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STAFF DIRECTORY

This updated directory reflects assignment changes based on 2005–2010 Expert Committees. The general USP telephone number, (301) 881-0666, may still be used for general inquiries or when a particular Expert Committee is not identified. The fax number is (301) 816-8373.

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USP ANNOUNCES A REVISED MONOGRAPH TO LEVOTHYROXINE SODIUM TABLETS. USP revised the monograph for Levothyroxine Sodium Tablets to support the action of the U.S. Food and Drug Administration to ensure the drug product retains its potency over its shelf life. USP published the revision to the *Assay* range in *Pharmacopeial Forum* 34(1) [Jan–Feb 2008] for public review and comment; the comment period ended on April 15, 2008. The proposed revision was approved for adoption by the relevant USP Expert Committee for inclusion in *USP 32–NF 27* to be published in November 2008. The revision will narrow the assay acceptance criteria from the current requirement “not less than 90.0 percent and not more than 110.0 percent of the labeled amount of levothyroxine sodium” to “not less than 95.0 percent and not more than 105.0 percent of the labeled amount of levothyroxine sodium.” The change will help improve the quality of the product so that consumers receive the level of medication needed to treat their thyroid disorders. Levothyroxine sodium tablets are used to treat underactive thyroid glands and other thyroid conditions. Levothyroxine sodium products are used by over 13 million patients.

On October 3, 2007, FDA notified the holders of approved NDAs and ANDAs for levothyroxine sodium drug products that it will require all approved levothyroxine sodium drug products to meet a 95.0 percent to 105.0 percent range of label claim throughout their labeled shelf-lives. The manufacturers should begin meeting these specifications no later than 24 months after the notification. This proposal is part of the FDA’s ongoing effort to address concerns about the performance of approved levothyroxine sodium products and to help ensure that levothyroxine sodium drug products maintain their quality throughout their shelf-lives. The FDA letter to the USP and additional information about the FDA proposal is available on the following FDA Center for Drug Evaluation and Research (CDER) website: <http://www.fda.gov/cder/drug/infopage/levothyroxine/default.htm>.

In addition to the companies licensed to market levothyroxine sodium tablets in the U.S., many non-U.S. markets have a local regulatory commitment to observe USP standards; manufacturers in these countries will need to meet the revised standard by the October 3, 2009 official date. It is of high clinical importance that these firms are aware of the change so that the supply of levothyroxine sodium tablets is not disrupted by compliance issues.

The tightened assay range in the USP monograph for Levothyroxine Sodium Tablets will become official on October 3, 2009, to correspond to the date provided by the FDA to the application holders. In this way, implementation of the USP monograph revision will be contemporaneous with the date when all FDA-approved products will be expected to meet the revised potency specifications. Please direct any comments or questions related to the revision to Dr. Elena Gonikberg, Senior Scientist (301-816-8251 or eg@usp.org).

USP PROPOSES CHANGES TO GENERAL CHAPTER <711> DISSOLUTION; REQUIREMENTS FOR THE SALICYLIC ACID DISSOLUTION CALIBRATOR TO BE DISCONTINUED. The Biopharmaceutics Expert Committee (BPC EC) has revised the General Chapter *Dissolution* <711> to remove USP Salicylic Acid Tablets RS from the Performance Verification Test (PVT) and to change the acceptance criteria for prednisone tablets. The revised chapter was published in *Pharmacopeial Forum* 34(5) with an intended official date of December 1, 2009 (the official date of the Second Supplement to USP 32–NF 27). This change was presented as an In Process Revision to allow considerable advance notice.

USP Prednisone Lot P PVT Reference Standard tablets will be replaced by USP Prednisone Lot Q Reference Standard tablets as they become available in the spring of 2009. The new procedure and criteria will become official for Lot Q on December 1, 2009. USP will provide a calculation spreadsheet in the “Compendial Tools” area of the website to assist with these calculations.

Please direct any questions to William Brown, Senior Scientist (301-816-8380 or web@usp.org) or Anthony DeStefano, Ph.D. (301-998-6303 or ajd@usp.org).

USP WEBSITE. USP is moving some information from the *PF* to the www.usp.org website. USP is undertaking this initiative to assure that all interested parties have access to this information. USP understands the information it publishes is critical to industry operations and needs to be broadly communicated to stakeholders in a timely manner. Because the website is available to everyone and is routinely maintained, it is the ideal vehicle for USP to use in order to achieve this goal.

The following information, previously published in the *Policies and Announcements* section of the *Pharmacopeial Forum*, is now accessible on USP’s website.

- IRA Commentary
- Compendial Notices
- *Stimuli to the Revision Process* Articles
- Pharmacopeial Education Courses
- Reference Standards Catalog

Other important information that resides on the USP website includes:

- Rules and Procedures of the Council of Experts
- Revision Bulletins
- Postponements
- Intent to Revise Letters
- Explanatory Notes and Announcements
- Errata Announcements

The USP intends to continue this effort and is targeting the following information to be posted only to the USP website in the near future:

- Reference Standards Abeyance List

• High Priority Monograph List

USP encourages stakeholders to sign up for the *Compendial Notices* e-mail service in order to receive notices of new postings to the USP website. To sign up for this service, go to <http://www.usp.org/support/products/uspNewslettersRequest.html?promo=compendial>.

PHARMACOPEIAL FORUM PUBLIC REVIEW AND COMMENT PERIOD DEADLINES. The USP welcomes and encourages interested parties to submit comments and

data regarding potential, proposed, or adopted (official) standards. In accordance with the Rules and Procedures of the 2005–2010 Council of Experts, USP has implemented a 90-day comment period by providing a deadline for each issue of *PF* unless otherwise stated in the individual briefing. The listing of comment period deadlines and the targeted official publications appears below.

Pharmacopeial Forum	Comment Deadline	Targeted Official Publication	Publication Date	Official Date
<i>PF</i> 34(2)	June 15, 2008	<i>USP 32–NF 27 1st Supplement</i>	February 2009	August 2009
<i>PF</i> 34(3)	August 15, 2008			
<i>PF</i> 34(4)	October 15, 2008	<i>USP 32–NF 27 2nd Supplement</i>	June 2009	December 2009
<i>PF</i> 34(5)	December 15, 2008			
<i>PF</i> 34(6)	February 15, 2009	<i>USP 33–NF 28</i>	November 2009	May 2010
<i>PF</i> 35(1)	April 15, 2009			
<i>PF</i> 35(2)	June 15, 2009	<i>USP 33–NF 28 1st Supplement</i>	February 2010	August 2010
<i>PF</i> 35(3)	August 15, 2009			

All official revisions are published in the annual edition or *Supplements* to *USP–NF* (twice yearly). Between these publications, official revisions are published in *PF* in the *Interim Revision Announcement*; these revisions are also incorporated in the upcoming *Supplement*. The official publication in which an *IRA* is incorporated will depend upon publication deadlines. The *IRAs* appearing in *PF* Numbers 5 and 6 of each vol-

ume will not appear until *Supplement 1*. See table below. The electronic version of *USP–NF* is updated as each *Supplement* becomes available and, therefore, contains all official text up to and including the contents of the latest *Supplement*. The table below outlines the publications and their release and official dates, and the book or supplement which supersedes them.

Publication Schedules

Publication	Release Date	Official Date	Superseded by
<i>IRA [PF 34(1)]</i>	Jan. 1, 2008	Feb. 1, 2008	<i>2nd Supplement to USP 31–NF 26</i>
<i>1st Supplement to USP 31–NF 26</i>	Feb. 1, 2008	Aug. 1, 2008	<i>2nd Supplement to USP 31–NF 26</i>
<i>IRA [PF 34(2)]</i>	Mar. 1, 2008	Apr. 1, 2008	<i>2nd Supplement to USP 31–NF 26</i>
<i>IRA [PF 34(3)]</i>	May 1, 2008	June 1, 2008	<i>USP 32–NF 27</i>
<i>2nd Supplement to USP 31–NF 26</i>	June 1, 2008	Dec. 1, 2008	<i>USP 32–NF 27</i>
<i>IRA [PF 34(4)]</i>	July 1, 2008	Aug. 1, 2008	<i>1st Supplement to USP 32–NF 27</i>
<i>IRA [PF 34(5)]</i>	Sept. 1, 2008	Oct. 1, 2008	<i>1st Supplement to USP 32–NF 27</i>
<i>IRA [PF 34(6)]</i>	Nov. 1, 2008	Dec. 1, 2008	<i>2nd Supplement to USP 32–NF 27</i>
<i>USP 32–NF 27</i>	Nov. 1, 2008	May 1, 2009	<i>1st Supplement to USP 32–NF 27</i>

PRIORITY NEW MONOGRAPH ITEMS. USP is seeking monographs for the following drug substances and drug products that are or soon will be off patent and thus are of the highest priority. USP also is seeking monographs for the excipients listed below.

Monographs are marked received upon receipt of the monograph proposal. Received monographs are removed from this list upon publication in *Pharmacopeial Forum* or when posted in the Pending Monographs section of the USP website (<http://www.usp.org/standards/pending/>). This list has been updated

as of August 18, 2008. For the most current list, please consult the Priority New Monograph Items List posted at <http://www.usp.org/USPNE/submitMonograph/newMon.html>.

Monograph sponsors should consult *USP's Guideline for Submitting Requests for Revision to the USP–NF* posted at <http://www.usp.org/USPNE/submitMonograph/subGuide.html>.

For additional information, contact Karen A. Russo, Ph.D., kar@usp.org.

Small Molecules (Drug Substances)—As of August 18, 2008

1. Allopurinol Sodium	2. Aminopropazine Fumarate	3. Aminopterin Sodium
4. Anagrelide Hydrochloride <i>(Received)</i>	5. Arsenic Trioxide	6. Auranofin
7. Azelaic Acid <i>(Received)</i>	8. Balsalazide Disodium	9. Bentoquatam
10. Benzphetamine Hydrochloride	11. Bivalirudin <i>(Received)</i>	12. Calcipotriene
13. Calcium Trisodium Pentetate	14. Calfactant	15. Candesartan Cilexetil <i>(Received)</i>
16. Carmustine <i>(Received)</i>	17. Cefditoren Pivoxil <i>(Received)</i>	18. Ceftibuten
19. Cetrorelix	20. Cevimeline	21. Chloroxine
22. Choline Salicylate	23. Cysteamine Bitartrate	24. Cytarabine Liposome
25. Dalfopristin	26. Dapirazole Hydrochloride	27. Desirudin
28. Desonide <i>(Received)</i>	29. Dexrazoxane	30. Dextromethorphan Polistirex
31. Difenoxin Hydrochloride	32. Difloxacin Hydrochloride	33. Entacapone <i>(Received)</i>
34. Epoprostenol Sodium <i>(Received)</i>	35. Erythromycin Phosphate	36. Erythromycin Thiocyanate
37. Esmolol Hydrochloride <i>(Received)</i>	38. Estazolam <i>(Received)</i>	39. Estramustine Phosphate Sodium
40. Ethanolamine Oleate	41. Etomidate <i>(Received)</i>	42. Etoposide Phosphate
43. Exemestane	44. Famciclovir <i>(Received)</i>	45. Felbamate
46. Fluoromethane F 18	47. Fosfomicin Tromethamine <i>(Received)</i>	48. Gadobenate Dimeglumine
49. Gadopentetic Acid	50. Gallium Nitrate	51. Ganirelix
52. Glyceryl Aminobenzoate	53. Guanidine Hydrochloride	54. Halobetasol Propionate <i>(Received)</i>
55. Haloperidol Decanoate <i>(Received)</i>	56. Hydrocodone Polistirex	57. Ibandronate Sodium
58. Imipramine Pamoate	59. Imiquimod	60. Irinotecan Hydrochloride <i>(Received)</i>
61. Isosulfan Blue	62. Latanoprost <i>(Received)</i>	63. Lomustine <i>(Received)</i>
64. Lopinavir <i>(Received)</i>	65. Metipranolol Hydrochloride	66. Miglitol
67. Milrinone Lactate	68. Misoprostol <i>(Received)</i>	69. Moexipril Hydrochloride
70. Nalbuphine Hydrochloride	71. Nalmefene Hydrochloride	72. Nateglinide <i>(Received)</i>
73. Nedocromil Sodium	74. Nicardipine Hydrochloride	75. Nilutamide
76. Nisoldipine	77. Olsalazine Sodium <i>(Received)</i>	78. Orlistat <i>(Received)</i>
79. Oxcarbazepine <i>(Received)</i>	80. Oxiconazole Nitrate	81. Pemirolast Potassium
82. Pentamidine Isethionate <i>(Received)</i>	83. Pioglitazone Hydrochloride	84. Piperonyl Butoxide
85. Pirbuterol Acetate <i>(Received)</i>	86. Poractant Alpha	87. Porfimer Sodium
88. Pramipexole Dihydrochloride	89. Quetiapine Fumarate <i>(Received)</i>	90. Ranitidine
91. Rivastigmine Tartrate <i>(Received)</i>	92. Ropinirole Hydrochloride	93. Rose Bengal Disodium
94. Rosiglitazone Maleate	95. Salmeterol Xinafoate <i>(Received)</i>	96. Sertraline Hydrochloride <i>(Received)</i>
97. Sodium Phenylbutyrate	98. Sodium Phosphates	99. Spectinomycin Sulfate
100. Streptozocin	101. Tacrolimus <i>(Received)</i>	102. Tenofovir Disoproxil Fumarate <i>(Received)</i>
103. Tiludronate Disodium	104. Tiopronin	105. Tranexamic Acid <i>(Received)</i>

Small Molecules (Drug Substances)—As of August 18, 2008 (Continued)

106. Tranylcypromine Sulfate (Received)	107. Trimetrexate Glucuronate	108. Venlafaxine Hydrochloride (Received)
109. Voriconazole (Received)	110. Zaleplon	111. Zinc Tridosium Pentetate
112. Zoledronic Acid	113. Zonisamide (Received)	

Small Molecules (Drug Products)—As of August 18, 2008

1. Abacavir Sulfate, Lamivudine, and Zidovudine Tablets	2. Acarbose Tablets	3. Acetaminophen, Butalbital, Caffeine, and Codeine Phosphate Capsules
4. Acetaminophen, Clemastine Fumarate, and Pseudoephedrine Hydrochloride Tablets	5. Acetazolamide Extended-Release Capsules	6. Albuterol and Ipratropium Bromide Inhalation Aerosol
7. Albuterol and Ipratropium Bromide Inhalation Solution	8. Albuterol Extended-Release Tablets	9. Albuterol Inhalation Aerosol
10. Albuterol Sulfate Inhalation Solution	11. Albuterol Sulfate Oral Solution	12. Alendronate Sodium Oral Solution
13. Alfuzosin Extended-Release Tablets	14. Allopurinol for Injection	15. Alprazolam Extended-Release Tablets
16. Alprostadil Urethral Suppository	17. Aminopropazine Fumarate and Neomycin Sulfate Tablets	18. Aminopropazine Fumarate Injection
19. Aminopropazine Fumarate Tablets	20. Aminopterin Sodium Tablets	21. Amiodarone Hydrochloride Injection
22. Amlodipine and Benazepril Hydrochloride Capsules	23. Amphotericin B Injection	24. Anagrelide Hydrochloride Capsules (Received)
25. Arsenic Trioxide Injection	26. Atovaquone and Proguanil Hydrochloride Tablets	27. Atovaquone Tablets
28. Auranofin Capsules	29. Azatadine Maleate and Pseudoephedrine Sulfate Extended-Release Tablets	30. Azelaic Acid Cream
31. Azithromycin for Injection (Received)	32. Azithromycin Tablets (Received)	33. Baclofen Injection
34. Balsalazide Disodium Capsules	35. Beclomethasone Dipropionate Inhalation Aerosol	36. Beclomethasone Dipropionate Nasal Suspension
37. Benazepril Hydrochloride and Hydrochlorothiazide Tablets	38. Bentoquatam Topical Suspension	39. Benzocaine and Cetylpyridinium Chloride Lozenges
40. Benzocaine and Menthol Lotion	41. Benzphetamine Hydrochloride Tablets	42. Bivalirudin Injection
43. Brompheniramine Maleate, Dextromethorphan Hydrobromide, and Pseudoephedrine Hydrochloride Oral Solution	44. Budesonide Inhalation Aerosol	45. Bupivacaine and Lidocaine Hydrochlorides Injection
46. Buprenorphine Hydrochloride Injection	47. Butalbital and Acetaminophen Capsules	48. Butalbital and Acetaminophen Tablets
49. Calcipotriene Cream	50. Calcipotriene Ointment	51. Calcipotriene Topical Solution
52. Calcitriol Capsules	53. Calcitriol Oral Solution	54. Calcium Acetate Capsules
55. Calcium Trisodium Pentetate Injection	56. Calfactant Intratracheal Suspension	57. Carbidopa and Levodopa Extended-Release Tablets (Received)
58. Carbidopa and Levodopa Tablets for Oral Suspension (Received)	59. Carbidopa, Levidopa, and Entacapone Tablets	60. Carmustine for Injection (Received)
61. Carmustine Implant	62. Cefdinir Tablets	63. Cefditoren Pivoxil Tablets
64. Ceftibuten Capsules	65. Ceftibuten for Oral Suspension	66. Ceftiofur Hydrochloride Oral Suspension
67. Cetirizine Hydrochloride Tablets (Received)	68. Cetrorelix Injection	69. Cevimeline Hydrochloride Capsules
70. Chloroxine Cream	71. Chlorpromazine Hydrochloride Extended-Release Capsules	72. Choline and Magnesium Salicylates Oral Solution
73. Choline and Magnesium Salicylates Tablets	74. Choline Salicylate Oral Solution (Received)	75. Ciclopirox Shampoo
76. Ciclopirox Topical Gel	77. Ciclopirox Topical Solution (Received)	78. Cimetidine Oral Solution
79. Ciprofloxacin Extended-Release Tablets	80. Ciprofloxacin Hydrochloride and Hydrocortisone Otic Suspension	81. Ciprofloxacin Otic Solution
82. Cisplatin Injection	83. Citalopram Hydrobromide Oral Solution	84. Citric Acid, Gluconolactone, and Magnesium Carbonate Irrigation
85. Cladribine Injection	86. Clemastine Fumarate Syrup	87. Clobetasol Propionate Gel
88. Clorazepate Dipotassium Capsules	89. Clorazepate Dipotassium Extended-Release Tablets	90. Clotrimazole and Betamethasone Dipropionate Lotion

Small Molecules (Drug Products)—As of August 18, 2008 (Continued)

91. Compound Undecylenic Acid Cream	92. Compound Undecylenic Acid Topical Powder	93. Conjugated Estrogens and Medroxyprogesterone Acetate Tablets
94. Cyclosporine Modified Capsules	95. Cyclosporine Modified Oral Solution	96. Cyclosporine Ointment
97. Cyclosporine Topical Solution	98. Cysteamine Bitartrate Capsules	99. Cytarabine Liposome Injection
100. Dalfopristin and Quinupristin Injection	101. Dantrolene Sodium Oral Suspension	102. Dapiprazole for Ophthalmic Solution
103. Desirudin for Injection	104. Desonide Cream	105. Dexrazoxane for Injection
106. Dextroamphetamine Sulfate Extended-Release Capsules	107. Dextromethorphan Polistirex Extended-Release Oral Suspension	108. Diazepam Injectable Emulsion
109. Diclofenac Sodium Ophthalmic Solution	110. Diethylpropion Hydrochloride Extended-Release Tablets	111. Difenoxin Hydrochloride and Atropine Sulfate Tablets
112. Difloxacin Hydrochloride Tablets	113. Dihydroergotamine Mesylate Metered Spray	114. Diltiazem Hydrochloride Injection
115. Dinoprostone Vaginal Suppositories	116. Diphenhydramine Hydrochloride and Acetaminophen Tablets	117. Divalproex Sodium Delayed-Release Capsules
118. Dorzolamide and Timolol Ophthalmic Solution	119. Dorzolamide Ophthalmic Solution	120. Doxepin Hydrochloride Cream
121. Doxycycline Oral Gel	122. Econazole Nitrate Cream	123. Edrophonium Chloride and Atropine Sulfate Injection
124. Enalapril Maleate and Felodipine Extended-Release Tablets	125. Enalaprilat Injection <i>(Received)</i>	126. Entacapone Tablets <i>(Received)</i>
127. Ephedrine Sulfate and Guaifenesin Tablets	128. Epirubicin Hydrochloride for Injection	129. Epirubicin Hydrochloride Injection
130. Epoprostenol for Injection	131. Epoprostenol Injection	132. Escitalopram Oxalate Tablets <i>(Received)</i>
133. Esmolol Hydrochloride Injection	134. Esomeprazole Magnesium Capsules	135. Estazolam Tablets <i>(Received)</i>
136. Estramustine Phosphate Sodium Capsules	137. Ethanolamine Oleate Injection	138. Etidronate Disodium Injection Concentrate
139. Etomidate Injection	140. Exemestane Tablets	141. Famotidine Orally Disintegrating Tablets
142. Felbamate Oral Suspension	143. Felbamate Tablets	144. Fentanyl Lozenges
145. Famciclovir Tablets	146. Fentanyl Transdermal System <i>(Received)</i>	147. Ferrous Fumarate and Docusate Sodium Extended-Release Capsules
148. Fluconazole Oral Suspension	149. Flunisolide Inhalation Aerosol	150. Flunisolide Nasal Spray
151. Fluocinolone Acetonide Shampoo	152. Fluorescein Sodium Ophthalmic Solution	153. Fluorometholone Ointment
154. Fluticasone Propionate Cream <i>(Received)</i>	155. Fluticasone Propionate Inhalation Powder	156. Fluticasone Propionate Ointment <i>(Received)</i>
157. Fluticasone Propionate Pressurized Inhaler	158. Fosarnet Sodium Injection	159. Fosfomycin for Oral Solution
160. Gabapentin Oral Solution	161. Gadobenate Dimeglumine Injection	162. Gallium Nitrate Injection
163. Ganciclovir Capsules	164. Ganirelix Acetate Injection	165. Gatifloxacin Injection
166. Gatifloxacin Tablets	167. Gentamicin Sulfate Oral Solution	168. Gentamicin Sulfate Soluble Powder
169. Glipizide Extended-Release Tablets	170. Guaifenesin and Pseudoephedrine Hydrochloride Extended-Release Tablets	171. Guaifenesin and Salts of Dextromethorphan and Pseudoephedrine Oral Solution
172. Guanidine Hydrochloride Tablets	173. Halobetasol Propionate Cream	174. Halobetasol Propionate Ointment
175. Haloperidol Decanoate Injection	176. Haloperidol Lactate Injection	177. Haloperidol Lactate Oral Concentrate
178. Hydralazine Hydrochloride and Hydrochlorothiazide Capsules	179. Hydrochlorothiazide Capsules	180. Hydrochlorothiazide Oral Solution
181. Hydrocodone Bitartrate and Acetaminophen Capsules	182. Hydrocodone Bitartrate and Acetaminophen Oral Solution	183. Hydrocodone Bitartrate and Aspirin Tablets
184. Hydrocodone Bitartrate and Guaifenesin Oral Solution	185. Hydrocodone Bitartrate and Homatropine Methylbromide Syrup	186. Hydrocortisone Acetate Dental Paste
187. Hydrocortisone Acetate Rectal Foam Aerosol	188. Hydrocortisone Butyrate Lotion	189. Hydroflumethiazide and Reserpine Tablets
190. Hydromorphone Hydrochloride Oral Solution <i>(Received)</i>	191. Hydroquinone Lotion	192. Ibandronate Sodium Tablets
193. Ibuprofen Capsules	194. Idarubicin Hydrochloride Injection	195. Imipramine Pamoate Capsules
196. Imiquimod Topical Cream	197. Ipratropium Bromide Inhalation Aerosol	198. Ipratropium Bromide Inhalation Solution
199. Irinotecan Hydrochloride Injection	200. Isosulfan Blue Injection	201. Isradipine Extended-Release Tablets
202. Itraconazole Injection	203. Itraconazole Oral Solution	204. Ketoconazole Cream

Small Molecules (Drug Products)—As of August 18, 2008 (Continued)

205. Ketoconazole Shampoo	206. Ketoprofen Capsules <i>(Received)</i>	207. Ketoprofen Extended-Release Capsules
208. Ketoprofen Tablets	209. Ketotifen Fumarate Ophthalmic Solution	210. Lactic Acid Lotion
211. Lamotrigine Tablets	212. Latanoprost Ophthalmic Solution	213. Leucovorin Calcium for Injection
214. Levetiracetam Tablets	215. Levocabastine Ophthalmic Suspension	216. Levofloxacin Solution
217. Lincomycin Hydrochloride and Spectinomycin Sulfate Soluble Powder	218. Liothyronine Injection	219. Lomustine Capsules
220. Lopinavir and Ritonavir Solution	221. Lopinavir Capsules	222. Lopinavir Solution
223. Loratadine Orally Disintegrating Tablets <i>(Received)</i>	224. Losartan Potassium Tablets <i>(Received)</i>	225. Mefloquine Hydrochloride Tablets <i>(Received)</i>
226. Melphalan for Injection	227. Mesalamine Suppositories	228. Mesoridazine Besylate Concentrate
229. Metaraminol Bitartrate Injection	230. Methacholine Chloride for Inhalation Solution	231. Methadone Hydrochloride Oral Concentrate
232. Methocarbamol and Aspirin Tablets	233. Methoxsalen Softgels	234. Methyclothiazide and Deserpidine Tablets
235. Methylphenidate Hydrochloride Chewable Tablets	236. Metipranolol Ophthalmic Solution	237. Metronidazole Capsules <i>(Received)</i>
238. Metronidazole Cream	239. Metronidazole Extended-Release Tablets	240. Metronidazole Hydrochloride for Injection
241. Metronidazole Lotion	242. Miconazole Nitrate Topical Aerosol	243. Midazolam Injection <i>(Received)</i>
244. Mifepristone Tablets	245. Miglitol Tablets	246. Milrinone Injection
247. Misoprostol Tablets <i>(Received)</i>	248. Moexipril Hydrochloride and Hydrochlorothiazide Tablets	249. Moexipril Hydrochloride Tablets
250. Molindone Hydrochloride Oral Solution	251. Morphine Sulfate for Injection Concentrate	252. Morphine Sulfate Oral Solution
253. Morphine Sulfate Oral Solution Concentrate	254. Morphine Sulfate Tablets	255. Mycophenolate Mofetil Capsules
256. Mycophenolate Mofetil Oral Solution	257. Mycophenolate Mofetil Tablets	258. Nalbuphine Hydrochloride Injection
259. Nalmefene Hydrochloride Injection	260. Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution	261. Naproxen Sodium Extended-Release Tablets
262. Nateglinide Tablets <i>(Received)</i>	263. Nedocromil Sodium Inhalation Aerosol	264. Neomycin Sulfate Oral Powder
265. Niacardipine Hydrochloride Capsules	266. Nilutamide Tablets	267. Nimodipine Capsules
268. Nisoldipine Extended-Release Tablets	269. Nitroglycerin Solution in Acrylic Adhesive	270. Nitroglycerin Transdermal System
271. Nizatidine Tablets	272. Ofloxacin in Dextrose Injection	273. Ofloxacin Injection
274. Olsalazine Sodium Capsules	275. Orphenadrine Citrate Extended Release Tablets <i>(Received)</i>	276. Orphenadrine Citrate, Aspirin, and Caffeine Tablets
277. Oxcarbazepine Suspension	278. Oxcarbazepine Tablets <i>(Received)</i>	279. Oxiconazole Cream
280. Pamidronate Disodium Injection	281. Pantoprazole Sodium for Injection	282. Pantoprazole Sodium Tablets
283. Paroxetine Hydrochloride Extended-Release Tablets	284. Paroxetine Oral Suspension	285. Pemirolast Potassium Ophthalmic Solution
286. Penicillin G Potassium Tablets for Oral Solution	287. Pentamidine Isethionate for Inhalation	288. Pentamidine Isethionate Injection <i>(Received)</i>
289. Pentazocine Hydrochloride and Acetaminophen Tablets	290. Phendimetrazine Tartrate Extended-Release Capsules	291. Phenobarbital Capsules
292. Phentermine Resin Complex Capsules	293. Phenylephrine Hydrochloride and Chlorpheniramine Maleate Extended-Release Capsules	294. Phenylephrine Hydrochloride, Chlorpheniramine Maleate, and Acetaminophen Extended-Release Tablets
295. Pilocarpine Hydrochloride Ophthalmic Gel	296. Pilocarpine Hydrochloride Ophthalmic Ointment	297. Pioglitazone Hydrochloride Tablets
298. Piperonyl Butoxide and Pyrethrins Aerosol Foam	299. Pirbuterol Acetate Inhalation Aerosol	300. Poractant Alpha Suspension
301. Porfimer Sodium for Injection	302. Povacrylate Solution	303. Povacrylate–Iodine Topical Solution
304. Povidone–Iodine Gauze	305. Povidone–Iodine Swabsticks	306. Povidone–Iodine Topical Aerosol Foam
307. Povidone–Iodine Vaginal Suppositories	308. Pramipexole Dihydrochloride Tablets	309. Prednisolone Sodium Phosphate Oral Solution

Small Molecules (Drug Products)—As of August 18, 2008 (Continued)

310. Prochlorperazine Maleate Extended-Release Capsules	311. Progesterone Capsules	312. Promethazine and Phenylephrine Hydrochlorides and Codeine Phosphate Syrup (Received)
313. Promethazine and Phenylephrine Hydrochlorides Syrup (Received)	314. Promethazine Hydrochloride and Codeine Phosphate Oral Solution (Received)	315. Promethazine Hydrochloride and Dextromethorphan Hydrobromide Syrup (Received)
316. Propafenone Hydrochloride Tablets	317. Pseudoephedrine Hydrochloride and Brompheniramine Maleate Extended-Release Tablets	318. Pseudoephedrine Hydrochloride and Naproxen Sodium Extended-Release Tablets
319. Pseudoephedrine Hydrochloride, Chlorpheniramine Maleate, and Codeine Phosphate Oral Solution	320. Pseudoephedrine Hydrochloride, Guaifenesin, and Codeine Phosphate Oral Solution	321. Pseudoephedrine Sulfate and Dexbrompheniramine Maleate Extended-Release Tablets
322. Pseudoephedrine Sulfate and Dexbrompheniramine Maleate Oral Solution	323. Pseudoephedrine Sulfate, Dexbrompheniramine Maleate, and Acetaminophen Extended-Release Tablets	324. Pyrilamine Maleate Injection
325. Quinapril Hydrochloride and Hydrochlorothiazide Tablets	326. Quinidine Sulfate Injection	327. Ramipril Capsules (Received)
328. Ranitidine Capsules	329. Rauwolfia Serpentina and Endroflumethiazide Tablets	330. Reserpine and Polythiazide Tablets
331. Rimantadine Hydrochloride Oral Solution	332. Risperidone Oral Solution (Received)	333. Risperidone Orally Disintegrating Tablets
334. Rivastigmine Tartrate Capsules (Received)	335. Rivastigmine Tartrate Oral Solution (Received)	336. Rocuronium Bromide Injection
337. Ropinirole Hydrochloride Tablets	338. Rosiglitazone Maleate Tablets	339. Salicylic Acid and Sulfur Cleansing Lotion
340. Salicylic Acid and Sulfur Lotion	341. Salicylic Acid and Sulfur Shampoo	342. Salicylic Acid Cream
343. Salicylic Acid Ointment	344. Salmeterol Inhalation Aerosol	345. Salmeterol Xinafoate Inhalation Powder
346. Scopolamine Transdermal System	347. Selegiline Hydrochloride Capsules	348. Sertraline Hydrochloride Oral Solution
349. Sibutramine Hydrochloride Capsules	350. Sodium Bicarbonate and Sodium Citrate for Oral Solution	351. Sodium Bicarbonate, Sodium Citrate, and Sodium Tartrate for Oral Suspension
352. Sodium Iodide Injection	353. Sodium Phenylbutyrate Oral Powder	354. Sodium Phenylbutyrate Tablets
355. Sodium Phosphates for Oral Suspension	356. Sodium Phosphates Tablets	357. Sodium Salicylate and Sulfur Shampoo
358. Sterile Talc Aerosol	359. Streptozocin for Injection	360. Sucralfate Oral Suspension
361. Sulconazole Nitrate Cream	362. Sulfacetamide Sodium and Fluorometholone Ophthalmic Suspension	363. Sulfacetamide Sodium and Prednisolone Sodium Phosphate Ophthalmic Solution
364. Sulfasalazine Oral Suspension	365. Sulisobenzene Lotion	366. Sumatriptan Injection
367. Sumatriptan Tablets (Received)	368. Tacrolimus Capsules (Received)	369. Tacrolimus Injection
370. Tacrolimus Ointment	371. Tamsulosin Hydrochloride Capsules (Received)	372. Technetium Tc 99m Teboroxime Injection
373. Tenofovir Disoproxil Fumarate Tablets (Received)	374. Terazosin Capsules (Received)	375. Terazosin Tablets (Received)
376. Terbinafine Hydrochloride Cream	377. Terbinafine Tablets (Received)	378. Terbinafine Topical Solution
379. Terconazole Vaginal Cream	380. Terconazole Vaginal Suppositories	381. Testosterone Transdermal Gel
382. Testosterone Transdermal System	383. Tetracycline Hydrochloride Periodontal Fiber	384. Theophylline Extended-Release Tablets
385. Tioconazole Vaginal Ointment	386. Tiopronin Tablets	387. Tolnaftate Topical Aerosol Solution
388. Topiramate Capsules (Received)	389. Topiramate Tablets (Received)	390. Toremide Injection
391. Toremide Tablets (Received)	392. Trandolapril and Verapamil Hydrochloride Extended-Release Tablets	393. Trandolapril Tablets
394. Tranexamic Acid Injection	395. Tranylcypromine Sulfate Tablets (Received)	396. Tretinoin Capsules
397. Tretinoin Microsphere Gel	398. Triamcinolone Acetonide Nasal Suspension	399. Trifluridine Ophthalmic Solution
400. Trimetrexate for Injection	401. Trimipramine Maleate Capsules	402. Triprolidine and Pseudoephedrine Hydrochlorides and Codeine Phosphate Syrup
403. Trolamine Salicylate Cream	404. Trolamine Salicylate Gel	405. Trolamine Salicylate Topical Emulsion
406. Undecylenic Acid Topical Foam Aerosol	407. Urea Cream	408. Vecuronium Bromide for Injection

Small Molecules (Drug Products)—As of August 18, 2008 (Continued)

409. Venlafaxine Extended-Release Capsules <i>(Received)</i>	410. Venlafaxine Tablets <i>(Received)</i>	411. Verapamil Hydrochloride Capsules
412. Verapamil Hydrochloride Extended-Release Capsules	413. Voriconazole Injection	414. Voriconazole Oral Suspension
415. Voriconazole Tablets	416. Yttrium Y-90 Chloride Solution	417. Yttrium Y-90 Glass Microspheres
418. Yttrium Y-90 Microspheres Injection	419. Zaleplon Capsules	420. Zidovudine and Lamivudine Tablets <i>(Received)</i>
421. Zinc Acetate Capsules	422. Zinc Tridosium Pentetate Injection	423. Ziprasidone Hydrochloride Capsules
424. Zoledronic Acid for Injection	425. Zonisamide Capsules <i>(Received)</i>	

Excipients—As of August 18, 2008

1. Acetone Sodium Bisulfite	2. Acetylated Monoglycerides	3. Aconitic Acid (Achilleic Acid)
4. Acrylic Acid-Octyl Acrylate Copolymer	5. Albumin Colloidal	6. Aliphatic Polyesters
7. Allantoin–Sodium Pyrrolidone Carboxylate	8. Aluminum Ammonium Sulfate	9. Aluminum Lactate
10. Aluminum Oxide	11. Aluminum Potassium Sulfate	12. Aluminum Silicate
13. Aluminum Sodium Sulfate	14. Aluminum Stearate	15. Ammonium Bicarbonate
16. Ammonium Calcium Alginate	17. Ammonium Phosphate	18. Batylalcohol Monostearate
19. Beeswax, Synthetic	20. Benzododecinium Bromide	21. Benzyl Chloride
22. Benzyl Nicotinate	23. Beta Naphthol	24. Brominated Vegetable Oil
25. Butadiene–Styrene Rubber	26. Butylated Hydromethylphenol	27. Butylene Glycol
28. Butylphthalyl Butylglycolate	29. Calcium Acid Pyrophosphate	30. Calcium Alginate
31. Calcium Alginate and Ammonium Alginate	32. Calcium Bromide	33. Calcium Chloride Solution
34. Calcium Phosphate, Monobasic	35. Calcium Propionate	36. Calcium Pyrophosphate
37. Calcium Sorbate	38. Calcium Stearoyl Lactylate	39. Caldiamide Sodium
40. Calteridol Calcium	41. Capric Acid	42. Caprylic/Capric Diglycerol Succinate
43. Carbon	44. Carboxymethyl Starch	45. Carboxymethylamylopectin Sodium
46. Carboxymethylcellulose Potassium	47. Cetostearyl Isononanoate	48. Chlorodifluoroethane
49. Cholic Acid	50. Cinnamaldehyde	51. Cocamide Diethanolamine
52. Cocamide Oxide	53. Cocoyl Caprylocaprates	54. Crystal Gum
55. Cutina	56. Cystine	57. Dammar Gum
58. Decanoic Acid	59. Decyl Oleate	60. Desoxycholic Acid
61. Dextrin Palmitate	62. Dextrins Modified	63. Diacetyl Tartaric Acid Esters of Mono- and Diglycerides
64. Dicyetyl Phosphate	65. Dichlorofluoromethane	66. Diethyl Sebacate
67. Difluoroethane	68. Diglycol Stearate	69. Diisobutyl Adipate
70. Diisopropyl Adipate	71. Diisopropylbenzothiazyl-2-Sulfenamide	72. Dilauryl Thiodipropionate
73. Dimethyl Dicarboxylate	74. Dimyristoyl Lecithin	75. Dimyristoyl Phosphatidylglycerol
76. Dipropylene Glycol	77. Disodium Edisylate	78. Disodium Guanylate
79. Disodium Inosinate	80. Disodium Monooleamide Sulfasuccinate	81. D-Mannose
82. Docusate Sodium/Sodium Benzoate	83. Erythrosine	84. Ethoxylated Mono- and Diglycerides
85. Ethoxyquin	86. Ethyl Hexanediol	87. Ethyl Linoleate
88. Ethyl Maltol <i>(Received)</i>	89. Ethylene Dichloride	90. Ethylurea
91. Ferric Ammonium Citrate	92. Ferric Citrate	93. Ferric Oxide, Brown
94. Ferric Phosphate	95. Ferric Pyrophosphate	96. Ferrous Citrate
97. Ferrous Glycinate	98. Ferrous Lactate	99. Fluorochlorohydrocarbons
100. Formic Acid	101. Furcelleran	102. Gentistic Acid
103. Geraniol	104. Glutamic Acid Hydrochloride	105. Gluten
106. Glycerol Ester of Gum Rosin (Ester Gum)	107. Glyceryl Laurate	108. Glyceryl Palmitate
109. Glyceryl Ricinoleate	110. Glyceryl Tristearate	111. Glycine Hydrochloride
112. Glycofurof	113. Glycol Stearate	114. Heptafluoropropane
115. Heptylparaben	116. Hexadecyl Isostearate	117. Hexane
118. Hexanetriol(-1,2,6-)	119. Hydrocarbon Gel	120. Hydroxyethylmethylcellulose
121. Hydroxylated Lecithin	122. Indigotine	123. Iron Carbonyl

Excipients—As of August 18, 2008 (Continued)

124. Iron Subcarbonate	125. Isobutylated–Isoprene Copolymer	126. Isooctylacrylate
127. Isopropyl Isostearate	128. Isopropyl Stearate	129. Isostearic Acid
130. Isostearyl Alcohol	131. Lactobionic Acid <i>(Received)</i>	132. Lactose Ferrin, Bovine
133. Lactylated Fatty Acid Esters of Glycerol and Propylene Glycol	134. Lactylic Esters of Fatty Acids	135. Lanolin (Wool Fat), Hydrogenated
136. Lanolin Alcohols, Acetylated	137. Lanolin Hydrous	138. L-Ascorbyl Stearate
139. Lauramine Oxide	140. Lauric Myristic Diethanolamide	141. Lauric Acid
142. Lauric Diethanolamide	143. Lavender Oil	144. L-Cysteine Monohydrochloride
145. Lecithin, Hydroxylated	146. L-Glutamic Acid <i>(Received)</i>	147. Linoleic Acid <i>(Received)</i>
148. L-Leucine	149. Macrogol Sorbitan Tristearate	150. Macrogolglycerol Cocoates
151. Macrogolglycerol Triisostearate	152. Magnesium Aluminum Silicate Hydrate	153. Magnesium Aspartame Dihydrate
154. Magnesium Aspartate	155. Magnesium Phosphate Tribasic	156. Magnesium Phosphate, Diabasic, Trihydrate
157. Magnesium Tartrate	158. Malt Syrup	159. Maltitol Syrup
160. Maltol Isobutyrate	161. Manganese Chloride	162. Manganese Citrate
163. Manganese Glycerophosphate	164. Manganese Hypophosphite	165. Medical Antifoam Emulsion C
166. Medronate Disodium	167. Medronic Acid	168. Methyl Chloride
169. Methylchloroisothiazolinone	170. Methylisothiazolinone	171. Microcrystalline Cellulose, Silicified <i>(Received)</i>
172. Mineral Spirits	173. Monoisostearyl Glyceryl Ester	174. Monopotassium Glutamate Monohydrate
175. Monosodium Citrate	176. Mullein Leaf	177. Myristyl Gamma–Picolinium Chloride
178. Myristyl Lactate	179. <i>N,N</i> -Bis(2-Hydroxyethyl)Stearamide	180. <i>N</i> -Acetyl-L-Methionine
181. Naphtha	182. <i>N</i> -Methylpyrrolidone <i>(Received)</i>	183. Non-Pareil Seeds
184. Nutmeg Oil	185. Octanoic Acid	186. Oxystearin
187. Pentasodium Triphosphate	188. Pentetate Calcium Trisodium	189. Pentetate Pentasodium
190. Phenprobamate	191. Phenylmercuric Acetate	192. Phenylmercuric Nitrate
193. Pine Oil	194. Polacrilin	195. Polyglycerol Esters of Fatty Acids
196. Polyglycerol Polyricinoleic Acid	197. Polyoxyethylene Castor Oil (USP has 35)	198. Polyoxyl Stearate (USP has 40)
199. Polypropylene Oleate	200. Polypropylene Stearyl Ether	201. Polysorbate 65
202. Polyvinylacetal Diethylanoacetate	203. Polyvinylpyrrolidone	204. Polyvinylpyrrolidone Ethylcellulose
205. Potassium Acid Tartrate	206. Potassium Bromate	207. Potassium Carbonate Solution
208. Potassium Dichloroisocyanurate	209. Potassium Gibberellate	210. Potassium Glycerophosphate
211. Potassium Iodate	212. Potassium Nitrite	213. Potassium Phosphate
214. Potassium Phosphate, Tribasic	215. Potassium Polymetaphosphate	216. Potassium Pyrophosphate
217. Potassium Stearate	218. Potassium Sulfate	219. Potassium Sulfite
220. Potassium Tripolyphosphate	221. Propyl Propionate	222. Propylene Glycol Diacetate
223. Propylene Glycol Mono- and Diesters	224. Rice Bran Wax	225. Rosin
226. Silicone	227. Sodium Acid Pyrophosphate	228. Sodium Aluminosilicate <i>(Received)</i>
229. Sodium Aluminum Phosphate Acidic	230. Sodium Aluminum Phosphate Basic	231. Sodium Aspartate
232. Sodium Bisulfate	233. Sodium Bisulfite	234. Sodium Carbonate Hydrate
235. Sodium Carboxymethyl Betaglucon	236. Sodium Caseinate	237. Sodium Chlorate
238. Sodium Citrate, Dibasic	239. Sodium Citrate, Monobasic	240. Sodium Dehydroacetate
241. Sodium Diacetate	242. Sodium Erythorbate	243. Sodium Ferric Pyrophosphate
244. Sodium Ferrocyanide	245. Sodium Hypophosphite <i>(Received)</i>	246. Sodium Laureth Sulfate
247. Sodium Lauroyl Sarcosinate	248. Sodium Lauryl Sulfoacetate	249. Sodium Magnesium Aluminosilicate
250. Sodium Magnesium Silicate	251. Sodium Malate	252. Sodium Metaphosphate, Insoluble
253. Sodium Metasilicate	254. Sodium Methylate	255. Sodium Polyphosphates Glassy
256. Sodium Potassium Tripolyphosphate	257. Sodium Pyrophosphate	258. Sodium Pyrrolidone Carboxylate
259. Sodium Sesquicarbonate	260. Sodium Sesquinoate	261. Sodium Stearoyl Lactylate
262. Sodium Thiomalate	263. Sodium Trimetaphosphate	264. Sodium Trioleate
265. Sodium Tripolyphosphate	266. Soy Polysaccharides	267. Stannous Tartrate
268. Starch, Pregelatinized Corn	269. Starch, Pregelatinized Tapioca	270. Stearalkonium Chloride

Excipients—As of August 18, 2008 (Continued)

271. Stearyl Citrate	272. Stearyl Monoglyceridyl Citrate	273. Succinylated Monoglycerides
274. Sucrose Acetate Isobutyrate	275. Sucrose Fatty Acid Esters	276. Sucrose Stearate <i>(Received)</i>
277. Sugar Fruit Fine	278. Sulfobutyl Ether Beta Cyclodextrin <i>(Received)</i>	279. Tallow
280. Tallow Glycerides	281. Tallow Oil	282. Tetrafluoroethane
283. Thioglycerol	284. Thyme Oil	285. Tribehenin
286. Triceteareth-4 Phosphate	287. Trichloroethylene	288. Trimyristin
289. Trisodium Citrate	290. Trolamine Lauryl Sulfate	291. Vegetable Oil
292. Wheat Flour	293. Wheat Germ Oil	294. Wheat Gluten <i>(Received)</i>
295. Whey		

INSTRUCTIONS TO AUTHORS

Contributions in the form of original research reports, evaluations of new and existing compendial methods, and other commentaries and articles relevant to drug standards or to *USP–NF* revision will be considered for publication in *Pharmacopeial Forum* under the section *Stimuli to the Revision Process*. Manuscripts are received with the explicit understanding that they have not been published previously in any language or medium and that they are not simultaneously under consideration by any other publication.

All manuscripts are subject to review by USP headquarters staff, Committee members, or qualified outside referees, and if accepted for publication they will be subject to editing by USP staff. Accepted manuscripts become the property of the USP Convention (USPC) and may not be subsequently published elsewhere without written permission from the USPC. Authors are also responsible for obtaining permission for reprinting any illustrations that have been published elsewhere.

Abstract—Include an abstract of not more than 250 words stating the purpose and the results or conclusions of the article.

Style and Usage—*Stimuli* articles generally follow the current *Chicago Manual of Style* except in scientific usage (numbers, abbreviations, etc.). For the latter, authors should use the current *AMA Manual of Style* or the current *ACS Style Guide*. Authors may usefully consult a current copy of *Pharmacopeial Forum*.

References—Consult the current *AMA Manual of Style*, which is generally consistent with the National Library of Medicine's *Recommended Formats for Bibliographic Citation*. A current copy of *Pharmacopeial Forum* will offer examples of reference formats.

Copyright—Copyright transfer documents will be sent to authors after manuscripts have been accepted for publication.

Contact Person—USP will designate a Scientific Liaison in the Documentary Standards Division as the corresponding author. This ensures that USP receives all comments generated by the *Stimuli* article. Authors should contact the Scientific Liaison if they would like to receive copies of comments generated by their *Stimuli* articles.

Submission Instructions—Manuscripts must be submitted both as an electronic file and as a printed copy of the electronic file. Submit the text in Microsoft® Word or another current word-processing application. The preferred format for graphics submitted electronically is tagged image file format (TIFF). Photocopies are not acceptable. Manuscripts submitted for publication should be addressed to:

Pharmacopeial Forum
Executive Secretariat, USP
12601 Twinbrook Pkwy.
Rockville, MD 20852

USP Responses to Comments on *Stimuli* Article, “The Application of Uncertainty to USP’s Compendial Reference Standards Program: Certified Reference Materials”

Reference Standards Expert Committee Subcommittee on Certified Reference Materials,^a Steven Lane, Shawn Dressman, Walter W. Hauck, William F. Koch,^b Roger L. Williams, *USP*

ABSTRACT *Pharmacopeial Forum* 33(6) [November–December 2007] included a *Stimuli* article titled “The Application of Uncertainty to USP’s Compendial Reference Standards Program: Certified Reference Materials.” This *Stimuli* article articulated efforts to advance official USP Reference Standards as Certified Reference Materials in accordance with guidances promulgated by national and international metrology organizations such as the International Standards Organization (ISO) and the International Bureau of Weights and Measures (BIPM). The article elicited comments that are abstracted here with USP responses.

INTRODUCTION

In *Pharmacopeial Forum* 33(6) USP authors published a *Stimuli* article titled “The Application of Uncertainty to USP’s Compendial Reference Standards Program: Certified Reference Materials” (1). This *Stimuli* article reviewed USP’s activities in creating comprehensive, practical, relevant, and timely documentary standards and reference materials that help ensure the strength, quality, and purity of medicines (drugs, biologics, and excipients) and foods (dietary supplements and food ingredients). The paper discussed the rationale and operational details of USP’s emerging certified reference material (CRM) program, as well as the compendial and regulatory applications of uncertainty of measurement and other relevant information associated with CRMs. This *Stimuli* article elicited two letters in response to the *Stimuli* article. We have extracted five key issues as expressed in these letters, namely, a policy statement on CRMs, the benefits of CRMs, the misuse and misunderstanding of CRMs, cost, and the formation of a project team. These general issues will be addressed first, followed by USP responses to specific concerns.

General Comments and USP Responses

1. Policy Statement on CRMs. USP believes that provision of the national primary standard(s) for an article is a mandate given to it in law in the US: cf. the adulteration provision of the Federal Food, Drug, and Cosmetic Act: “A drug or device shall be deemed to be adulterated . . . if it purports to be or is represented as a drug the name of which is recognized in an official compendium [including *USP* and *NF*], and its strength differs from, or its quality or purity falls below, the standards set forth in such compendium” [emphasis added] (2). USP wishes to execute this mandate to the fullest possible extent. It is the intent of the measurement science program at USP to support the scientific deliberations of the Council of Experts; to ensure that the USP Official Reference Standard

collection is maintained and grows in concert with USP monographs and the needs of our stakeholders globally; and to advance the metrological science of our reference standards, including the issuance of CRMs as the application and intended use demands. CRMs provide a means to establish trueness and traceability to the measurement system, thereby allowing and enabling consistency and comparability of measurements and results across time and space, and supporting sound administrative and legal decisions. USP CRMs will be first and foremost USP Reference Standards and in every way responsive to the requirements set forth in *USP–NF*.

2. The Benefits of CRMs. A CRM is a material that is sufficiently homogeneous and stable with reference to specified properties and is established to be fit for its intended use in measurement. Further, it is accompanied by documentation, issued by an authoritative body, providing one or more specified property values, with associated uncertainties and traceabilities, using valid procedures (3).

Three additional definitions are critical to this discussion: metrology, metrological traceability and uncertainty:

Metrology is the science of measurement, embracing both experimental and theoretical determinations in any field of science and technology. Metrology has three distinct branches, all of which have relevance to the development, application, and use of CRMs. *Fundamental* metrology includes the establishment of measurement units, new measurement methods, realization of measurement standards and the transfer of traceability. *Applied* metrology concerns the application of measurement science to manufacturing, ensuring the suitability of measurement instruments, their calibration, and quality control of measurements. Finally, *legal* metrology concerns regulatory requirements of measurements and measuring instruments.

Metrological traceability is the property of a measurement result whereby the result can be related to a stated reference through a documented unbroken chain of calibrations, each of which contributes to the measurement uncertainty.

Measurement uncertainty is a non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used.

^a For membership see Appendix.

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The Use of Inductively Coupled Plasma–Optical Emission Spectroscopy in the Determination of Heavy Metals in Cospovidone and Povidone as a Replacement for the Concomitant Visual Comparison Test

Sergio Lira,^a Peter Brush,^b Laurence Senak,^a Chi-san Wu,^a and Edward Malawer^{c,d}

ABSTRACT The determination and quantification of heavy metals by the concomitant visual comparison test in the *US Pharmacopeia (USP)* is more than 100 years old. Critical experimental examination of this method reveals two flaws: the loss of analytes at elevated temperatures upon ashing the sample and the varied responses of several metals (including silver, arsenic, cadmium, mercury, tin, bismuth, and antimony) to the sulfide reagent. As a result of these two flaws, the presence of heavy metals in pharmaceutical excipients such as cospovidone can be significantly underreported. The purpose of this *Stimuli* article is to demonstrate these deficiencies in the current method and to propose an alternative method, inductively coupled plasma–optical emission spectroscopy (ICP–OES) for cospovidone and related materials. The satisfactory recovery of all 10 heavy metals specified in the *USP* general test is demonstrated by the ICP method.

INTRODUCTION

The determination of heavy metals by concomitant visual comparison is a general test in *US Pharmacopeia (USP)* General Chapter *Heavy Metals* (231) and in the *European Pharmacopoeia (EP)* and is required for compliance to monographs such as that for cospovidone, the pharmaceutical grade of cross-linked poly(vinyl pyrrolidone). The pharmacopoeias have long recognized the need for heavy metals testing as a component of ingredient safety testing, and thus the concomitant visual comparison test dates back more than 100 years (1). Weaknesses in this method and potential solutions have appeared in the literature recently. For example during an attempt to harmonize, *USP*, *EP*, and *Japanese Pharmacopoeia (JP)* monographs for heavy metals, Blake noted that loss of metals was a significant problem associated with the current procedure (2). The Blake study facilitated a critical review of the heavy metals test as practiced in *USP*. A subsequent report examined the importance of testing for metals and setting of limits in pharmaceutical excipients (3). As a solution to the deficiencies of current heavy metals test methods, Lewen et al. have proposed the use of inductively coupled plasma–mass spectrometry (ICP–MS) for the screening of metals in active pharmaceutical compounds (4).

The *USP* and *EP* methods are similar but not exactly the same (5, 6). Both methods require a sample preparation step that involves sample ignition followed by sample ashing at 600 °C (*USP*) or 800 °C (*EP*). After it is ashed, the residue is then pH adjusted and a thioacetamide reagent, either freshly generated hydrogen sulfide solution or thioacetamide–glycerin base TS, is added to the sample tube. A 10 ppm lead standard is prepared in the same way for use in the visual color comparison. Lead is one of the few heavy metals with minimal loss during high-temperature ashing and responds well to the thioacetamide reagent. The color of the sample solution should not

be darker than that of the standard solution. The directions in both *USP* and *EP* state that 10 metals colored by the sulfide ion under these test conditions are: lead, mercury, bismuth, arsenic, antimony, tin, cadmium, silver, copper, and molybdenum. To compound the issue of metals lost in ashing the sample, recent reports and the present work show that this method is adequately sensitive for only a few of the ten metals just listed. The loss of heavy metals during ashing has helped promote the development of a new method for the analysis of heavy metals by inductively coupled plasma–optical emission spectroscopy (ICP–OES).

The proposed method employs acid digestion of the sample followed by analysis using ICP–OES. One gram of sample is added to a digestion vessel and is placed in a microwave digester. The sample vessel is charged with nitric acid and sulfuric acid and then is ramped up to a temperature of approximately 280 °C. When the digestion of the sample is complete, the remaining sulfuric acid is evaporated (at 350 °C) so that less than 1 gram of acid remains. The final solution is then diluted to about 20 g with distilled water. The sample is analyzed for lead, mercury, bismuth, arsenic, antimony, tin, cadmium, silver, copper, and molybdenum using ICP. This report shows that recovery using the ICP method is acceptable for all 10 heavy metals listed in *USP* and *EP* tests.

PART I: AN EXAMINATION OF DEFICIENCIES IN THE CURRENT *USP* MONOGRAPH FOR HEAVY METAL ANALYSIS IN POVIDONE AND CROSPVIDONE

As noted, two deficiencies limit the use of the current *USP* monograph for the determination and quantification of heavy metals in povidone and cospovidone. In the first part of the investigation, the authors studied the effect of heating and temperature on volatilization of the metals in question. Ten test sample solutions were made, each of which contained 10 ppm of one of the 10 heavy metals under evaluation: lead, mercury, bismuth, arsenic, antimony, tin, cadmium, silver, copper, and molybdenum. These solutions contained no sample and only a spike of the heavy metal in question. Each of the ten test solutions was then subdivided into three equal portions. One of the

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Compendial Calculations: Recommendations for Improving *USP–NF* Calculations^a

Compendial Calculations Project Team: Philip Travis (Chair), *Midwest Compendial Discussion Group*; Jason Lu, *Calibration & Validation Group*; Don Magin and Bukhosi Ndlovu, *New Jersey Pharmaceutical Quality Control Association*; Andy Sopirak, *Pharmaceutical Research & Manufacturers of America*; Marina Aerova, *Western Compendial Discussion Group*

ABSTRACT This *Stimuli* article summarizes the recommendations of the Prescription/Nonprescription Stakeholder Forum's Compendial Calculations Project Team for improving mathematical information (and related topics) within *USP–NF*. The recommendations are intended to improve the mathematical functionality of *USP–NF* for common applications within the pharmaceutical industry and to standardize the formulas and variables within *USP–NF*. The recommendations are made to the Chair, Council of Experts, for further consideration, subject to the Council's Rules and Procedures.

BACKGROUND

In 2003 a proposal was submitted by Merck & Co. Inc., to clarify and standardize the calculations within the *United States Pharmacopeia (USP)*. This proposal was developed further by the Pharmaceutical Research & Manufacturers of America (PhRMA), and a *Stimuli* article titled "Compendial Calculations: Improving Calculations in *USP–NF*" was submitted to *Pharmacopeial Forum (PF)* in 2004 (1). In early 2005 USP published two *Stimuli* articles, "Common Pharmacopeial Calculations in *USP* Monographs" and "The Use of Relative Response Factors to Determine Impurities" (2, 3). Although some of the suggestions differed, representatives from the pharmaceutical industry and USP agreed that improvements were desirable.

In association with the USP Prescription/Nonprescription Stakeholder Forum, the Compendial Calculations Project Team (Project Team) was formed in 2006. The charge of the Project Team was to open a dialog between industry stakeholders and USP to review the three *Stimuli* articles as the foundation for a discussion about next steps and the path forward for compendial calculations. Once the charge was established, two primary goals were set: 1) to standardize common calculations, clarify ambiguous factors, and add missing calculations; and 2) to improve allied USP systems and eliminate redundancy.

INTRODUCTION

This article summarizes the recommendations of the Project Team as a path forward in developing the calculations and improving the overall usability of *USP–NF*.

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I. Universal Improvements

Variables

The variables used within monograph calculations should be standardized. Where possible, the variables should align with the recommendations provided in the *USP–NF* Calculation Templates for General Chapters (*Attachment 1*).

Example: Current Procedure for Microcrystalline Cellulose, Identification B

Calculate the degree of polymerization, P , by the formula:

$$(95)[\eta]_c/W_s[(100 - \%LOD)/100]$$

in which $[\eta]_c$ is the intrinsic viscosity; W_s is the weight, in g, of the Microcrystalline Cellulose taken; and $\%LOD$ is the value obtained from the test for *Loss on drying*.

Standardized Variables:

$$\frac{(95)[\eta]_c}{W(1 - A)}$$

in which W is the weight, in g, of the Microcrystalline Cellulose taken; and A is the percent *Loss on drying* value, as a decimal.

General Chapter References

Where appropriate, methods that apply technology covered by the General Chapters should reference those chapters. For example, General Chapter *Spectrophotometry and Light-scattering* (851) is not always included with UV/VIS methods of analysis.

Appearance

Maintain a clear separation of mathematical functions to avoid confusion with the order of operations.

General Chapter *Containers—Packaging Auxiliary Components* <670>

Michael N. Eakins, Vice-Chair, *Packaging and Storage Expert Committee*^a

ABSTRACT The Packaging and Storage Expert Committee proposes a new General Chapter, *Containers—Packaging Auxiliary Components* <670>, to support or enhance container–closure systems. The initial content will consist of cotton, rayon, and polyester pharmaceutical coil used to prevent breakage of tablets or capsules during shipment. Further additions to the chapter are envisaged (e.g., desiccants) at a future date. This *Stimuli* article reviews the historical development of <670> and reviews some of the General Chapter's content.

HISTORY AND OVERVIEW OF GENERAL CHAPTER <670>

Although cotton is a natural fiber, both rayon and polyester are synthetic fibers manufactured from cellulose and petroleum, respectively. The products display different moisture-absorptive properties. Cotton and rayon are moisture absorptive and are most commonly used in bottles of tablets and capsules, but polyester is nonabsorbent and is most commonly used with soft-gel capsules.

The addition of pharmaceutical coil to *USP* was proposed in *Pharmacopeial Forum* in 1997 (1), but the monographs titled *Purified Cotton Filler* (2) and *Purified Rayon Filler* (3) did not advance to *USP*. Instead, industry has relied on the *USP* monographs for *Purified Cotton* (4) and *Purified Rayon* (5) as the basis for ad hoc standards for the use of these materials as pharmaceutical coil by selecting those tests that are relevant to the product. FDA has endorsed this general approach in the guidance document on *Container–Closure Systems for Packaging Human Drugs and Biologics* (6) with the caveats that cotton coil need not meet the monograph requirements for sterility, fiber length, or absorbency; rayon coil need not meet the monograph requirements for fiber length or absorbance; and appropriate tests and acceptance criteria for identification and for moisture content should be established for both cotton and rayon. Monographs for both cotton and rayon in other pharmacopeias do contain tests for identification and moisture. For example, the *European Pharmacopoeia* includes a test for *Absorbent Cotton* (7), and the *Indian Pharmacopoeia* includes tests for both *Absorbent Cotton* and *Purified Rayon* (8, 9).

The sections on cotton and rayon pharmaceutical coil include chemical methods for identification and a color stain test that can distinguish between cotton, rayon, and polyester fibers. The section on cotton pharmaceutical coil has retained the test methods and specifications for acidity or alkalinity, residue on ignition, water-soluble substances, fatty matter, dyes, and other foreign matter from the *USP* monograph on *Purified Cotton* (4). Similarly, the section on rayon pharmaceutical coil has retained the test methods and specifications for acidity or alkalinity, residue on ignition, acid-insoluble ash, water-soluble substances, dyes, and other foreign matter from the *USP* monograph on *Purified Rayon* (5). A test and specification for volatile content also have been included for

both cotton and rayon pharmaceutical coil. The specification for cotton pharmaceutical coil of not more than 8.0% is the same as for the specification for Absorbent Cotton in the *European Pharmacopoeia* monograph (7), and the specification for rayon pharmaceutical coil has been set at not more than 11.0% (1).

Cotton is bleached during the purification process, typically with hydrogen peroxide that is subsequently removed by washing. Accordingly, a limit test for residual hydrogen peroxide has been included in the chapter because excess residual peroxide has been observed to produce stability problems in tablets. Chemicals such as furfural and other aldehydes can cause gelatin crosslinking, which produces a rubbery, water-insoluble film or pellicle that acts as a barrier and delays drug release (10, 11). Rayon pharmaceutical coil has been found to be a potential source of such chemicals, and a warning has been added to the chapter regarding its use with gelatin capsules.

Polyester is a family of polymers that contains the ester functional group in the main chain and is one of the most widely used synthetic fibers in the world. It is produced by reacting terephthalic acid or dimethyl terephthalate with monoethylene glycol in the presence of a catalyst, e.g., antimony trioxide. One of the most common forms of polyester is polyethylene terephthalate or PET, and a section of General Chapter *Containers—Plastics* <661> (12) is devoted to PET. This chapter includes infrared (IR) and differential scanning calorimetry tests on PET containers for identity and on extracts of the plastic obtained by various solvents. For polyester pharmaceutical coil, an IR method suitable for fibers has been included as an identity test as well as a method and limit for moisture content. Test methods and specifications for acidity or alkalinity, residue on ignition, and other foreign matter have been provided. To assist in handling, the polyester threads are usually coated with a solution containing lubricants, emulsifiers, and antistatic agents. Polyester should comply with applicable sections of 21 Code of Federal Regulations (CFR) Part 177 for Indirect Food Additives, Sections 1630 and 2800 (13, 14).

CONCLUSION

A draft of General Chapter *Containers—Packaging Auxiliary Components* <670> is published in this number of *Pharmacopeial Forum*, and *USP* invites comments. Please contact Desmond Hunt, PhD, Scientist, US Pharmacopeia, 12601

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Description of the Upcoming Change in Data Analysis for USP Dissolution Performance Verification Tests

Walter W. Hauck,^a Anthony J. DeStefano, William E. Brown, Erika S. Stippler, Darrell R. Abernethy, Roger L. Williams, *USP*, and the Biopharmaceutics Expert Committee^b

ABSTRACT As part of its evaluation of the performance verification tests used periodically to affirm the integrity of the USP Performance test when General Chapter *Dissolution* (711) is relied upon, the Biopharmaceutics Expert Committee of the Council of Experts, working with staff, decided to change the form of the accept/reject decision from one based on the result for each tablet to one based on the mean and coefficient of variation of results from a set of tablets. This paper describes the new approach. The paper also describes an implementation period for the approach, coupled with a period during which USP will discontinue use of the Salicylic Acid tablet in a performance verification test.

INTRODUCTION

USP has embarked on a vigorous program to evaluate its performance verification tests (PVTs) in order to maximize their value in ensuring the integrity of the dissolution and other procedures (e.g., 1, 2). For the dissolution procedure described in General Chapter *Dissolution* (711) and applied to nonsolution orally administered dosage forms, this has led to two major changes.

First, Salicylic Acid tablets will be discontinued as an available official USP Reference Standard (RS) for use in a PVT. The transition is expected at the end of CY 2009. Adequate information will be made available to users to allow a smooth transition, and USP's remaining PVT tablets (Prednisone and Chlorpheniramine Maleate Extended-Release RS tablets) will continue to be supplied as before.

Second, the form of the accept/reject decision for the PVT will change. A 2007 *Stimuli* article proposed the change from one based on per-tablet results—which correspond to individual positions in an assembly—to one based on the mean and coefficient of variation (CV) of a set of RS tablet results (3). Note that an assembly is the complete dissolution test equipment including 6 to 12 apparatus positions, depending on the manufacturer. Responses to the authors of the five comments received regarding the *Stimuli* article were published in a subsequent *Stimuli* article (4). One comment suggested that the test be done in a two-stage fashion. This is similar to the current procedure for General Chapter *Dissolution* (711) (5) and for General Chapter *Uniformity of Dosage Units* (905) (6). A two-stage test is an optional part of the proposal described here.

USP's Biopharmaceutics Expert Committee (BPC) reviewed the current proposal and concluded that USP should proceed with implementation of the revised form of the PVT acceptance criteria, as described in the 2007 *Stimuli* article (3), and include the option of a two-stage test. The purpose of this *Stimuli* article is to describe the revised approach that will apply to PVTs used to assess the integrity of the dissolution

procedure as described in General Chapter (711). The background information provided to the BPC, including operating characteristic curves, will be submitted for publication elsewhere (article in preparation).

Single-Stage Test

The current acceptance criteria for the dissolution PVT are per RS tablet. That is, the result for each tablet/position must fall within the acceptance range, which arises from collaborative studies of RS tablets and is based on both inter- and intra-laboratory variability. The proposal is to replace the current approach with one based on the mean and CV of results from a set of tablets judged relative to acceptance ranges obtained from the collaborative study. The new approach will follow ISO International Standard 5725-6 (7). In Technical Specification 21748 ISO recommended a minimum of 15 degrees of freedom for the variability (8). USP elected to increase the number of tablets in the PVT from that currently required but to a lesser extent than that called for by the 15-degree-of-freedom recommendation.

The following are step-by-step instructions for the single-stage test. Sufficient detail is provided so readers can both understand the procedure and, if desired, perform the calculations. USP will make available on its Web site a spreadsheet that will accept data from the 12 to 16 individual results from steps 1 and 2 and perform all the calculations.

1. For each position in the assembly, test one USP PVT RS (Prednisone RS tablets for Apparatus 1 and 2, and Chlorpheniramine Maleate Extended-Release RS tablets for Apparatus 3 at each dip rate), and record the percent dissolved at each sampling time point(s) specified for that apparatus (i.e., 30 min for Apparatus 1 and 2 and each of the times specified for Apparatus 3). After transforming the percent dissolved results to the log scale, determine the mean and variance. For assemblies with 12 positions (12 dissolution vessels), no further testing is required.
2. For assemblies with fewer than 12 positions, repeat Step 1 with an additional set of tablets. Again after transforming the percent dissolved results to the log scale, determine the mean and variance.

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^b For a list of the members of the Biopharmaceutics Expert Committee, please see Appendix A.

USP Responses to Comments on *Stimuli* Article, “Uncertainty Statements Regarding USP Reference Standards”

William F. Koch, PhD,^a Walter W. Hauck, PhD, Shawn F. Dressman, PhD, Darrell R. Abernethy, MD, PhD,
Roger L. Williams, MD, *USP*

ABSTRACT *Pharmacopeial Forum* 34(2) [March–April 2008] included a *Stimuli* article titled “Uncertainty Statements Regarding USP Reference Standards.” This *Stimuli* article commented favorably on USP’s pilot project for the production of Certified Reference Materials. The article elicited a response that posed four questions, which are abstracted here with USP responses.

INTRODUCTION

Pharmacopeial Forum 34(2) included a *Stimuli* article titled “Uncertainty Statements Regarding USP Reference Standards” (1). The article suggested that “this development will increase the transparency and quality of USP Reference Standards.” The *Stimuli* article elicited four questions from FDA (letter dated 5 June 2008) that are abstracted here with USP responses.

Question 1

In the section titled “Measurement Results Obtained over Time” on page 479 of the *Stimuli* article, the basis of the comparison of three different reference standards (RS) is not quite clear to the reader. If the in-house primary RS is a solution that has been stored for the entire six-year period, the storage conditions to maintain stability is not described in this section. If the in-house secondary RS is a solution, it is not explained either if this is stored in the same manner as the in-house primary RS. This section does not describe whether a fresh solution of the USP Human Insulin RS was prepared from powder when comparison studies were made. If these assumptions are true, the in-house secondary RS may give good results compared to the in-house primary RS because the samples were treated identically between measurements. Furthermore, if the USP Human Insulin RS was made fresh for each analysis, variations in preparations likely could cause the observed fluctuations in the data.

USP Response

FDA raises excellent points for which the answers involve details not available to USP. The important message to be derived from this line of inquiry is that there are several sources of uncertainty and variability that enter into stability studies and reference material comparisons. All sources of these variabilities must be understood and controlled to draw definite conclusions. USP emphasizes that most measurements are in fact comparisons or ratios involving at least two materials: the “known” (also known as the standard or calibrant) and the “unknown” (also known as the sample of interest or measur-

and). Hence, the importance of enhanced knowledge of the property value of the standard, including its expanded uncertainty, is undeniable. Without this information, the analyst cannot determine whether the primary or secondary standard is shifting—or both—and this lack of information in consequence breaks the traceability chain, as described in a previous *Stimuli* article response (2).

Question 2

The sentence “Consequently, the estimate of uncertainty is not related to the individual measurement result” under “Estimation of Content” on page 479, is not very informative. If the authors describe factors to which the estimate of uncertainty is related, the point will be clearer. The sentence could be revised to: “Consequently the estimate of uncertainty includes measurement repeatability determined from replicate measurements on single samples, measurement reproducibility between labs and operators, and vial-to-vial heterogeneity of the RS.”

USP Response

The treatment of data and associated uncertainties required to draw conclusions about comparisons of materials is well documented in a variety of scholarly texts and internationally recognized standards including ISO 5725 (3), which USP relies on as guidance for our statistical analyses. The assessment of both Type A and Type B sources of variability, is an essential requirement of Certified Reference Materials.

Question 3

Vial-to-vial homogeneity is a critical quality attribute of any RS, and it is appropriate to provide such information to the end user. If the collaborative study is properly designed, then an uncertainty due to heterogeneity can be provided to the user in the form of a relative standard deviation associated with heterogeneity. However, if the specified RS uncertainty is computed from data that include multiple vials, then the grand means and standard deviations already include this information in the estimate of uncertainty. Thus, if the end user performs a proper error analysis, the influence of heterogeneity should be included. On the other hand, if the end user uses

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Redesign of the *United States Pharmacopeia* and *National Formulary*

Todd L. Cecil, PhD, USP^a

ABSTRACT A revision of the style and format of *USP–NF* was proposed in 2006 to increase the readability and usability of the compendia. This *Stimuli* article presents feedback received from reviewers and describes the final redesign. This article informs users about forthcoming changes that will be incorporated in *USP–NF* and provides the rationale for these changes.

INTRODUCTION

In *Pharmacopeial Forum (PF)* 32(6) [Nov.–Dec. 2006] a *Stimuli* article proposed a new style and format for *USP* and *NF* monographs (1). The *PF* article proposed a new monograph design for public review and comment. *USP* received comments from 11 individuals, organizations, and agencies. *USP* also charged 2 project teams of the Prescription/Nonprescription Stakeholder Forum with the task of providing industry commentary on the proposal. This *Stimuli* article summarizes all of the comments received, and the recommendations of the Compendial Calculations Project team are included elsewhere in this issue of *PF*.

All comments can be distilled into 7 major topic areas. These areas include: ICH terminology; Description section; Assay section; Impurities section; Specific tests section; General Recommendations; and Consistency.

ICH Terminology

The redesign has attempted to incorporate terms defined by the International Conference on Harmonization (ICH) in the Q3 (2–4) and Q6 (5, 6) series of guidelines. ICH nomenclature is incorporated into *USP* monographs by several design elements.

The Q6A guideline defines a *Specification* as containing “Universal Tests” (Description, Identification, Assay, and Impurities) and “Specific Tests.” Each test contains a “Procedure” and “Acceptance Criteria.” The Universal Tests and Specific Tests are included as the section headers in the newly redesigned monographs. Within test sections the redesigned monographs include Procedures and Acceptance Criteria. Where there is more than one procedure in a “Test,” each procedure is preceded by a bullet.

Within the Impurities Test, ICH Q3A(r) (2) and Q3B(r) (3) define impurities as belonging to 1 of 3 types: Organic Impurities, Inorganic Impurities, and Residual Solvents. The redesigned *USP* monographs reflect this by incorporating specific subsections in the Impurities Test for Organic Impurities, Inorganic Impurities, and, in rare cases, Residual Solvents. In addition to these sections, *USP* has specifically identified a “Performance Tests” section and an “Other Components” section. Neither of these sections is defined by ICH, but for reasons explained below these sections were added to the redesign.

Comments on ICH Terminology

The incorporation of the ICH nomenclature was generally approved by the commenters, but 3 comments suggested minor changes for application in the *Pharmacopeia*. These comments will be addressed later in the article.

Two commenters suggested that where multiple procedures exist for a given test, they should be termed “Test 1, Test 2” instead of “Procedure 1, Procedure 2.” The commenters suggested that this modification would minimize changes to filings with regulatory agencies and to internal SOPs. *USP* chose not to incorporate this suggestion. The term *Procedure* is preferred because it is consistent with ICH nomenclature. In addition, the consistent careful application of the terms “Specification, Test, Procedure, and Acceptance Criteria” is a cornerstone of the redesign effort and should lead to better understanding of *USP* and *NF* monographs.

Three commenters requested the elimination of the “Performance Tests” section and the incorporation of these tests in the “Specific Tests” section of a monograph. The requested change reflects the ICH Q6A guideline. *USP* is retaining the Performance Tests section as a separate section because the procedures included in this section typically deviate from the singlet testing paradigm that is the basis of most tests in *USP*.

Description Section

The “Description” as defined by ICH Q6A (5) creates problems for compendial monographs. ICH Q6A defines “Description” as “a qualitative statement about the state (e.g., solid, liquid) and color of the new drug substance . . .” However in *USP* and *NF* the Description and Solubility information has been extracted from monographs and collated into a separate section in the publication. This approach was instituted in 1980 and is considered the appropriate location for this information. The redesign proposal included a section called “Description” that reflected current *USP–NF* style, which deviated from the ICH definition. Several commenters requested changing the test section title from “Description” to “Definition.” This change represents a departure from strictly constructed ICH terminology. The redesign will incorporate the test section of “Definition” because it follows general *USP* usage and intention and avoids confusion with the Description and Solubility section. A single commenter suggested that moving solubility into the monograph was appropriate, but this proposal had little support from the majority of correspondents and will not be incorporated in the redesign.

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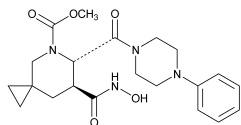
USP Dictionary of USAN and International Drug Names 2008 USP DICTIONARY SUPPLEMENT 4

IMPORTANT—Save this Supplement. This and all supplements appearing in *PF* are needed to keep the 2008 edition of the USP Dictionary (USPD) up-to-date. The cumulative contents of the supplements to the current (2008) edition will be included in the next complete edition of the Dictionary.

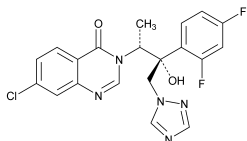
Newly Approved United States Adopted Names (USAN), Released for Publication

The following are newly established United States Adopted Names (USAN). These names will not be listed cumulatively; see preceding and succeeding numbers of *PF* for other new USAN to supplement the Dictionary main volume.

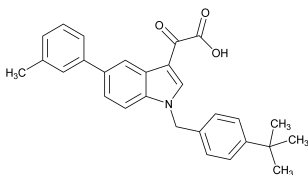
Aderbasib [2007] (a der' ba sib). $C_{21}H_{28}N_4O_5$. 416.47. (1) 5-Azaspiro[2.5]octane-5-carboxylic acid, 7-[(hydroxyamino)carbonyl]-6-[(4-phenyl-1-piperazinyl)carbonyl]-, methyl ester, (6*S*,7*S*)-; (2) Methyl (6*S*,7*S*)-7-[(hydroxyamino)carbonyl]-6-[(4-phenylpiperazin-1-yl)carbonyl]-5-azaspiro[2.5]octane-5-carboxylate. *CAS*-791828-58-5. INN. *Antineoplastic; ErbB Sheddase (ADAM) Inhibitor*. \diamond INCB 007839



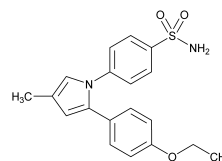
Albaconazole [2008] (al' ba kon' a zole). $C_{20}H_{16}ClF_2N_5O_2$. 431.82. (1) 4(3*H*)-Quinazolinone, 7-chloro-3-[(1*R*,2*R*)-2-(2,4-difluorophenyl)-2-hydroxy-1-methyl-3-(1*H*-1,2,4-triazol-1-yl)propyl]-; (2) 7-Chloro-3-[(1*R*,2*R*)-2-(2,4-difluorophenyl)-2-hydroxy-1-methyl-3-(1*H*-1,2,4-triazol-1-yl)propyl]quinazolin-4(3*H*)-one. *CAS*-187949-02-6. INN. *Treatment of fungal infections*. \diamond UR-9825



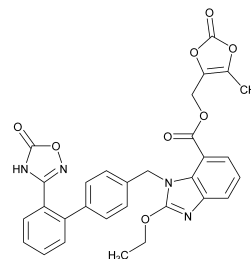
Aleplasinin [2007] (al' e plas' in in). $C_{28}H_{27}NO_3$. 425.50. (1) 1*H*-Indol-3-acetic acid, 1-[[[4-(1,1-dimethylethyl)phenyl]methyl]-5-(3-methylphenyl)- α -oxo-]; (2) 1-[4-(1,1-Dimethylethyl)benzyl]-5-(3-methylphenyl)-1*H*-indol-3-yl]oxoacetic acid. *CAS*-481629-87-2. INN. *Treatment of Alzheimer's disease* \diamond PAZ-417



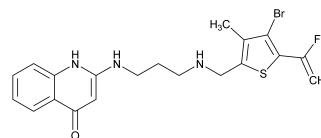
Apricoxib [2008] (a' pri kox' ib). $C_{19}H_{20}N_2O_3S$. 356.40. (1) Benzenesulfonamide, 4-[2-(4-ethoxyphenyl)-4-methyl-1*H*-pyrrol-1-yl]-; (2) 4-[2-(4-Ethoxyphenyl)-4-methyl-1*H*-pyrrol-1-yl]benzenesulfonamide. *CAS*-197904-84-0. INN. *Treatment of pain and inflammation, oncology*. \diamond TG01; R-109339; CS-706



Azilsartan Medoxomil [2007] (ay' zil sar' tan me dox' oh mil). $C_{30}H_{24}N_4O_8$. 568.50. (1) 1*H*-Benzimidazole-7-carboxylic acid, 1-[[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)[1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl ester; (2) (5-Methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-ethoxy-1-((2'-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)biphenyl-4-yl)methyl)-1*H*-benzo[d]imidazole-7-carboxylate. *CAS*-863031-21-4. INN. *Treatment of hypertension*. \diamond TAK-491

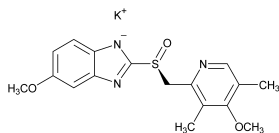


Bederocin [2007] (be der' oh sin). $C_{20}H_{21}BrFN_3OS$. 450.40. (1) 4(1*H*)-Quinolinone, 2-[[[3-[[[4-bromo-5-(1-fluoroethyl)-3-methyl-2-thienyl]methyl]amino]propyl]amino]-]; (2) 2-[[[3-[[[4-bromo-5-(1-fluoroethyl)-3-methylthiophen-2-yl]methyl]amino]propyl]amino]quinolin-4(1*H*)-one. *CAS*-757942-43-1. INN. *Antibacterial agent*. \diamond REP 8839



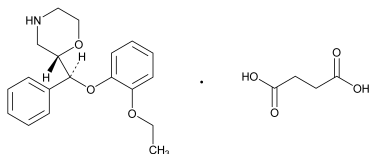
Carlecortemel-L [2007] (kar' le kor tem' sel - el). StemEx[®] is a suspension of human umbilical cord blood-derived, *ex vivo* expanded CD133+ cells in an infusion solution, composed of PBS buffer containing 1 mM EDTA and 0.5% HSA, to a fixed concentration of $2.3\text{--}3.3 \times 10^6$ cells/ml and packed in a culture bag. *Treatment of high risk hematologic malignancies*. StemEx (Gamida Cell); StemEx (Teva, Israel)

methylpyridin-2-yl)methyl]sulfinyl}-1*H*-benzimidazole potassium salt. CAS-161796-84-5. Treatment of GERD patients with a history of erosive esophagitis.



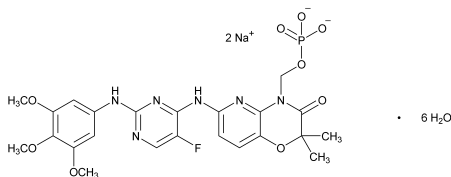
Esreboxetine Succinate [2007] (es' re box' e tine sux' i nate).

C₁₉H₂₃NO₃·C₄H₆O₄. 431.48. (1) Butanedioic acid, compd. with (2*S*)-2-[(*S*)-(2-ethoxyphenoxy)phenylmethyl]morpholine (1:1); (2) (+)-(2*S*)-2-[(*S*)-(2-Ethoxyphenoxy)phenylmethyl]morpholine hydrogen butanedioate. CAS-635724-55-9. Treatment of chronic neuropathic pain. \diamond PNU-165442G



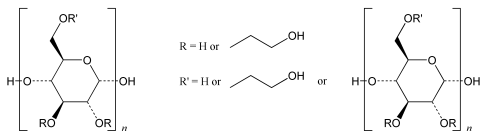
Fostamatinib Disodium [2008] (fos' ta ma' ti nib dye soe' dee um).

C₂₃H₂₄FN₆Na₂O₉P·6H₂O. 732.50. (1) 2*H*-Pyrido[3,2-*b*]-1,4-oxazin-3(4*H*)-one, 6-[[[5-fluoro-2-[(3,4,5-trimethoxyphenyl)amino]-4-pyrimidinyl]amino]-2,2-dimethyl-4-[(phosphonoxy)methyl]-, disodium salt, hexahydrate; (2) [6-(5-Fluoro-2-[(3,4,5-trimethoxyphenyl)amino]pyrimidin-4-yl)amino]-2,2-dimethyl-3-oxo-2,3-dihydro-4*H*-pyrido[3,2-*b*]-1,4-oxazin-4-yl]-methyl disodium phosphate hexahydrate. CAS-914295-16-2. Treatment of rheumatoid arthritis, immune thrombocytopenic purpura, and B-cell lymphoma. \diamond R935788 sodium; R788 sodium



Hydroxyethyl Starch 130/0.4 [2008] (hye drox' ee eth' il starch). (1)

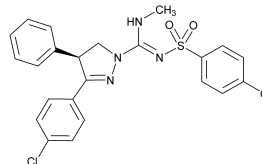
Starch 2-hydroxyethyl ether; (2) A starch composed of more than 90% amylopectin that has been etherified to the extend that an average of 3.8 to 4.5 of the OH groups present in every 10 D-glucopyranose units of the starch polymer have been converted into OCH₂CH₂OH groups. Molecular weight is approximately 130,000 daltons. CAS-9005-27-0. Prophylaxis of hypervolemia. Voluven (Fresenius Kabi Deutschland GmbH) \diamond HES 130/0.4



Ibipinabant [2007] (eye' bi pin' a bant). C₂₃H₂₀Cl₂N₄O₂S. 487.40.

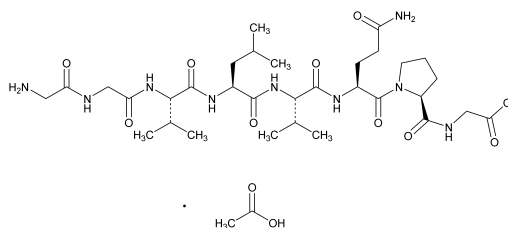
(1) 1*H*-Pyrazole-1-carboximidamide, 3-(4-chlorophenyl)-*N*-[(4-chlorophenyl)sulfonyl]-4,5-dihydro-*N'*-methyl-4-phenyl-, (4*S*,*E*); (2) (*E*)-(4*S*)-3-(4-Chlorophenyl)-*N'*-[(4-chlorophenyl)-

sulfonyl]-*N*-methyl-4-phenyl-4,5-dihydro-1*H*-pyrazole-1-carboximidamide. CAS-464213-10-3. INN. Treatment of obesity. \diamond SLV-319; BMS-646256



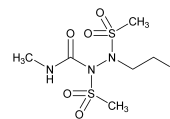
Larazotide Acetate [2007] (la raz' oh tide as' e tate).

C₃₂H₅₅N₉O₁₀·C₂H₄O₂. 785.89. [Larazotide is INN.] (1) Glycine, glycyglycyl-L-valyl-L-leucyl-L-valyl-L-glutamyl-L-prolyl-, monoacetate; (2) Glycyglycyl-L-valyl-L-leucyl-L-valyl-L-glutamyl-L-prolylglycine acetate. CAS-881851-50-9; CAS-258818-34-7 [larazotide]. Treatment of Celiac disease and treatment of Inflammatory Bowel Disease. \diamond AT-1001



Laromustine [2007] (lar' oh mus' teen). C₆H₁₄ClN₃O₅S₂. 307.80. (1)

Methanesulfonic acid, 1-(2-chloroethyl)-2-[(methylamino)carbonyl]-2-(methylsulfonyl)hydrazide; (2) 2'-(2-Chloroethyl)-*N*-methyl-1',2'-bis(methylsulfonyl)carbamo-hydrazide; (3) 1,2-Bis(methylsulfonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine. CAS-173424-77-6. INN. Antineoplastic; treatment of acute myeloid leukemia. Cloretazine (Vion) \diamond VNP40101M; 101M



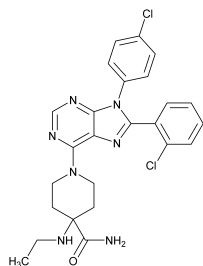
Linacotide [2007] (lin ak' loe tide). C₅₉H₇₉N₁₅O₂₁S₆. 1526.80. (1) L-

Tyrosine, L-cysteinyl-L-cysteinyl-L- α -glutamyl-L-tyrosyl-L-cysteinyl-L-cysteinyl-L-asparaginyl-L-prolyl-L-alanyl-L-cysteinyl-L-threonylglycyl-L-cysteinyl-, cyclic (1 \rightarrow 6),(2 \rightarrow 10),(5 \rightarrow 13)-tris(disulfide); (2) [9-L-Tyrosine]heat-stable enterotoxin (*Escherichia coli*)-(6-19)-peptide. CAS-851199-59-2. Treatment of irritable bowel syndrome with constipation (IBS-C), chronic constipation and other gastrointestinal disorders.

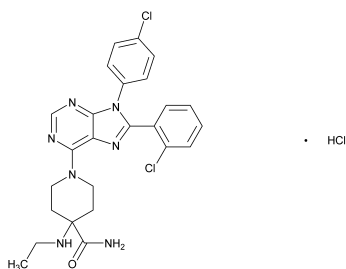


Otenabant [2007] (oh ten' a bant). C₂₅H₂₅Cl₂N₇O. 510.42. (1) 4-

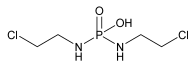
Piperidinecarboxamide, 1-[8-(2-chlorophenyl)-9-(4-chlorophenyl)-9*H*-purin-6-yl]-4-(ethylamino)-; (2) 1-[8-(2-Chlorophenyl)-9-(4-chlorophenyl)-9*H*-purin-6-yl]-4-(ethylamino)piperidine-4-carboxamide. CAS-686344-29-6. INN. Treatment of obesity. \diamond CP-945,598



Otenabant Hydrochloride [2007] (oh ten' a bant hye' droe klor' ide). $C_{25}H_{25}Cl_2N_7O.HCl$. 546.88. (1) 4-Piperidinecarboxamide, 1-[8-(2-chlorophenyl)-9-(4-chlorophenyl)-9H-purin-6-yl]-4-(ethylamino)-, monohydrochloride; (2) 1-[8-(2-Chlorophenyl)-9-(4-chlorophenyl)-9H-purin-6-yl]-4-(ethylamino)piperidine-4-carboxamide monohydrochloride. CAS-686347-12-6. Treatment of obesity. \diamond CP-945,598

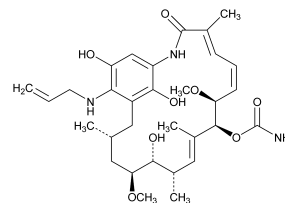


Palifosfamide [2008] (pal' i fos' fa mide). $C_4H_{11}Cl_2N_2O_2P$. 221.00. (1) Phosphorodiamidic acid, *N,N'*-bis(2-chloroethyl)-; (2) *N,N'*-Bis(2-chloroethyl)phosphorodiamidic acid. CAS-31645-39-3. INN. Antineoplastic. \diamond IPM; ZIO-201

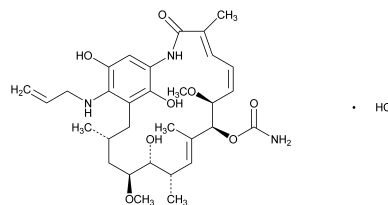


Ranagengliotucel-T [2007] (ran' a jen glye' oh too' sel - el). Autologous vaccine cocktail of TGF- β blocked, whole brain cancer tumor cells. Cell therapy treatment for brain cancer. Glionix (No-vaRx)

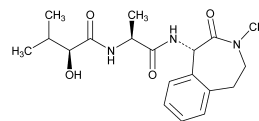
Retaspimycin [2008] (ret' asp i mye' sin). $C_{31}H_{45}N_3O_8$. 587.70. (1) Geldanamycin, 18,21-didehydro-17-demethoxy-18,21-dideoxo-18,21-dihydroxy-17-(2-propenylamino)-; (2) (4*E*,6*Z*,8*S*,9*S*,10*E*,12*S*,13*R*,14*S*,16*R*)-13,20,22-Trihydroxy-8,14-dimethoxy-4,10,12,16-tetramethyl-3-oxo-19-(prop-2-enylamino)-2-azabicyclo[16.3.1]docosa-1(21),4,6,10,18(22),19-hexaen-9-yl carbamate. CAS-857402-23-4. INN. Treatment of patients with metastatic and/or unresectable gastrointestinal stromal tumors (GIST); treatment of patients with relapsed and/or refractory stage IIIb (with pleural or pericardial effusions) or IV NSCLC. \diamond IPI-504



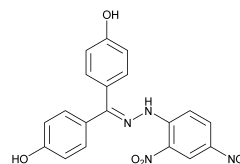
Retaspimycin Hydrochloride [2008] (ret' asp i mye' sin). $C_{31}H_{45}N_3O_8.HCl$. 624.20. (1) Geldanamycin, 18,21-didehydro-17-demethoxy-18,21-dideoxo-18,21-dihydroxy-17-(2-propenylamino)-, monohydrochloride; (2) (4*E*,6*Z*,8*S*,9*S*,10*E*,12*S*,13*R*,14*S*,16*R*)-13,20,22-Trihydroxy-8,14-dimethoxy-4,10,12,16-tetramethyl-3-oxo-19-(prop-2-enylamino)-2-azabicyclo[16.3.1]docosa-1(21),4,6,10,18(22),19-hexaen-9-yl carbamate hydrochloride. CAS-857402-63-2. Antineoplastic, Hsp 90 inhibitor. \diamond IPI-504



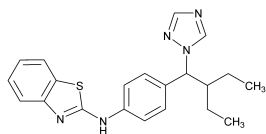
Semagacestat [2007] (sem' a gas' e stat). $C_{19}H_{27}N_3O_4$. 361.44. (1) Butanamide, 2-hydroxy-3-methyl-*N*-[(1*S*)-1-methyl-2-oxo-2-[[[(1*S*)-2,3,4,5-tetrahydro-3-methyl-2-oxo-1*H*-3-benzazepin-1-yl]amino]ethyl]-, (2*S*)-]; (2) (2*S*)-2-Hydroxy-3-methyl-*N*-[(2*S*)-1-[[[(1*S*)-3-methyl-2-oxo-2,3,4,5-tetrahydro-1*H*-3-benzazepin-1-yl]amino]-1-oxopropan-2-yl]butanamide; (3) *N*'-[(2*S*)-2-Hydroxy-3-methylbutanoyl]-*N*'-[(1*S*)-3-methyl-2-oxo-2,3,4,5-tetrahydro-1*H*-3-benzazepin-1-yl]-*L*-alaninamide; (4)A. CAS-425386-60-3. INN. Treatment of Alzheimer's disease. \diamond LY450139



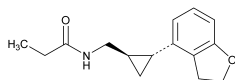
Sivifene [2007] (siv' i feen). $C_{19}H_{14}N_4O_6$. 394.34. (1) Methanone, bis(4-hydroxyphenyl)-, (2,4-dinitrophenyl)hydrazone; (2) 4,4'-[[2-(2,4-Dinitrophenyl)hydrazinylidene]methylene]diphenol. CAS-2675-35-6. INN. Treatment of high-grade squamous intraepithelial lesions of the cervix and other neoplasms. \diamond A-007



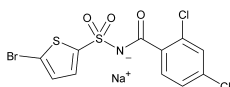
Talarozole [2007] (ta lar' oh zole). $C_{21}H_{23}N_3S$. 377.51. (1) 2-Benzothiazolamine, *N*-[4-[2-ethyl-1-(1*H*-1,2,4-triazol-1-yl)butyl]phenyl]-; (2) *N*-[4-[(1*R*)-2-Ethyl-1-(1*H*-1,2,4-triazol-1-yl)butyl]phenyl]benzothiazol-2-amine. CAS-201410-53-9. INN. Treatment of keratinization disorders; acne and psoriasis. Ram-bazole (Barrier) \diamond R115866



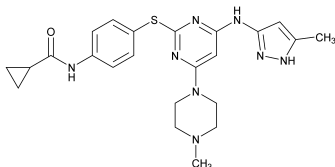
Tasimelteon [2007] (tas' i mel' tee on). $C_{15}H_{19}NO_2$. 245.32. (1) Propanamide, *N*-[[[(1*R*,2*R*)-2-(2,3-dihydro-4-benzofuranyl)cyclopropyl]methyl]-; (2) *N*-[[[(1*R*,2*R*)-2-(2,3-Dihydro-1-benzofuran-4-yl)cyclopropyl]methyl]propanamide. *CAS*-609799-22-6. INN. *Sleep disorders*. \diamond VEC-162; BMS-214778



Tasisulam Sodium [2007] (tas' i soo' lam). $C_{11}H_5BrCl_2NO_3S_2Na$. 437.09. [Tasisulam is INN.] (1) Benzamide, *N*-[(5-bromo-2-thienyl)sulfonyl]-2,4-dichloro-, sodium salt; (2) Sodium *N*-[(5-bromothiophen-2-yl)sulfonyl]-2,4-dichlorobenzamide. *CAS*-519055-63-1; *CAS*-519055-62-0 [tasisulam]. *Antineoplastic*. \diamond LY-573636.Na

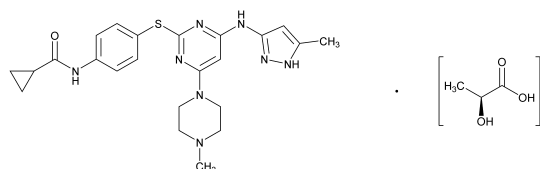


Tozasertib [2008] (toe' za ser' tib). $C_{23}H_{28}N_8OS$. 464.59. (1) Cyclopropanecarboxamide, *N*-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1*H*-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-; (2) *N*-[4-({4-(4-methylpiperazin-1-yl)-6-[(5-methyl-1*H*-pyrazol-3-yl)amino]pyrimidin-2-yl} sulfanyl)phenyl]cyclopropanecarboxamide. *CAS*-639089-54-6. *Antineoplastic*.

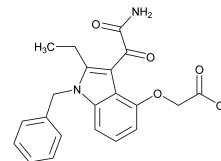


Tozasertib Lactate [2008] (toe' za ser' tib lak' tate). $C_{23}H_{28}N_8OS \cdot xC_3H_6O_3$. 464.59 (base). (1) Propanoic acid, 2-hydroxy-, (2*S*)-, compd. with *N*-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1*H*-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]cyclopropanecarboxamide; (2) *N*-[4-[[4-(4-Methylpiperazin-1-yl)-6-[(5-methyl-1*H*-pyrazol-3-yl)amino]pyrimidin-2-yl]-

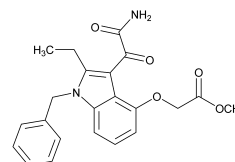
sulfanyl]phenyl]cyclopropanecarboxamide (2*S*)-2-hydroxypropanoate. *CAS*-899827-04-4. *Antineoplastic*. \diamond MK-0457; VX-680



Varespladib [2008] (var esp' la dib). $C_{21}H_{20}N_2O_5$. 380.40. (1) Acetic acid, 2-[[3-(2-amino-2-oxoacetyl)-2-ethyl-1-(phenylmethyl)-1*H*-indol-4-yl]oxy]-; (2) {3-(Amino-oxoacetyl)-1-benzyl-2-ethyl-1*H*-indol-4-yl]oxy}acetic acid. *CAS*-172732-68-2. INN. *Treatment of dyslipidemia*.



Varespladib Methyl [2008] (var esp' la dib meth' il). $C_{22}H_{22}N_2O_5$. 394.40. (1) Acetic acid, [[3-(amino-oxoacetyl)-2-ethyl-1-(phenylmethyl)-1*H*-indol-4-yl]oxy]-, methyl; ester; (2) Methyl {3-(amino-oxoacetyl)-1-benzyl-2-ethyl-1*H*-indol-4-yl]oxy}acetate. *CAS*-172733-08-3. *Treatment of dyslipidemia*. \diamond A-002; LY333013; S-3013



Veltuzumab [2007] (vel tooz' ue mab). $C_{6458}H_{9918}N_{1706}O_{2026}S_{46}$. (1) Immunoglobulin G1, anti-(human CD20 (antigen)) (human-mouse monoclonal hA20 heavy chain), disulfide with human-mouse monoclonal hA20 κ -chain, dimer; (2) Immunoglobulin G1, anti-(human B-lymphocyte antigen CD20 (Membrane-spanning 4-domains subfamily A member 1, Leu-16, Bp35)); [218-arginine,360-glutamic acid,362-methionine]humanized mouse monoclonal hA20 γ 1 heavy chain (224-213')-disulfide with humanized mouse monoclonal hA20 κ light chain (230-230':233-233')-bisdissulfide dimer. Molecular weight is approximately 145,300 daltons. *CAS*-728917-18-8. INN. *Treatment of non-Hodgkin's lymphoma*. \diamond IMMU-106

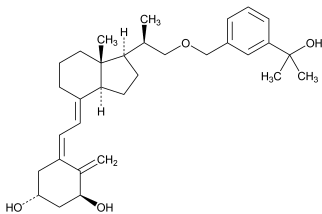
Revisions of United States Adopted Names (USAN)

The following are revisions of existing United States Adopted Names (USAN) and other names.

Atocalcitol

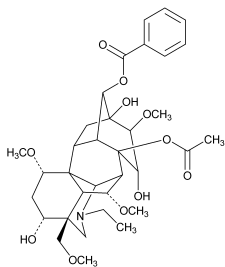
Change chemical name to read:

(1*S*,3*R*,5*Z*,7*E*,20*R*)-20-[3-(2-Hydroxypropan-2-yl)benzyloxymethyl]-9,10-secopregna-5,7,10(19)-triene-1*α*,3*β*-diol



Aconitine

Add structure, chemical name, chemical formula, and molecular weight:

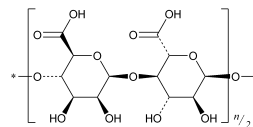


C₃₄H₄₇NO₁₁ 645.74

(1*α*,3*α*,6*α*,14*α*,15*α*,16*β*)-20-Ethyl-1,6,16-trimethoxy-4-(methoxymethyl)aconitane-3,8,13,14,15-pentol 8-acetate 14-benzoate

Alginate acid

Add structure, chemical name, and chemical formula:

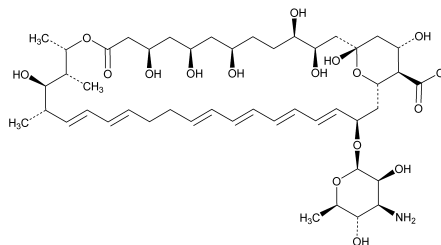


(C₆H₈O₆)_n

Alginate acid, Poly

Nystatin

Add structure, chemical names, chemical formula, and molecular weight:



C₄₇H₇₅NO₁₇ 926.09

Nystatin A

14,39-Dioxabicyclo[33.3.1]nonatriaconta-19,21,25,27,29,31-hexaene-36-carboxylic acid, 33-[(3-amino-3,6-dideoxy-β-D-mannopyranosyl)oxy]-1,3,4,7,9,11,17,37-octahydroxy-15,16,18-trimethyl-13-oxo- (1*S*,3*R*,4*R*,7*R*,9*R*,11*R*,15*S*,16*R*,17*R*,18*S*,19*E*,21*E*,25*E*,27*E*,29*E*,31*E*,33*R*,35*S*,36*R*,37*S*)- (1*S*,3*R*,4*R*,7*R*,9*R*,11*R*,15*S*,16*R*,17*R*,18*S*,19*E*,21*E*,25*E*,27*E*,29*E*,31*E*,33*R*,35*S*,36*R*,37*S*)- (1*S*,3*R*,4*R*,7*R*,9*R*,11*R*,15*S*,16*R*,17*R*,18*S*,19*E*,21*E*,25*E*,27*E*,29*E*,31*E*,33*R*,35*S*,36*R*,37*S*)-33-[(3-amino-3,6-dideoxy-β-D-mannopyranosyl)oxy]-1,3,4,7,9,11,17,37-octahydroxy-15,16,18-trimethyl-13-oxo-14,39-dioxabicyclo[33.3.1]nonatriaconta-19,21,25,27,29,31-hexaene-36-carboxylic acid

Proposed and Recommended International Nonproprietary Names

International Nonproprietary Names (INN) are devised by the World Health Organization (WHO).

Under its charter, the WHO is empowered simply to *recommend* specific actions or procedures to its Member States. This limitation is incorporated into the WHO program concerned with the selection of international nonproprietary names for pharmaceutical substances, in that the WHO first publishes the selected names as *proposals* ("Proposed International Nonproprietary Names"). A period of four months from the date of publication in *WHO Drug Information* is allowed for entering comments on, or objections to, any proposal on the part of

Member States or other interested parties. In general, an objection reflects a belief that the proposal concerned is confusingly close to (i.e., conflicts with) a name already in use, perhaps in only a restricted area in which the party has a proprietary interest in the form of trademark rights. In the event that no objection is received, the WHO proceeds with listing and publishing the names so devised as *recommendations* ("Recommended International Nonproprietary Names"), which many Member States then recognize as the sole or preferred nonproprietary name for use within their respective territories.

Proposed International Nonproprietary Names—List 99

The following 68 names have been selected by the World Health Organization (WHO) as Proposed International Nonproprietary Names.

This list, with chemical names or descriptions and the molecular formulae, appears in *WHO Drug Information*, Vol. 22, No. 2, 2008.

Suggested INN	Category	Suggested INN	Category
Aderbasib	<i>Antineoplastic</i>	Lensiprazine	<i>Antidepressant</i>
Adoprazine	<i>Antidepressant</i>	Levomefolic Acid	<i>Folic Acid Analogue</i>
Afutuzumab	<i>Immunomodulator</i>	Levomilnacipran	<i>Antidepressant</i>
Alipogene Tiparvovec	<i>Gene Therapy Product (In Lipoprotein Disorders)</i>	Linagliptin	<i>Antidiabetic</i>
Apricoxib	<i>Selective Cyclo-Oxygenase Inhibitor</i>	Lixisenatide	<i>Antidiabetic</i>
Bafetinib	<i>Antineoplastic</i>	Macitentan	<i>Endothelin Receptor Antagonist</i>
Bederocin	<i>Antibacterial</i>	Melogliptin	<i>Antidiabetic</i>
Befiradol	<i>Analgesic</i>	Mimopezil	<i>Acetyl Cholinesterase Inhibitor</i>
Bevasiranib	<i>Antineoplastic</i>	Mipomersen	<i>Antihypercholesterol Agent</i>
Catridecacog	<i>Blood Coagulation Factor</i>	Olesoxime	<i>Neurodegenerative Disorders</i>
Citatumumab Bogatox	<i>Antineoplastic</i>	Ombrabulin	<i>Antineoplastic</i>
Conatumumab	<i>Antineoplastic</i>	Otenabant	<i>Cannabinoid Receptor Antagonist</i>
Custirsen	<i>Antineoplastic</i>	Palifosfamide	<i>Antineoplastic</i>
Danusertib	<i>Antineoplastic</i>	Palovarotene	<i>Retinoid Acid Receptor Agonist</i>
Darotrium Bromide	<i>Anticholinergic</i>	Radezolid	<i>Antibacterial</i>
Demiditraz	<i>Acaricide (Veterinary Use)</i>	Rafivirumab	<i>Antiviral (Rabies Prophylaxy)</i>
Denenicokin	<i>Immunomodulator</i>	Retaspimycin	<i>Antineoplastic</i>
Derquantel	<i>Anthelmintic</i>	Saracatinib	<i>Antineoplastic</i>
Disitertide	<i>Transforming Growth Factor Beta-1 Inhibitor</i>	Semagacestat	<i>Gamma Secretase Inhibitor</i>
Drinabant	<i>Cannabinoid Receptor Antagonist</i>	Semuloparin Sodium	<i>Anticoagulant</i>
Dulanermin	<i>Antineoplastic</i>	Sivifene	<i>Antiestrogen</i>
Edoxaban	<i>Anti-thrombotic</i>	Talarozole	<i>Cytochrome P450 Cyp26 Inhibitor</i>
Elagolix	<i>Gnrh Antagonist</i>	Talmapimod	<i>Immunomodulator</i>
Elesclomol	<i>Antineoplastic (Adjunctive Agent)</i>	Tanezumab	<i>Analgesic</i>
Entinostat	<i>Antineoplastic</i>	Tasimeleone	<i>Melatonin Receptor Antagonist</i>
Eprotirome	<i>Antihyperlipidaemic</i>	Tasisulam	<i>Antineoplastic</i>
Esreboxetine	<i>Antidepressant</i>	Taspoglutide	<i>Antidiabetic</i>
Etaracizumab	<i>Antineoplastic</i>	Tecovirimat	<i>Antiviral</i>
Foravirumab	<i>Antiviral (Rabies Prophylaxy)</i>	Teneligliptin	<i>Antidiabetic</i>
Ibipinabant	<i>Cannabinoid Receptor Antagonist</i>	Tildipirosin	<i>Antibiotic</i>
Inolitazone	<i>Antineoplastic</i>	Tosedostat	<i>Antineoplastic</i>
Lancovutide	<i>Expectorant (In Cystic Fibrosis)</i>	Troplasmafinogen Alfa	<i>Fibrinolytic And Thrombolytic</i>
Larazotide	<i>Zonulin Antagonist (In Celiac Disease)</i>	Ustekinumab	<i>Immunomodulator</i>
		Vadimezan	<i>Antineoplastic (Adjunctive Agent)</i>
		Velneperit	<i>Neuropeptide Y Receptor Antagonist</i>

Recommended International Nonproprietary Names—List 60

The following 77 names have been selected by the World Health Organization (WHO) as Recommended International Nonproprietary

Names. This list, with chemical names or descriptions and the molecular formulae, appears in *WHO Drug Information*, Vol. 22, No. 3, 2008.

Adiplon
Agatolimod
Alacizumab Pegol
Aleplasinin
Almorexant
Amolimogene Bepiplasmid
Amsilarotene
Anacetrapib
Anrukizumab
Baminercept
Bentamapimod
Berubicin
Besifloxacin
Betrixaban
Briobacept
Cabazitaxel
Cariprazine
Carmegliptin
Cobiprostone
Conestat Alfa
Dacetuzumab
Daporinad
Darinaparsin
Dexneбиволол
Emricasan
Eribaxaban
Ezatiostat
Fasobegron
Favipiravir
Fermagate

Flopristin
Folitixorin
Ibodutant
Imeglimin
Laromustine
Levoneбиволол
Linopristin
Lucatumumab
Milatuzumab
Mirabegron
Monepantel
Nelivaptan
Nesbuvir
Odanacatib
Omacetaxine Mepesuccinate
Otelixizumab
Pegloticase
Preladenant
Radiprodil
Remogliflozin Etabonate
Retosiban
Riociguat
Rolofylline
Tenatumomab
Tertomotide
Tigatuzumab
Velaglucerase Alfa
Veltuzumab
Viquidacin