material extracted (g)]/10

2106 **Acceptance criteria:**

2107 NMT 25% by weight

2108 **For tubing:**

2109 ~~NMT 30% by weight~~<sup>▲ (USP 1-Aug-2020)</sup>

2110 Change to read:

2111 **POLYPROPYLENE**

2112 **Identification**

2113 [NOTE—The identification of polypropylene needs compliance with only  
2114 one test procedure to be established.]

2115 •**A. INFRARED SPECTROPHOTOMETRY (197F)**

2116 Refer to **(854)**.<sup>▲ (USP 1-Aug-2020)</sup>

2117 **Apparatus:**

2118 Use an infrared spectrophotometer capable of correcting for the blank  
2119 spectrum and able to measure in transmission mode or equipped with an  
2120 internal reflectance accessory and an appropriate internal reflectance  
2121 plate.

2122     **Sample preparation**

2123     **Transmission mode:**

2124       Prepare a specimen of appropriate thickness (about 100 µm) without  
2125       visible defects (cracks or holes). The specimens can be compressed to  
2126       form a thin, uniform film by exposure to elevated temperatures and  
2127       pressures (2000 psi or more). The temperatures at which the thin films  
2128       are generated represent a trade-off between producing a melt (which  
2129       dictates the lowest temperature necessary) and degrading the sample  
2130       (which dictates the highest temperature allowed). Ultimately, the  
2131       temperatures that are used are appropriate if the film produced is  
2132       conducive to the infrared analysis.

2133     **Internal reflectance mode:**

2134       Prepare a flat section and trim it as necessary to obtain a segment that  
2135       is convenient for mounting in the internal reflectance accessory. Taking  
2136       care to avoid scratching the surfaces, wipe the specimen with dry paper  
2137       or, if necessary, a soft cloth dampened with methanol, and permit the  
2138       surfaces to dry. Then securely mount the specimen on the internal  
2139       reflection plate, ensuring adequate surface contact.

2140     **Procedure:**

2141       Place the mounted specimen sections in the sample compartment of the  
2142       infrared spectrophotometer or the internal reflectance accessory, and  
2143       place the assembly in the specimen beam of the infrared  
2144       spectrophotometer. For internal reflectance, adjust the specimen  
2145       position and mirrors within the accessory to permit maximum light  
2146       transmission of the unattenuated reference beam. (For a double-beam  
2147       instrument, attenuate the reference beam after completing the  
2148       adjustment in the accessory to permit full-scale deflection during the  
2149       scanning of the specimen.) Determine the infrared spectrum from 3800  
2150       cm<sup>-1</sup> to 650 cm<sup>-1</sup> (2.6–15 µm).

2151     **Acceptance criteria:**

2152       The specimen exhibits an absorption spectrum that is substantially  
2153       equivalent to that of the [USP Homopolymer Polypropylene RS](#).  
2154       Substantial, as opposed to exact, equivalence allows for minor spectral  
2155       differences arising from the natural compositional and/or physical

2156 variation among polymers of this class. Substantial equivalence is  
2157 achieved when all differences between the sample and RS spectra can be  
2158 explained in the context of such natural compositional and/or physical  
2159 variations.

2160 **•B. THERMAL ANALYSIS**

2161 Refer to [\(891\)](#).

2162 **Sample preparation:**

2163 Place an appropriately sized sample in the test specimen pan. [NOTE—  
2164 Intimate contact between the pan and the thermocouple is essential for  
2165 obtaining reproducible results.]

2166 **Procedure:**

2167 Determine the thermal analysis curve under nitrogen, using  
2168 heating/cooling conditions specified for the polymer type and using  
2169 equipment capable of performing the determinations as described in  
2170 [\(891\)](#). Heat the specimen from ambient to 30° above the melting point.  
2171 Maintain the temperature for 10 min, then cool to 50° below the peak  
2172 crystallization temperature at a rate of 10°–20°/min.

2173 **Acceptance criteria:**

2174 The melting peak temperature in the thermal analysis curve does not  
2175 differ from that of [USP Homopolymer Polypropylene RS](#) by more than  
2176 12.0°.

2177 **Physicochemical Tests**

2178 **Water extraction, Solution S1:**

2179 Place 25 g of the test material in a borosilicate glass flask with a ground-  
2180 glass neck. Add 500 mL of *Purified Water*, and boil under reflux  
2181 conditions for 5 h. Allow to cool, and pass the extracting solution  
2182 through a sintered-glass filter. Collect the filtrate in a 500-mL volumetric  
2183 flask and dilute with *Purified Water* to volume; the diluted solution is  
2184 designated *Solution S1*. Use *Solution S1* within 4 h of preparation.

2185 **Absorbance**

2186 Refer to [\(857\)](#).

2187 **Procedure:**

2188 Determine the spectrum between 220 and 340 nm in *Solution S1*.

2189 **Acceptance criteria:**

2190 NMT 0.2. If the specification for absorbance is exceeded, then the  
2191 material can still be considered compliant with this chapter if the  
2192 chemicals responsible for the test results can be established (identity  
2193 and concentration) and the chemicals are characterized to establish that  
2194 the probable risk posed by all the chemicals, considered individually, is  
2195 within acceptable parameters.

2196 **Acidity or alkalinity**

2197 **BRP indicator solution:**

2198 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
2199 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

2200 **Methyl orange solution:**

2201 Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
2202 with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
2203 *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
2204 1 N hydrochloric acid is required to change the color from yellow to red.

2205 **Procedure:**

2206 To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*.  
2207 Determine the titration volume of 0.01 N sodium hydroxide required to  
2208 change the color of the indicator to blue. To a separate, 100-mL portion  
2209 of *Solution S1* add 0.2 mL of *Methyl orange solution*. Determine the  
2210 titration volume of 0.01 N hydrochloric acid required to reach the  
2211 beginning of the color change of the indicator from yellow to orange.

2212 **Acceptance criteria:**

2213 NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color  
2214 of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is  
2215 required to reach the beginning of the color change of the indicator from  
2216 yellow to orange.

2217 **Total organic carbon**

2218 **Procedure:**

2219 The total organic carbon TOC content of *Solution S1* is measured  
2220 according to the general methodologies outlined in <643>. However,

2221 although (643) is designed for the testing of high-purity water with low  
2222 TOC values, material extracts may have TOC values that are higher than  
2223 those of *Purified Water* because of extracted organic substances. Thus,  
2224 the method used to perform the TOC analyses should have a limit of  
2225 detection of 0.2 mg/L (ppm) and should have a demonstrated linear  
2226 dynamic range from 0.2 to 20 mg/L (which encompasses the TOC limit).  
2227 A linear range with a higher upper concentration can be used if linearity  
2228 is established. If sample extracts exceed this upper linear range, they  
2229 must be diluted appropriately for analysis.  
2230

**Acceptance criteria:**

2231 The difference between the sample and blank TOC concentrations is NMT  
2232 5 mg/L. If the specification for TOC is exceeded, then the material can  
2233 still be considered compliant with this chapter if the chemicals  
2234 responsible for the test results can be established (identity and  
2235 concentration) and the chemicals are characterized to establish that the  
2236 probable risk posed by all the chemicals, considered individually, is  
2237 within acceptable parameters.

**Extractable Metals**

**Aluminum:**

2240 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

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

2242 Report the measured value in *Solution S3* at values above 0.01 mg/L  
2243 (ppm), corresponding to 0.025 µg/g. If the measured values are below  
2244 these values, report the result as less than 0.01 mg/L (ppm),  
2245 corresponding to less than 0.025 µg/g.

**Chromium:**

2247 *Solution S3* contains NMT 0.02 mg/L (ppm), corresponding to 0.05 µg/g.

**Titanium:**

2249 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

**Zinc:**

2251 *Solution S3* contains NMT 0.4 mg/L (ppm), corresponding to 1 µg/g.

2252 Test results for additional relevant extractable metals are similarly

2253 reported. ▲ (USP 1-Aug-2020)

2254 **Plastic Additives**

2255 The test results from these analyses are reported.

2256 **Phenolic antioxidants**

2257 **Solvent mixture:**

2258 Acetonitrile and tetrahydrofuran (50:50, v/v)

2259 **Toluene extraction, Solution S2:**

2260 Place 2.0 g of the test material in a 250-mL borosilicate glass flask with  
2261 a ground-glass neck. Add 80 mL of toluene and boil under a reflux  
2262 condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add,  
2263 with continued stirring, 120 mL of methanol. Pass the resulting solution  
2264 through a sintered-glass filter. Rinse the flask and the filter with 25 mL  
2265 of a mixture of 40 mL of toluene and 60 mL of methanol, add the  
2266 rinsings to the filtrate, and dilute with the same mixture of solvents to  
2267 250 mL to produce *Solution S2*. Prepare a blank solution.  
2268

**Sample solution S8:**

2269 Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°.  
2270 Dissolve the resulting residue with 5.0 mL of the *Solvent mixture* to  
2271 produce *Sample solution S8*. Prepare a blank solution from the blank  
2272 solution corresponding to *Solution S2*.  
2273

**Sample solution S9:**

2274 Evaporate 50 mL of *Solution S2* to dryness under vacuum at 45°.  
2275 Dissolve the residue with 5.0 mL of methylene chloride to produce  
2276 *Sample solution S9*. Prepare a blank solution from the blank solution  
2277 corresponding to *Solution S2*.  
2278

**Reference solutions:**

2279 Of the following reference solutions, prepare only those that are  
2280 necessary for the analysis of the phenolic antioxidants stated in the  
2281 composition of the substance to be examined.  
2282

**Reference solution A:**

2283 0.1 mg/mL of [USP Butylated Hydroxytoluene RS](#) and 0.24 mg/mL of [USP](#)  
2284 [Plastic Additive 1 RS](#) prepared in the *Solvent mixture*

**Reference solution B:**

2286      0.24 mg/mL of [USP Plastic Additive 2 RS](#) and 0.24 mg/mL of [USP Plastic](#)  
2287      [Additive 3 RS](#) prepared in the *Solvent mixture*

2288      **Reference solution C:**

2289      0.24 mg/mL of [USP Plastic Additive 4 RS](#) and 0.24 mg/mL of [USP Plastic](#)  
2290      [Additive 5 RS](#) prepared in methylene chloride

2291      **Reference solution D:**

2292      0.1 mg/mL of [USP Butylated Hydroxytoluene RS](#) prepared in the *Solvent*  
2293      *mixture*

2294      **Reference solution E:**

2295      0.24 mg/mL of [USP Plastic Additive 1 RS](#) prepared in the *Solvent*  
2296      *mixture*

2297      **Reference solution F:**

2298      0.24 mg/mL of [USP Plastic Additive 6 RS](#) prepared in the *Solvent*  
2299      *mixture*

2300      **Reference solution G:**

2301      0.24 mg/mL of [USP Plastic Additive 2 RS](#) prepared in the *Solvent*  
2302      *mixture*

2303      **Reference solution H:**

2304      0.24 mg/mL of [USP Plastic Additive 3 RS](#) prepared in the *Solvent*  
2305      *mixture*

2306      **Reference solution I:**

2307      0.24 mg/mL of [USP Plastic Additive 4 RS](#) prepared in methylene chloride

2308      **Reference solution J:**

2309      0.24 mg/mL of [USP Plastic Additive 5 RS](#) prepared in methylene chloride

2310      **•TEST A:**

2311      If the substance to be examined contains additive butylated  
2312      hydroxytoluene and/or additive ethylene bis[3,3-bis[3-(1,1-  
2313      dimethylethyl)-4-hydroxyphenyl]butanoate] ([USP Plastic Additive 1](#)  
2314      [RS\)](#)<sup>▲</sup>, then carry out *Test A.*<sup>▲</sup> (USP 1-Aug-2020)

2315      **Mobile phase:**

2316      Acetonitrile and *Purified Water* (70:30, v/v)

2317      **Chromatographic system**

2318 (See *Chromatography* [\(621\)](#), *General Procedures, Liquid*  
2319 *Chromatography.*)

2320 **Detector:**

2321 UV 280 nm

2322 **Column:**

2323 4.6-mm × 25-cm; 5-μm packing L1

2324 **Flow rate:**

2325 2 mL/min

2326 **Injection volume:**

2327 20 μL

2328 **Run time:**

2329 30 min

2330 **System suitability**

2331 **Resolution:**

2332 Minimum 5.0 between the additive butylated hydroxytoluene and [USP](#)  
2333 [Plastic Additive 1 RS](#) (ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-  
2334 hydroxyphenyl]butanoate]) peaks, *Reference solution A*  
2335 *Sample solution S8* shows only peaks caused by antioxidants stated in  
2336 the composition and minor peaks that also correspond to the blank  
2337 solution.

2338 **Analysis**

2339 **Samples:**

2340 *Sample solution S8*, corresponding blank solution, *Reference solution A*,  
2341 and *Reference solution D*, *Reference solution E*, or both.

2342 **Acceptance criteria:**

2343 The peak areas of *Sample solution S8* are less than the corresponding  
2344 peak areas of *Reference solution D* or *Reference solution E*.

2345 •**TEST B:**

2346 If the substance to be examined contains one or more of the following  
2347 antioxidants: pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-  
2348 hydroxyphenyl)propionate] ([USP Plastic Additive 2 RS](#)); 2,2',2'',6,6',6''-  
2349 hexa-*tert*-butyl-4,4',4''-[(2,4,6-trimethyl-1,3,5-benzene-  
2350 triyl)trismethylene]triphenol ([USP Plastic Additive 3 RS](#)); octadecyl-3-

2351 (3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate ([USP Plastic Additive 4](#)  
2352 [RS](#)); tris(2,4-di-*tert*-butylphenyl) phosphite ([USP Plastic Additive 5](#)  
2353 [RS](#));<sup>▲</sup> (USP 1-Aug-2020) 1,3,5-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-s-triazine-  
2354 2,4,6(1*H*,3*H*,5*H*)-trione ([USP Plastic Additive 6 RS](#)),<sup>▲</sup> then carry out *Test*

2355 [B.](#)<sup>▲</sup> (USP 1-Aug-2020)

### Mobile phase:

2357 Acetonitrile, tetrahydrofuran, and *Purified Water* (60:30:10, v/v/v)

### Chromatographic system:

2359 Carry out the test as described in *Test A* with the following modifications.

#### Detector:

2361 UV 280 nm

#### Flow rate:

2363 1.5 mL/min

#### Injection volume:

2365 20 µL

### System suitability

#### Resolution:

2368 Minimum 2.0 between [USP Plastic Additive 2 RS](#) (pentaerythrityl  
2369 tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate]) and [USP](#)  
2370 [Plastic Additive 3 RS](#) (2,2',2'',6,6',6''-hexa-*tert*-butyl-4,4',4''-[(2,4,6-  
2371 trimethyl-1,3,5-benzene-triyl)trismethylene]triphenol peaks), *Reference*  
2372 *solution B*

2373 *Sample solution S8* shows only peaks caused by antioxidants stated in  
2374 the composition and minor peaks that also correspond to the blank  
2375 solution.

### Analysis

#### Samples:

2378 *Sample solution S8*, corresponding blank solution, *Reference solution B*,  
2379 and any *Reference solutions* of the antioxidants listed above that are  
2380 stated in the composition

#### Acceptance criteria:

2382 The peak areas of *Sample solution S8* are less than the corresponding  
2383 areas of the *Reference solutions* of the antioxidants that are listed above  
2384 and that are stated in the composition.

2385 **•TEST C:**

2386 If the substance to be examined contains [USP Plastic Additive 4 RS](#)  
2387 (octadecyl-3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate) and/or [USP](#)  
2388 [Plastic Additive 5 RS](#) (tris(2,4-di-*tert*-butylphenyl) phosphite), <sup>▲</sup>then  
2389 carry out *Test C.* ▲ (USP 1-Aug-2020)

2390 **Mobile phase:**

2391 Methanol, 2-propanol, and *Purified Water* (50:45:5, v/v/v)

2392 **Chromatographic system:**

2393 Carry out the test as described in *Test A* with the following modifications.

2394 **Detector:**

2395 UV 280 nm

2396 **Flow rate:**

2397 1.5 mL/min

2398 **Injection volume:**

2399 20 µL

2400 **System suitability**

2401 **Resolution:**

2402 Minimum 2.0 between [USP Plastic Additive 4 RS](#) (octadecyl-3-(3,5-di-  
2403 *tert*-butyl-4-hydroxyphenyl)propionate) and [USP Plastic Additive 5 RS](#)  
2404 (tris(2,4-di-*tert*-butylphenyl) phosphite) peaks, *Reference solution C*  
2405 *Sample solution S8*<sup>▲</sup>*S9* ▲ (USP 1-Aug-2020) shows only peaks due to antioxidants

2406 stated in the composition and minor peaks that also correspond to the  
2407 blank solution.

2408 **Analysis**

2409 **Samples:**

2410 *Sample solution S9*, corresponding blank solution, *Reference solution C*,  
2411 and either *Reference solution I* or *Reference solution J*

2412 **Acceptance criteria:**

2413 The peak areas of *Sample solution S9* are less than the corresponding  
2414 peak areas of *Reference solution I* or *Reference solution J*.

2415    **Nonphenolic antioxidants**

2416    **Methylene chloride, acidified:**

2417    To 100 mL of methylene chloride add 10 mL of hydrochloric acid, shake,  
2418    allow to stand, and separate the two layers. Use the lower layer.

2419    **Iodine in ethanol detection solution:**

2420    Dissolve 10 g of iodine in 100 mL of alcohol absolute. Store protected  
2421    from light.

2422    **Sample solution S10:**

2423    Evaporate 100 mL of *Solution S2* to dryness under vacuum at 45°.  
2424    Dissolve the resulting residue with 2 mL of *Methylene chloride, acidified*.

2425    **Reference solution M:**

2426    6.0 mg/mL of [USP Plastic Additive 8 RS](#) prepared in methylene chloride.  
2427    Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

2428    **Reference solution N:**

2429    6.0 mg/mL of [USP Plastic Additive 9 RS](#) prepared in methylene chloride.  
2430    Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

2431    **Reference solution O:**

2432    6.0 mg/mL of [USP Plastic Additive 10 RS](#) prepared in methylene chloride.  
2433    Dilute 2 mL of the solution with *Methylene chloride, acidified* to 10 mL.

2434    **Reference solution P:**

2435    6.0 mg/mL of [USP Plastic Additive 10 RS](#), and 6.0 mg/mL of [USP Plastic](#)  
2436    [Additive 9 RS](#) prepared in methylene chloride. Dilute 2 mL of the solution  
2437    with *Methylene chloride, acidified* to 10 mL.

2438    **Chromatographic system**

2439    (See *Chromatography* (621), *General Procedures, Thin-Layer*  
2440    *Chromatography*.)

2441    **Plate:**

2442    TLC silica gel GF<sub>254</sub>

2443    **Mobile phase A:**

2444    Hexane

2445    **Mobile phase B:**

2446        Methylene chloride

2447     **Application volume:**

2448        20 µL

2449     **Development A:**

2450        Over a path of 18 cm with *Mobile phase A*; dry in air

2451     **Development B:**

2452        Over a path of 17 cm with *Mobile phase B*; dry in air

2453     **Detector:**

2454        UV 254 nm. Spray with *Iodine in ethanol detection solution* and examine

2455        after 10–15 min.

2456     **System suitability**

2457     **Resolution:**

2458        The chromatogram shows two clearly separated spots, *Reference*

2459        *solution P*.

2460     **Analysis**

2461     **Samples:**

2462        *Sample solution S10* and the reference solutions corresponding to all of

2463        the phenolic and nonphenolic antioxidants expected to be present in the

2464        test material

2465     **Acceptance criteria:**

2466        Any spots in the chromatogram of *Sample solution S10* are not more

2467        intense than the spots in the same positions in the chromatograms of

2468        the *Reference solutions*.

2469     **Amides and stearates**

2470     **Sample solution:**

2471        Use *Sample solution S10* described in *Nonphenolic antioxidants*.

2472     **Reference solution R:**

2473        2.0 mg/mL of [USP Stearic Acid RS](#) prepared in methylene chloride

2474     **Reference solution S:**

2475        2.0 mg/mL of [USP Plastic Additive 12 RS](#) prepared in methylene chloride

2476     **Reference solution T:**

2477      2.0 mg/mL of [USP Plastic Additive 13 RS](#) prepared in methylene chloride  
2478      **Chromatographic system**

2479      (See *Chromatography* (621), *General Procedures, Thin-Layer*  
2480      *Chromatography*.)

2481      **Plate:**

2482      TLC silica gel GF<sub>254</sub>

2483      • **TEST A**

2484      **Mobile phase:**

2485      2,2,4-trimethylpentane and anhydrous ethanol (75:25, v/v)

2486      **Application volume:**

2487      10 µL

2488      **Development:**

2489      Over a path of 10 cm with *Mobile phase*; dry in air

2490      **Detector:**

2491      Spray with a 2-g/L solution of 2,6-dichlorophenol-indophenol sodium in  
2492      dehydrated alcohol and heat in an oven at 120° for a few minutes to  
2493      intensify the spots.

2494      **Analysis**

2495      **Samples:**

2496      *Sample solution S10* and *Reference solution R*

2497      **Acceptance criteria:**

2498      Any spot corresponding to additive stearic acid in *Sample solution S10* is  
2499      identical in position (*R<sub>f</sub>* about 0.5) but is not more intense than the spot  
2500      in the same position in *Reference solution R*.

2501      • **TEST B**

2502      **Mobile phase A:**

2503      Hexane

2504      **Mobile phase B:**

2505      Methylene chloride and methanol (95:5, v/v)

2506      **Application volume:**

2507      10 µL

2508 **Development A:**

2509 Over a path of 13 cm with *Mobile phase A*; dry in air

2510 **Development B:**

2511 Over a path of 10 cm with *Mobile phase B*; dry in air

2512 **Detector:**

2513 Spray with a 40-g/L solution of phosphomolybdic acid in alcohol,

2514 dehydrated, and heat in an oven at 120° until spots appear.

2515 **Analysis**

2516 **Samples:**

2517 *Sample solution S10, Reference solution S, and Reference solution T*

2518 **Acceptance criteria:**

2519 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*.

2523 Change to read:

## 2524 **POLYVINYL CHLORIDE**

### 2525 **Identification**

2526 [NOTE—The identification of polyvinyl chloride needs compliance with  
2527 only one test procedure to be established]

#### 2528 •**A. INFRARED SPECTROPHOTOMETRY {<sup>(197F)</sup>}**

2529 Refer to {<sup>(854)</sup>}.<sup>▲</sup> (USP 1-Aug-2020)

### 2530 **Apparatus:**

2531 Use an infrared spectrophotometer capable of correcting for the blank  
2532 spectrum and able to measure in transmission mode or equipped with an  
2533 internal reflectance accessory and an appropriate internal reflectance  
2534 plate.

### 2535 **Sample preparation**

### 2536 **Transmission mode:**

2537 Prepare a specimen of appropriate thickness without visible defects  
2538 (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  $\text{cm}^{-1}$  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 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

2573 this class. Substantial equivalence is achieved when all differences  
2574 between the sample and RS spectra can be explained in the context of  
2575 such natural compositional and/or physical variations.

2576 **•B. THERMAL ANALYSIS**

2577 Refer to [\(891\)](#).

2578 **Sample preparation:**

2579 Place an appropriately sized sample in the test specimen pan. [NOTE—  
2580 Intimate contact between the pan and the thermocouple is essential for  
2581 obtaining reproducible results.]

2582 **Procedure:**

2583 Determine the thermal analysis curve under nitrogen, using  
2584 heating/cooling conditions specified for the polymer type and using  
2585 equipment capable of performing the determinations as described in  
2586 [\(891\)](#). Heat the specimen from –20° to 120° at a heating rate of about  
2587 10°/min. Quickly cool the specimen to room temperature.

2588 **Acceptance criteria:**

2589 The thermal analysis curve of the specimen is similar to the thermal  
2590 analysis curve of [USP Polyvinyl Chloride RS](#), and the melting peak  
2591 temperature obtained from the thermal analysis curve of the specimen  
2592 does not differ from that of the RS by more than 8.0°. Note that the  
2593 results of the DSC analysis are strongly dependent on the amount of  
2594 plasticizer in the test article.

2595 **Physicochemical Tests**

2596 **Water extraction, Solution S1:**

2597 Place 25 g of the test material into a borosilicate glass flask. Add 500 mL  
2598 of *Purified Water*, cover the flask's neck with aluminum foil or a  
2599 borosilicate beaker, and heat in an autoclave at 121 ± 2° for 20 min.  
2600 Allow the solution to cool and the solids to settle, decant the solution  
2601 into a 500-mL volumetric flask, and dilute with *Purified Water* to volume;  
2602 the diluted solution is designated *Solution S1*.

2603 **~~Alcohol extraction, Solution S5~~**

2604 ~~Place 10 g of the test material in a borosilicate glass flask with a ground-~~  
2605 ~~glass neck. Add 100 mL of alcohol, absolute, and heat at 50° for 5 h.~~

2606 Allow to cool and the solids to settle, then decant the solution, producing  
2607 ~~Solution S5. Use Solution S5 within 4 h of preparation.~~ ▲ (USP 1-Aug-2020)

2608 **Absorbance**

2609 Refer to [\(857\)](#).

2610 **Procedures**

2611 **Solution S1:**

2612 Evaporate 100 mL of *Solution S1* to dryness. Dissolve the residue in 5  
2613 mL of hexane. If necessary, pass through a filter that has been  
2614 previously rinsed with hexane. Determine the spectrum between 250  
2615 and 330 nm in the dissolved residue.

2616 **Solution S6:**

2617 If the polyvinyl chloride contains 1-phenyleicosane-1,3-dione and is used  
2618 as a container for dry dosage forms for oral administration, dilute  
2619 *Solution S6* (1 in 10) with ethanol prior to measurement. In all other  
2620 situations, analyze *Solution S6* with no further preparation. Determine  
2621 the spectrum between 250 and 330 nm in the dissolved residue.

2622 **Acceptance criteria**

2623 **Solution S1:**

2624 NMT 0.25 for containers for non-injectable aqueous solutions. NMT 0.30  
2625 for containers for dry dosage forms for oral administration.

2626 **Solution S6:**

2627 NMT 0.2 for tin-stabilized materials used as containers for non-injectable  
2628 aqueous solutions. NMT 0.4 for other materials used as containers for  
2629 non-injectable aqueous solutions. NMT 1.0 for materials that do not  
2630 contain 1-phenyleicosane-1,3-dione used as containers for dry dosage  
2631 forms for oral administration. NMT 0.4 for materials containing 1-  
2632 phenyleicosane-1,3-dione used as containers for dry dosage forms for  
2633 oral administration.

2634 **Total organic carbon**

2635 **Procedure:**

2636 The TOC content of *Solution S1* is measured according to the general  
2637 methodologies outlined in [\(643\)](#). However, although [\(643\)](#) is designed for  
2638 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<sup>a</sup> (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<sup>a</sup> acceptance criteria<sup>a</sup> (USP 1-Aug-2020) 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%

2672     **Sorbitol:**

2673       NMT 1.5%

2674     **2,4-Dinonylphenyl phosphite or di(4-nonylphenyl) phosphite or**

2675     **tris(nonylphenyl) phosphite:**

2676       NMT 1%

2677     **Calcium carbonate:**

2678       For materials used for containers for dry dosage forms for oral

2679       administration, NMT 1%

2680     **Silica:**

2681       For materials used for containers for dry dosage forms for oral

2682       administration, NMT 1%

2683     **Colorants:**

2684       May contain a colorant or pigment or may be opacified by titanium

2685       dioxide

2686     **Stabilizers**

2687       They may contain one of the following groups of stabilizers (where

2688       isooctyl is, for example, 2-ethylhexyl).

2689     **Tin as di(isooctyl) 2,2'-(dioctylstannylene)bis(thio)]-diacetate**

2690     **containing about 27% of tri(isooctyl)2,2',2"-**

2691     **[(mono octylstannylidyne)tris(thio) triacetate:**

2692       NMT 0.25%

2693     **Tin as a mixture containing NMT 76% of di(isooctyl) 2,2'**

2694     **[(dioctylstannylene)bis(thio)]-diacetate and NMT 85% of**

2695     **tri(isooctyl)2,2',2"-[(mono octylstannylidyne)tris(thio) triacetate:**

2696       NMT 0.25%

2697     **1-Phenyleicosane-1,3-dione (benzoylstearoylmethane):**

2698       NMT 1%

2699     **Tin in tin-stabilized materials**

2700     **Reference solution U:**

2701      0.81 mg/mL of [USP Plastic Additive 18 RS](#) prepared in tetrahydrofuran is  
2702      diluted from 20 to 100 mL with ethanol.

2703      **Standard solution:**

2704      Add 0.1 mL of *Solution S6<sup>▲</sup>Reference solution U<sub>▲</sub> (USP 1-Aug-2020)* to a test tube.  
2705      Add 0.05 mL of 1 M hydrochloric acid, 0.5 mL of potassium iodide  
2706      solution, and 5 mL of ethanol to the test tube. Mix thoroughly and wait  
2707      for 5 min. Add 9 mL of water and 0.1 mL of a 5-g/L solution of sodium  
2708      sulfite and mix thoroughly. Add 1.5 mL of dithizone solution freshly  
2709      diluted 100-fold with methylene chloride, shake for 15 s, and allow to  
2710      stand for 2 min.

2711      **Sample solution:**

2712      Take 0.1 mL of *Reference solution U<sup>▲</sup>Solution S6<sub>▲</sub> (USP 1-Aug-2020)* through the  
2713      same procedure as the 0.1 mL of *Solution S6<sup>▲</sup>Reference solution U<sub>▲</sub> (USP 1-  
2714      Aug-2020)*.

2715      **Analysis**

2716      **Samples:**

2717      *Standard solution* and *Sample solution*  
2718      Compare the violet color in the lower layer of the *Sample solution* to the  
2719      violet color in the lower layer of the *Standard solution*.

2720      **Acceptance criteria:**

2721      NMT 0.25 weight %. The color in the *Sample solution* should not be as  
2722      intense as the color in the *Standard solution*.

2723      **Tin in non-tin-stabilized materials**

2724      **Standard solution:**

2725      Take 0.05 mL of *Reference solution U* through the same procedure as  
2726      the 0.1 mL of *Solution S6*.

2727      **Sample solution:**

2728      Add 5 mL of *Solution S6* to a test tube. Add 0.05 mL of 1 M hydrochloric  
2729      acid, 0.5 mL of potassium iodide solution, and 5 mL of ethanol to the  
2730      test tube. Mix thoroughly and wait for 5 min. Add 9 mL of water and 0.1  
2731      mL of a 5-g/L solution of sodium sulfite and mix thoroughly. If the  
2732      solution is not colorless, add the sodium sulfite in 0.05-mL fractions. Add

2733      1.5 mL of dithizone solution freshly diluted 100-fold with methylene  
2734      chloride, shake for 15 s and allow to stand for 2 min.

2735      **Analysis**

2736      **Samples:**

2737      *Standard solution and Sample solution*

2738      Compare the violet color in the lower layer of the *Sample solution* to the  
2739      violet color in the lower layer of the *Standard solution*. ~~The color in the~~  
2740      ~~*Sample solution* should not be as intense as the color in the *Standard*~~  
2741      ~~solution.~~▲ (USP 1-Aug-2020)

2742      **Acceptance criteria:**

2743      ▲NMT 25 µg/g (ppm).▲ (USP 1-Aug-2020) The color in the *Sample solution* should  
2744      not be as intense as the color in the *Standard solution*. ~~Non-tin-stabilized~~  
2745      ~~materials, NMT 25 µg/g (ppm).~~▲ (USP 1-Aug-2020)

2746      **Related Substances**

2747      **Vinyl chloride**

2748      **Internal standard solution:**

2749      Using a microsyringe, inject 10 µL of ethyl ether into 20.0 mL of *N,N*-  
2750      dimethylacetamide, immersing the tip of the needle in the solvent.  
2751      Immediately before use, dilute the solution with *N,N*-dimethylacetamide  
2752      to 1000 times its volume.

2753      **Sample solution:**

2754      Place 1.0 g of the test material in a 50-mL vial, and add 10.0 mL of the  
2755      *Internal standard solution*. Close the vial, and secure with a stopper.  
2756      Shake, avoiding contact between the stopper and the liquid. Place the  
2757      vial in a water bath at 60 ± 1° for 2 h.

2758      **Vinyl chloride primary solution:**

2759      [NOTE—Prepare under a ventilated hood.] Place 50.0 mL of *N,N*-  
2760      dimethylacetamide in a 50-mL vial, stopper the vial, secure the stopper,  
2761      and weigh to the nearest 0.1 mg. Fill a 50-mL polyethylene or  
2762      polypropylene syringe with gaseous vinyl chloride, allow the gas to  
2763      remain in contact with the syringe for about 3 min, empty the syringe,  
2764      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  $\mu$ L of the solution obtained contains about 1.2  $\mu$ g 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  $\mu$ L, 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  $\mu$ g of vinyl chloride. Shake, avoiding contact between the stopper and the liquid. Place the vials in a water bath at  $60 \pm 1^\circ$  for 2 h.

**Chromatographic system**

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

**Column:**

Stainless steel 3-mm  $\times$  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:**

150°

**Carrier gas:**

Nitrogen

**Flow rate:**

30 mL/min

2798     **Analysis**

2799     **Samples:**

2800         *Sample solution and Reference solutions*

2801         Inject 1 mL of the head space of each vial containing the *Sample*

2802         *solution and the Reference solutions.* Calculate the amount of vinyl  
2803         chloride in the *Sample solution* by comparing the test result of the  
2804         *Sample solution* with the test results of the *Reference solutions*.

2805         Calculate the amount of vinyl chloride in the test material by dividing  
2806         the amount of vinyl chloride in the *Sample solution* by 1.0 g, producing  
2807         a result in µg/g or ppm.

2808     **Acceptance criteria:**

2809         NMT 1 ppm. Note that vinyl chloride is not an additive but is monitored  
2810         as a residual monomer.

2811     **Chlorine content**

2812     **Preparation:**

2813         Prepare the sample using *Oxygen Flask Combustion* (471). Perform the  
2814         combustion with 50.0 mg of the test material. Absorb the combustion  
2815         products with 20 mL of 1 M sodium hydroxide.

2816     **Analysis:**

2817         Add 2.5 mL of nitric acid, 10 mL of 0.1 M silver nitrate solution, 5 mL of  
2818         ferric ammonium sulfate solution, and 1 mL of dibutyl phthalate to the  
2819         *Preparation* solution. Titrate with 0.005 M ammonium thiocyanate  
2820         solution until a reddish-yellow color is obtained. Carry out a blank  
2821         titration.

2822     **Calculation:**

2823         Calculate the titration volume by subtracting the volume of titrant used  
2824         in the blank from the volume of titrant used in the *Preparation*. Each  
2825         milliliter of titrant volume is equal to 6.25 mg of polyvinyl chloride. The  
2826         chlorine content, in weight %, is calculated as follows:

Chlorine content (weight %) = {[titrant volume (in mL) × 6.25 mg/mL]/weight of sample (mg)} × 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.]

## **•A. INFRARED SPECTROPHOTOMETRY (~~INFRARED ABSORPTION(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

2858 or, if necessary, a soft cloth dampened with methanol, and permit the  
2859 surfaces to dry. Then securely mount the specimen on the internal  
2860 reflection plate, ensuring adequate surface contact.  
2861

**Tetrahydrofuran extraction, Solution S6:**

2862 Dissolve 5.0 g of the test material in 80 mL of tetrahydrofuran and dilute  
2863 with the same solvent to a volume of 100 mL. Filter if necessary; the  
2864 solution may remain opaque. Slowly and dropwise add 70 mL of ethanol  
2865 to 20 mL of this solution. Cool the mixture in ice for 1 h. Filter or  
2866 centrifuge the mixture, collecting residue A. Wash residue A with  
2867 ethanol. Collect the washings and add them to the solution remaining  
2868 after filtration or centrifugation. Transfer the solution to a 100-mL  
2869 volumetric flask and dilute to volume with ethanol. This process  
2870 produces *Solution S6*. Prepare a blank solution.  
2871

**Procedure:**

2872 Dissolve residue A from *Solution S6* in 5 mL of tetrahydrofuran. Apply a  
2873 few drops of this solution to a sodium chloride plate and evaporate to  
2874 dryness in an oven at 100°–105°. Determine the infrared spectrum from  
2875 3800  $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$  (2.6–15 mm).  
2876

**Acceptance criteria:**

2877 The specimen exhibits an absorption spectrum that is substantially  
2878 equivalent to that of [USP Polyvinyl Chloride, Plasticized RS](#). Substantial,  
2879 as opposed to exact, equivalence allows for minor spectral differences  
2880 arising from the natural compositional and/or physical variation among  
2881 polymers of this class. Substantial equivalence is achieved when all  
2882 differences between the sample and RS spectra can be explained in the  
2883 context of such natural compositional and/or physical variations.  
2884

**•B. THERMAL ANALYSIS**

2885 Refer to [\(891\)](#).

**Sample preparation:**

2887 Place an appropriately sized sample in the test specimen pan. [NOTE—  
2888 Intimate contact between the pan and the thermocouple is essential for  
2889 obtaining reproducible results.]]  
2890

**Procedure:**

2891 Determine the thermal analysis curve under nitrogen, using  
2892 heating/cooling conditions specified for the polymer type and using  
2893 equipment capable of performing the determinations as described in  
2894 [\(891\)](#). Heat the specimen from  $-20^{\circ}$  to  $120^{\circ}$  at a heating rate of about  
2895  $10^{\circ}/\text{min}$ . Quickly cool the specimen to room temperature.  
2896

**Acceptance criteria:**

2897 The thermal analysis curve of the specimen is similar to the thermal  
2898 analysis curve of [USP Polyvinyl Chloride, Plasticized RS](#), and the glass  
2899 transition temperature obtained from the thermal analysis curve of the  
2900 specimen does not differ from that of the RS. The nature of these  
2901 polymers and compositional variety, material-to-material variations in  
2902 the melting peak temperature can be anticipated. [NOTE— that the  
2903 results of the DSC analysis are strongly dependent on the amount of  
2904 plasticizer in the test article.]

**Physicochemical Tests**

**Water extraction, Solution S1:**

2907 Place 25 g of the test material into a borosilicate glass flask. Add 500 mL  
2908 of *Purified Water*, cover the flask's neck with aluminum foil or a  
2909 borosilicate beaker, and heat in an autoclave at  $121 \pm 2^{\circ}$  for 20 min.  
2910 Allow the solution to cool and the solids to settle, decant the solution  
2911 into a 500-mL volumetric flask, and dilute with *Purified Water* to volume;  
2912 the diluted solution is designated *Solution S1*.  
2913

**Absorbance**

2914 Refer to [\(857\)](#).

**Procedure:**

2916 Evaporate 100 mL of *Solution S1* to dryness. Dissolve the resulting  
2917 residue in 5 mL of hexane to produce the hexane sample. Pass the  
2918 hexane sample, if necessary, through a filter previously rinsed with  
2919 hexane. Determine the spectrum between 250 and 310 nm in the  
2920 hexane sample.

**Acceptance criteria:**

2922 NMT 0.25. If the specification for absorbance is exceeded, then the  
2923 material can still be considered compliant with this chapter if the

2924 chemicals responsible for the test results can be established (identity  
2925 and concentration) and the chemicals are characterized to establish that  
2926 the probable risk posed by all the chemicals, considered individually, is  
2927 within acceptable parameters.

2928 **Acidity or alkalinity**

2929 **BRP indicator solution:**

2930 1.0 mg/mL of bromothymol blue, 0.2 mg/mL of methyl red, and 0.2  
2931 mg/mL of phenolphthalein in alcohol. Filter the resulting solution.

2932 **Methyl orange solution:**

2933 Dissolve 100 mg of methyl orange in 80 mL of *Purified Water*, and dilute  
2934 with alcohol to 100 mL. Test for sensitivity: Add 0.1 mL of *Methyl orange*  
2935 *solution* to 100 mL of carbon dioxide-free *Purified Water*. NMT 0.1 mL of  
2936 1 N hydrochloric acid is required to change the color from yellow to red.

2937 **Procedure:**

2938 To 100 mL of *Solution S1* add 0.15 mL of *BRP indicator solution*.  
2939 Determine the titration volume of 0.01 N sodium hydroxide required to  
2940 change the color of the indicator to blue. To 100 mL of *Solution S1* add  
2941 0.2 mL of *Methyl orange solution*. Determine the titration volume of 0.01  
2942 N hydrochloric acid required to reach the beginning of the color change  
2943 of the indicator from yellow to orange.

2944 **Acceptance criteria:**

2945 NMT 1.5 mL of 0.01 N sodium hydroxide is required to change the color  
2946 of the indicator to blue. NMT 1.0 mL of 0.01 N hydrochloric acid is  
2947 required to reach the beginning of the color change of the indicator from  
2948 yellow to orange.

2949 **Total organic carbon**

2950 **Procedure:**

2951 The TOC content of *Solution S1* is measured according to the general  
2952 methodologies outlined in <643>. However, although <643> is designed for  
2953 the testing of high-purity water with low TOC values, material extracts  
2954 may have TOC values that are higher than those of *Purified Water*  
2955 because of extracted organic substances. Thus, the method used to  
2956 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.~~ ▲ (USP 1-Aug-2020)

**Plastic Additives**

2989 Additives are di(2-ethylhexyl) phthalate, *N'N*"-diacylethylenediamines,  
2990 epoxidized soya oil, and epoxidized linseed oil. Vinyl chloride monomer  
2991 (VCM) is also monitored, although it is a residual monomer and not an  
2992 additive.

2993 **Solution A1:**

2994 Add 2.0 g of the test material to 200 mL of peroxide-free ether and heat  
2995 under a reflux condenser for 8 h. Separate the resulting residue B and  
2996 extraction solution A by filtration. Evaporate extraction solution A to  
2997 dryness under reduced pressure in a water bath at 30°, producing  
2998 residue C. Dissolve residue C in 10 mL of toluene to produce *Solution*  
2999 *A1*.

3000 **Precipitate B2:**

3001 Dissolve residue B in 60 mL of ethylene chloride heating on a water bath  
3002 under a reflux condenser, producing solution D. Filter the resulting  
3003 solution D. Add the filtered solution D dropwise and with vigorous  
3004 shaking to 600 mL of heptanes heated almost to boiling. Separate by hot  
3005 filtration the coagulum B1 and the organic solution E. Allow solution E to  
3006 cool; separate the precipitate B2 that forms upon cooling, and pass  
3007 through a tared sintered-glass filter (pore size of 16–40 µm).

3008 **Reference solutions U, V, W:**

3009 10.0-mg/mL solutions of [USP Plastic Additive 14 RS](#), [USP Plastic Additive](#)  
3010 [15 RS](#), and [USP Plastic Additive 16 RS](#), respectively, in toluene

3011 **Chromatographic system**

3012 (See *Chromatography* (621), *General Procedures, Thin-Layer*  
3013 *Chromatography*.)

3014 **Plate:**

3015 TLC silica gel GF<sub>254</sub> (1-mm thick)

3016 **Procedure:**

3017 Apply 0.5 mL of *Solution A1* to the plate as a 30-mm × 3-mm band.  
3018 Apply 5 µL each of *Reference solutions U, V*, and *W* to the plate. Develop  
3019 the plate over a path of 15 cm using toluene. Dry the plate carefully.

3020 **Additive di(2-ethylhexyl) phthalate:**

3021 UV 254 nm. Locate the zone corresponding to additive di(2-ethylhexyl)  
3022 phthalate, [USP Plastic Additive 14 RS](#) ( $R_F$  about 0.4). Remove the area of  
3023 silica gel corresponding to this zone, mix with 40 mL of ethyl ether, and  
3024 shake for 1 min. Filter, rinse filter with two quantities each of 10 mL of  
3025 ethyl ether, add the rinsings to the filtrate, and evaporate to dryness.  
3026

**Additives epoxidized soya oil and epoxidized linseed oil:**

3027 Expose the plate to iodine vapor for 5 min. Examine the chromatogram,  
3028 and locate the band corresponding to additives epoxidized soya oil, [USP](#)  
3029 [Plastic Additive 15 RS](#), and epoxidized linseed oil, [USP Plastic Additive 16](#)  
3030 [RS](#) ( $R_F = 0$ ). Remove the area of silica gel corresponding to this band.  
3031 Similarly, remove a corresponding area of silica gel as a blank reference.  
3032 Separately mix both samples with separate 40-mL portions of methanol,  
3033 shaking for 15 min. Filter, rinse the filter with two quantities of 10 mL of  
3034 methanol, add the rinsings to the filtrate, and evaporate to dryness.  
3035

**Additive *N,N'*-diacylethylenediamines:**

3036 Wash precipitate B2 with alcohol, absolute. Dry to constant mass over  
3037 diphosphorus pentoxide, and weigh the filter.

**Acceptance criteria**

**Di(2-ethylhexyl)phthalate:**

3040 Residue is NMT 40 mg.

**Epoxidized soya oil:**

3042 The difference between the masses of both residues is NMT 10 mg.

**Epoxidized linseed oil:**

3044 The difference between the masses of both residues is NMT 10 mg.

***N,N'*-Diacylethylenediamines:**

3046 Residue is NMT 20 mg.

**Related Substances**

**Vinyl chloride**

**Internal standard solution:**

3050 Using a microsyringe, inject 10  $\mu$ L of ethyl ether into 20.0 mL of *N,N*-  
3051 dimethylacetamide, immersing the tip of the needle in the solvent.

3052      Immediately before use, dilute the solution with *N,N*-dimethylacetamide  
3053      to 1000 times its volume.

3054      **Sample solution:**

3055      Place 1.0 g of the test material in a 50-mL vial, and add 10.0 mL of the  
3056      *Internal standard solution*. Close the vial, and secure with a stopper.  
3057      Shake, avoiding contact between the stopper and the liquid. Place the  
3058      vial in a water bath at  $60 \pm 1^\circ$  for 2 h.

3059      **Vinyl chloride primary solution:**

3060      [NOTE—Prepare under a ventilated hood.] Place 50.0 mL of *N,N*-  
3061      dimethylacetamide in a 50-mL vial, stopper the vial, secure the stopper,  
3062      and weigh to the nearest 0.1 mg. Fill a 50-mL polyethylene or  
3063      polypropylene syringe with gaseous vinyl chloride, allow the gas to  
3064      remain in contact with the syringe for about 3 min, empty the syringe,  
3065      and fill again with 50 mL of gaseous vinyl chloride. Fit a hypodermic  
3066      needle to the syringe, and reduce the volume of gas in the syringe from  
3067      50 to 25 mL. Inject the remaining 25 mL of vinyl chloride slowly into the  
3068      vial, shaking gently and avoiding contact between the liquid and the  
3069      needle. Weigh the vial again; the increase in mass is about 60 mg (1  $\mu$ L  
3070      of the solution obtained contains about 1.2  $\mu$ g of vinyl chloride). Allow to  
3071      stand for 2 h. Store the primary solution in a refrigerator.

3072      **Vinyl chloride standard solution:**

3073      To 1 volume of the *Vinyl chloride primary solution* add 3 volumes of *N,N*-  
3074      dimethylacetamide.

3075      **Reference solutions:**

3076      Place 10.0 mL of the *Internal standard solution* in each of six 50-mL  
3077      vials. Close the vials, and secure the stoppers. Inject 1, 2, 3, 5, and 10  
3078       $\mu$ L, respectively, of the *Vinyl chloride standard solution* into 5 of the  
3079      vials. The 6 solutions thus obtained contain, respectively, 0, 0.3, 0.6,  
3080      0.9, 1.5, and 3  $\mu$ g of vinyl chloride. Shake, avoiding contact between the  
3081      stopper and the liquid. Place the vials in a water bath at  $60 \pm 1^\circ$  for 2 h.

3082      **Chromatographic system**

3083      (See *Chromatography* (621), *General Procedures, Gas Chromatography*.)

3084      **Column:**

3085      Stainless steel 3-mm × 3-m packed with silanized diatomaceous earth  
3086      for gas chromatography impregnated with 5% m/m of  
3087      dimethylstearylamine and 5% m/m of polyethylene glycol 400

3088      **Temperatures**

3089      **Injection port:**

3090      100°

3091      **Column:**

3092      45°

3093      **Detector:**

3094      FID 150°

3095      **Carrier gas:**

3096      Nitrogen

3097      **Flow rate:**

3098      30 mL/min

3099      **Analysis**

3100      **Samples:**

3101      *Sample solution and Reference solutions*

3102      Inject 1 mL of the head space of each vial containing the *Sample*

3103      *solution and the Reference solutions.* Calculate the amount of vinyl

3104      chloride in the *Sample solution* by comparing the test result of the

3105      *Sample solution* with the test results of the *Reference solutions*.

3106      Calculate the amount of vinyl chloride in the test material by dividing

3107      the amount of vinyl chloride in the *Sample solution* by 1.0 g, producing

3108      a result in µg/g or ppm.

3109      **Acceptance criteria:**

3110      NMT 1 ppm. Note that vinyl chloride is not an additive but is monitored

3111      as a residual monomer.

3112      **ADDITIONAL REQUIREMENTS**

3113      •**USP REFERENCE STANDARDS (11)**

3114      **Polymer standards**

- 3115      [USP Cyclic Olefin Copolymer RS](#)
- 3116      [USP Cyclic Olefin Polymer RS](#)
- 3117      [USP Polyamide 6 RS](#)
- 3118      [USP Polycarbonate RS](#)
- 3119      [USP High-Density Polyethylene RS](#)
- 3120      [USP Homopolymer Polypropylene RS](#)
- 3121      [USP Low-Density Polyethylene RS](#)
- 3122      [USP Polyethylene Terephthalate RS](#)
- 3123      [USP Polyethylene Terephthalate G RS](#)
- 3124      [USP Poly\(ethylene-vinyl acetate\) RS](#)
- 3125      [USP Polyvinyl Chloride RS](#)
- 3126      [USP Polyvinyl Chloride, Plasticized RS](#)

## **Plastic additive standards**

- 3128      [USP Plastic Additive 1 RS](#)  
Ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate].  
[CAS-32509-66-3].
- 3131      [USP Plastic Additive 2 RS](#)  
Pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate].  
[CAS-6683-19-8].
- 3135      [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].
- 3139      [USP Plastic Additive 4 RS](#)  
Octadecyl 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate.  
[CAS-2082-79-3].
- 3142      [USP Plastic Additive 5 RS](#)  
Tris(2,4-di-*tert*-butylphenyl) phosphite.  
[CAS-31570-04-4].
- 3145      [USP Plastic Additive 6 RS](#)  
1,3,5-Tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-s-triazine-2,4,6(1*H*,3*H*,5*H*)-trione.  
[CAS-27676-62-6].
- 3149      [USP Plastic Additive 8 RS](#)

- 3150 Dioctadecyl disulfide.  
3151 [CAS-2500-88-1].  
3152 [USP Plastic Additive 9 RS](#)  
3153 Didodecyl 3,3'-thiodipropionate.  
3154 [CAS-123-28-4].  
3155 [USP Plastic Additive 10 RS](#)  
3156 Dioctadecyl 3,3'-thiodipropionate.  
3157 [CAS-693-36-7].  
3158 [USP Plastic Additive 11 RS](#)  
3159 Copolymer of dimethyl succinate and (4-hydroxy-2,2,6,6-tetramethylpiperidin-1-yl)ethanol.  
3160  
3161 [CAS-65447-77-0].  
3162 [USP Plastic Additive 12 RS](#)  
3163 Oleamide.  
3164 [CAS-301-02-0].  
3165 [USP Plastic Additive 13 RS](#)  
3166 Erucamide.  
3167 [CAS-112-84-5].  
3168 [USP Plastic Additive 14 RS](#)  
3169 Di(2-ethylhexyl) phthalate.  
3170 [CAS-117-81-7].  
3171 [USP Plastic Additive 15 RS](#)  
3172 Epoxidized soya oil.  
3173 [CAS-8013-07-8].  
3174 [USP Plastic Additive 16 RS](#)  
3175 Epoxidized linseed oil.  
3176 [CAS-8016-11-3].  
3177 [USP Plastic Additive 18 RS](#)  
3178 Mixture of Di(isooctyl) 2,2'-(dioctylstannylene)-bis(thio)diacetate and  
3179 Tri(isooctyl) 2,2',2''-[monooctylstannylidyne]tris(thio)]triacetate.  
3180 [CAS-26401-97-8; CAS-26401-86-5].  
3181 **Related substances standards**  
3182 [USP Bisphenol A RS](#)[CAS-80-05-07].  
3183 [USP Butylated Hydroxytoluene RS](#)[CAS-128-37-0].  
3184 [USP Caprolactam RS](#)[CAS-105-60-2].

3185

USP Stearic Acid RS[CAS-57-11-4].

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