

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.)

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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. ^(USP 1-Aug-2020) 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.) ^(USP 1-Aug-2020) If
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. ^(USP 1-Aug-2020)~~

13 Add the following:

14 ▲

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[▲]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[▲] acceptance
68 criteria[▲] (USP 1-Aug-2020) 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 [▲]and acceptance criteria[▲] (USP 1-Aug-2020) 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 [▲]plastic[▲] (USP 1-Aug-2020) additives [▲]and
81 relevant extracted metals[▲] (see (1661)).[▲] (USP 1-Aug-2020)

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 [▲](USP 1-Aug-2020) 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**

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

	addressing the purity criteria and 111
	limitations pertaining to use 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

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

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Table 1. Application of Tests

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

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120 ^a This table provides the appropriate application of the chemical tests for oral and topical
121 dosage forms. [NOTE—For aqueous-based oral drug products that contain
122 cosolvents (or if, for any reason, it may be expected to extract greater
123 amounts of substances from plastic packaging components than
124 water), additional extractables information may be needed to
125 determine suitability. If additional information is required, perform
126 Additives tests as directed in this table.]

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	Polyvinyl Chloride, Plasticized
Solution		Absorbance Acidity/alkalinity	Absorbance Acidity/alkalinity	Absorbance ^a Acidity/alkalinity	Absorbance Acidity/alkalinity	Absorbance Acidity/alkalinity	Absorbance Acidity/alkalinity	Absorbance, Acidity/alkalinity
S1	Water	TOC	TOC	TOC	TOC	TOC	TOC	TOC
Solution		Phenolic antioxidants, nonphenolic antioxidants, amides, and stearates ^a	N/A	N/A	N/A	Phenolic antioxidants, amides, and stearic acid ^a	N/A	N/A
S2	Toluene							
Solution		Extractable metals: Al, As, Cd, Co, Cr, ^b 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,	Extractable metals: Al, As, Ba, ^d Cd, Co, Hg,	Extractable metals: As, Ba, Ca, Cd, Co, Hg,
S3	Acid							

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	Polyvinyl Chloride, Plasticized
		Ni, Pb, Ti, V, Zn, and Zr ^a	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
Solution			Extractable metals: Sb and Ge		Extractable metals: Sb and Ge			
S4	Alkali	N/A	Ge	N/A	Ge	N/A	N/A	N/A
Solution								
S5	Alcohol	N/A	N/A	N/A	Absorbance	N/A	N/A	N/A
Solution								
S6	Tetrahydrofuran	N/A	N/A	N/A	N/A	N/A	Absorbance	N/A
Solution								
S7	Phenol	N/A	Free-base function	N/A	N/A	N/A	N/A	N/A

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^a 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.

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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**

180 The extractable metals testing described in this chapter is required for all
181 plastic materials of construction used in packaging systems.
182 Specifically, all materials must be tested for those extractable metals
183 listed in [Table 3](#).[▲] (USP 1-Aug-2020)

184 Change to read:

185 **CYCLIC OLEFINS**

186 **Identification**

187 ● **A. INFRARED SPECTROPHOTOMETRY** (~~INFRARED ABSORPTION (197F)~~)

188 [▲]Refer to *Mid-Infrared Spectroscopy (854)*.[▲] (USP 1-Aug-2020)

189 **Apparatus:**

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

194 **Sample preparation**

195 **Transmission mode:**

196 Prepare a specimen of appropriate thickness without visible defects
197 (cracks or holes). The specimens can be compressed to form a thin,
198 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 cm^{-1} to 650 cm^{-1} (2.6–15 μm).

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 **● ~~B. 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](#));[▲] (USP 1-Aug-2020) 1,3,5-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-s-triazine-
413 2,4,6(1*H*,3*H*,5*H*)-trione ([USP Plastic Additive 6 RS](#)),[▲] then carry out *Test*
414 *B*.[▲] (USP 1-Aug-2020)

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-
462 *tert*-butyl-4-hydroxyphenyl)propionate) and [USP Plastic Additive 5 RS](#)
463 (tris(2,4-di-*tert*-butylphenyl) phosphite) peaks, *Reference solution C*

464 *Sample solution S8*^{S9} (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](#)
495 [Additive 9 RS](#) prepared in methylene chloride. Dilute 2 mL of the solution
496 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*
503 *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 GF₂₅₄

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- μ m packing L8

557 **Flow rate:**

558 2 mL/min

559 **Injection volume:**

560 20 μ L

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 GF₂₅₄

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 cm^{-1} to 650 cm^{-1} (2.6–15 μm).

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[^]0.25-mm_▲ (USP 1-Aug-2020) × 30-m[^]0.25-μm_▲ (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).[▲] (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⁻¹ to 650 cm⁻¹ (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° to 300° 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° . 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~~^{0.32-mm}_(USP 1-Aug-2020) × ~~0.32-mm~~^{30-m}_(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 µg/g.

1076 Analyte (µg/g) = [analyte in *Sample solution* (mg/L) × 10]/weight of
1077 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 cm^{-1} to 650 cm^{-1} (2.6–15 μm).

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
1347 a ground-glass neck. Add 80 mL of toluene and boil under a reflux
1348 condenser for 1.5 h, stirring constantly. Allow to cool to 60° and add,
1349 with continued stirring, 120 mL of methanol. Pass the resulting solution
1350 through a sintered-glass filter. Rinse the flask and the filter with 25 mL

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*^{S9} (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](#)
1520 [Additive 9 RS](#) prepared in methylene chloride. Dilute 2 mL of the solution
1521 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*
1528 *Chromatography*.)

1529 **Plate:**

1530 TLC silica gel GF₂₅₄

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 GF₂₅₄

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 cm^{-1} to 650 cm^{-1} (2.6–15 μm).

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 cm^{-1} to 650 cm^{-1} (2.6–15 μm).

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° to 120° 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° .

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*
1960 *Chromatography.*)

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](#)
1974 [3 RS](#), Reference solution K

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](#)
2004 [Additive 5 RS](#), Reference solution L

2005 **Analysis**

2006 **Samples:**

2007 *Sample solution S13*, corresponding blank solution, and *Reference*
2008 *solution L*.

2009 **Acceptance criteria:**

2010 *Sample solution S13* shows only peaks caused by antioxidants in
2011 *Reference solution L* and minor peaks that also correspond to the blank
2012 solution. The peak areas of *Sample solution S13* are less than the
2013 corresponding peak areas of *Reference solution L*.

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*
2027 *Chromatography*.)

2028 **Plate:**

2029 TLC silica gel GF₂₅₄

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 GF₂₅₄

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~~[▲] (USP 1-Aug-2020)

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).[▲] (USP 1-Aug-2020)

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^{-1} to 650 cm^{-1} (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.

2238 **Extractable Metals**

2239 **Aluminum:**

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

2241 **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.

2246 **Chromium:**

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

2248 **Titanium:**

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

2250 **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*

2285 **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](#))[▲], then carry out *Test A*.[▲] (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);~~[▲] (USP 1-Aug-2020) 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-s-triazine-
2354 2,4,6(1H,3H,5H)-trione (USP Plastic Additive 6 RS),[▲] then carry out Test
2355 **B.**[▲] (USP 1-Aug-2020)

2356 **Mobile phase:**

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

2358 **Chromatographic system:**

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

2360 **Detector:**

2361 UV 280 nm

2362 **Flow rate:**

2363 1.5 mL/min

2364 **Injection volume:**

2365 20 µL

2366 **System suitability**

2367 **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.

2376 **Analysis**

2377 **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

2381 **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), 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*▲*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 GF₂₅₄

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 GF₂₅₄

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_f 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*
2520 *solution S10* are identical in position (R_f about 0.2) but are not more
2521 intense than the corresponding spots in *Reference solution S* and
2522 *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 ~~(197F)~~**

2529 [▲]Refer to (854).[▲] (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,

2539 uniform film by exposure to elevated temperatures and pressures (2000
2540 psi or more). The temperatures at which the thin films are generated
2541 represent a trade-off between producing a melt (which dictates the
2542 lowest temperature necessary) and degrading the sample (which
2543 dictates the highest temperature allowed). Ultimately, the temperatures
2544 that are used are appropriate if the film produced is conducive to the
2545 infrared analysis.

2546 **Internal reflectance mode:**

2547 Prepare a flat section and trim it as necessary to obtain a segment that
2548 is convenient for mounting in the internal reflectance accessory. Taking
2549 care to avoid scratching the surfaces, wipe the specimen with dry paper
2550 or, if necessary, a soft cloth dampened with methanol, and permit the
2551 surfaces to dry. Then securely mount the specimen on the internal
2552 reflection plate, ensuring adequate surface contact.

2553 **Tetrahydrofuran extraction, Solution S6:**

2554 Dissolve 5.0 g of the test material in 80 mL of tetrahydrofuran and dilute
2555 to a volume of 100 mL with the same solvent. Filter if necessary; the
2556 solution may remain opaque. Slowly and dropwise add 70 mL of ethanol
2557 to 20 mL of this solution. Cool the mixture in ice for 1 h. Filter or
2558 centrifuge the mixture, collecting residue A. Wash residue A with
2559 ethanol. Collect the washings and add them to the solution remaining
2560 after filtration or centrifugation. Transfer the solution to a 100-mL
2561 volumetric flask and dilute with ethanol to volume. This process
2562 produces *Solution S6*. Prepare a blank solution.

2563 **Procedure:**

2564 Dissolve residue A from *Solution S6* in 5 mL of tetrahydrofuran. Apply a
2565 few drops of this solution to a sodium chloride plate and evaporate to
2566 dryness in an oven at 100°–105°. Determine the infrared spectrum from
2567 3800 cm⁻¹ to 650 cm⁻¹ (2.6–15 μm).

2568 **Acceptance criteria:**

2569 The specimen exhibits an absorption spectrum that is substantially
2570 equivalent to that of [USP Polyvinyl Chloride RS](#). Substantial, as opposed
2571 to exact, equivalence allows for minor spectral differences arising from
2572 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 $10^{\circ}/\text{min}$. 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 $121 \pm 2^{\circ}$ 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

2639 may have TOC values that are higher than those of *Purified Water*
2640 because of extracted organic substances. Thus, the method used to
2641 perform the TOC analyses should have a limit of detection of 0.2 mg/L
2642 (ppm) and should have a demonstrated linear dynamic range from 0.2
2643 to 20 mg/L (which encompasses the TOC limit). A linear range with a
2644 higher upper concentration can be used if linearity is established. If
2645 sample extracts exceed this upper linear range, they must be diluted
2646 appropriately for analysis.

2647 **Acceptance criteria:**

2648 NMT 5 mg/L. If the specification for TOC is exceeded, then the material
2649 can still be considered compliant with this chapter if the chemicals
2650 responsible for the test results can be established (identity and
2651 concentration) and the chemicals are characterized to establish that the
2652 probable risk posed by all the chemicals, considered individually, is
2653 within acceptable parameters.

2654 **Plastic** (USP 1-Aug-2020) **Additives and Stabilizers:**

2655 The supplier of the material must be able to provide sufficient
2656 compositional information to establish whether the material meets the
2657 specifications acceptance criteria (USP 1-Aug-2020) for additives and stabilizers.

2658 **Plastic additives**

2659 **Epoxidized soya oil of which the oxiran oxygen content is 6%–8%**
2660 **and the iodine value is NMT 6:**

2661 For tin-stabilized materials, NMT 2%. For non-tin-stabilized materials,
2662 NMT 3%.

2663 **Calcium, magnesium, or zinc salts for aliphatic fatty acids with**
2664 **more than seven carbon atoms:**

2665 NMT 1.5% of one salt or NMT 1.5% of a mixture of salts

2666 **Lubricants:**

2667 For individual lubricants: waxes, NMT 4%; liquid paraffin, NMT 1.5%;
2668 hydrogenated oils or esters of aliphatic fatty acids, NMT 2%. Total
2669 lubricants: NMT 4%.

2670 **Macrogol esters:**

2671 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 **[(monoocylstannylidene)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''-[(monoocylstannylidene)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~~ **Reference solution U** (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~~ **Solution S6** (USP 1-Aug-2020) through the
2713 same procedure as the 0.1 mL of ~~Solution S6~~ **Reference solution U** (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 $60 \pm 1^\circ$ 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

2765 needle to the syringe, and reduce the volume of gas in the syringe from
2766 50 to 25 mL. Inject the remaining 25 mL of vinyl chloride slowly into the
2767 vial, shaking gently and avoiding contact between the liquid and the
2768 needle. Weigh the vial again; the increase in mass is about 60 mg (1 μ L
2769 of the solution obtained contains about 1.2 μ g of vinyl chloride). Allow to
2770 stand for 2 h. Store the primary solution in a refrigerator.

2771 **Vinyl chloride standard solution:**

2772 To 1 volume of the *Vinyl chloride primary solution* add 3 volumes of *N,N*-
2773 dimethylacetamide.

2774 **Reference solutions:**

2775 Place 10.0 mL of the *Internal standard solution* in each of six 50-mL
2776 vials. Close the vials, and secure the stoppers. Inject 1, 2, 3, 5, and 10
2777 μ L, respectively, of the *Vinyl chloride standard solution* into 5 of the
2778 vials. The 6 solutions thus obtained contain, respectively, 0, 0.3, 0.6,
2779 0.9, 1.5, and 3 μ g of vinyl chloride. Shake, avoiding contact between the
2780 stopper and the liquid. Place the vials in a water bath at $60 \pm 1^\circ$ for 2 h.

2781 **Chromatographic system**

2782 (See *Chromatography* (621), *General Procedures, Gas Chromatography*.)

2783 **Column:**

2784 Stainless steel 3-mm \times 3-m packed with silanized diatomaceous earth
2785 for gas chromatography impregnated with 5% m/m of
2786 dimethylstearylamine and 5% m/m of polyethylene glycol 400

2787 **Temperatures**

2788 **Injection port:**

2789 100 $^\circ$

2790 **Column:**

2791 45 $^\circ$

2792 **Detector:**

2793 150 $^\circ$

2794 **Carrier gas:**

2795 Nitrogen

2796 **Flow rate:**

2797 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 $\mu\text{g/g}$ 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:

2827 Chlorine content (weight %) = {[titrant volume (in mL) × 6.25
2828 mg/mL]/weight of sample (mg)} × 100%

2829 **Acceptance criteria:**

2830 NLT 80% by weight, expressed as polyvinyl chloride

2831 **Change to read:**

2832 **POLYVINYL CHLORIDE, PLASTICIZED**

2833 **Identification**

2834 [NOTE—The identification of polyvinyl chloride, plasticized needs
2835 compliance with only one test procedure to be established.]

2836 ● **A. INFRARED SPECTROPHOTOMETRY** (~~INFRARED ABSORPTION (197F)~~)

2837 ▲Refer to (854).▲ (USP 1-Aug-2020)

2838 **Apparatus:**

2839 Use an infrared spectrophotometer capable of correcting for the blank
2840 spectrum and able to measure in transmission mode or equipped with an
2841 internal reflectance accessory and an appropriate internal reflectance
2842 plate.

2843 **Sample preparation**

2844 **Transmission mode:**

2845 Prepare a specimen of appropriate thickness without visible defects
2846 (cracks or holes). The specimens can be compressed to form a thin,
2847 uniform film by exposure to elevated temperatures and pressures (2000
2848 psi or more). The temperatures at which the thin films are generated
2849 represent a trade-off between producing a melt (which dictates the
2850 lowest temperature necessary) and degrading the sample (which
2851 dictates the highest temperature allowed). Ultimately, the temperatures
2852 that are used are appropriate if the film produced is conducive to the
2853 infrared analysis.

2854 **Internal reflectance mode:**

2855 Prepare a flat section and trim it as necessary to obtain a segment that
2856 is convenient for mounting in the internal reflectance accessory. Taking
2857 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 cm⁻¹ to 650 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).

2886 **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° to 120° 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.]

2905 **Physicochemical Tests**

2906 **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).

2915 **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.

2921 **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

2957 (ppm) and should have a demonstrated linear dynamic range from 0.2
2958 to 20 mg/L (which encompasses the TOC limit). A linear range with a
2959 higher upper concentration can be used if linearity is established. If
2960 sample extracts exceed this upper linear range, they must be diluted
2961 appropriately for analysis.

2962 **Acceptance criteria:**

2963 The difference between the sample and blank TOC concentrations is NMT
2964 5 mg/L. If the specification for TOC is exceeded, then the material can
2965 still be considered to be compliant with this chapter if the chemicals
2966 responsible for the test results can be established (identity and
2967 concentration) and the chemicals are characterized to establish that the
2968 probable risk posed by all the chemicals, considered individually, is
2969 within acceptable parameters.

2970 **Extractable Metals**

2971 ~~**Arsenic, cadmium, lead, mercury, cobalt, nickel, and vanadium:**~~

2972 ~~Report the measured value in *Solution S3* at values above 0.01 mg/L~~
2973 ~~(ppm), corresponding to 0.025 µg/g. If the measured values are below~~
2974 ~~these values, report the result as less than 0.01 mg/L (ppm),~~
2975 ~~corresponding to less than 0.025 µg/g.~~

2976 ~~**Barium:**~~

2977 ~~*Solution S3* contains NMT 0.25 mg/L (ppm), corresponding to 5 µg/g.~~

2978 ~~**Calcium:**~~

2979 ~~*Solution S3* contains NMT 35 mg/L (ppm), corresponding to 0.07 weight~~
2980 ~~%.~~

2981 ~~**Tin:**~~

2982 ~~*Solution S3* contains NMT 1 mg/L (ppm), corresponding to 20 µg/g.~~

2983 ~~**Zinc:**~~

2984 ~~*Solution S3* contains NMT 100 mg/L (ppm), corresponding to 0.2 weight~~
2985 ~~%.~~

2986 Test results for additional relevant extractable metals are similarly
2987 reported. [▲] (USP 1-Aug-2020)

2988 **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 GF₂₅₄ (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.

3038 **Acceptance criteria**

3039 **Di(2-ethylhexyl)phthalate:**

3040 Residue is NMT 40 mg.

3041 **Epoxidized soya oil:**

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

3043 **Epoxidized linseed oil:**

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

3045 ***N,N''*-Diacylethylenediamines:**

3046 Residue is NMT 20 mg.

3047 **Related Substances**

3048 **Vinyl chloride**

3049 **Internal standard solution:**

3050 Using a microsyringe, inject 10 μ 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 μ L
3070 of the solution obtained contains about 1.2 μ 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 μ 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 μ 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](#)
3127 **Plastic additive standards**

- 3128 [USP Plastic Additive 1 RS](#)
3129 Ethylene bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxyphenyl]butanoate].
3130 [CAS-32509-66-3].
3131 [USP Plastic Additive 2 RS](#)
3132 Pentaerythrityl tetrakis[3-(3,5-di-*tert*-butyl-4-
3133 hydroxyphenyl)propionate].
3134 [CAS-6683-19-8].
3135 [USP Plastic Additive 3 RS](#)
3136 2,2',2'',6,6',6''-Hexa-*tert*-butyl-4,4',4''-[(2,4,6-trimethyl-1,3,5-
3137 benzenetriyl)trismethylene]triphenol.
3138 [CAS-1709-70-2].
3139 [USP Plastic Additive 4 RS](#)
3140 Octadecyl 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionate.
3141 [CAS-2082-79-3].
3142 [USP Plastic Additive 5 RS](#)
3143 Tris(2,4-di-*tert*-butylphenyl) phosphite.
3144 [CAS-31570-04-4].
3145 [USP Plastic Additive 6 RS](#)
3146 1,3,5-Tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-*s*-triazine-
3147 2,4,6(1*H*,3*H*,5*H*)-trione.
3148 [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-
3160 tetramethylpiperidin-1-yl)ethanol.
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''-[monoctylstannylidyne)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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