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# Guidance for Industry

## Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing

**U.S. Department of Health and Human Services  
Food and Drug Administration  
Office of the Commissioner**

**December 2008  
Electronic Submission**

# Guidance for Industry Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
Office of the Commissioner**

**December 2008  
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## Guidance for Industry<sup>1</sup>

115

### Providing Regulatory Submissions in Electronic Format –

116

### Drug Establishment Registration and Drug Listing

117

118 This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It  
119 does not create or confer any rights for or on any person and does not operate to bind FDA or the public.  
120 You can use an alternative approach if the approach satisfies the requirements of the applicable statutes  
121 and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for  
122 implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate  
123 number listed on the title page of this guidance.

124

125

#### 126 I. INTRODUCTION

127

128 This is one in a series of guidance documents intended to assist persons making regulatory  
129 submissions to FDA in electronic format. This guidance is designed to assist manufacturers with  
130 electronic submissions of drug establishment registration and drug listing information. The  
131 guidance and accompanying technical documents explain:

- 132 • The statutory requirement to submit electronically drug establishment registration and  
133 drug listing information;
- 134 • How to create a Structured Product Labeling (SPL)<sup>2</sup> file for submitting drug  
135 establishment registration and drug listing information to FDA through the Electronic  
136 Submissions Gateway (ESG) using defined code sets and codes, i.e., a language  
137 recognized by the computer system; and
- 138 • On June 1, 2009, FDA will no longer accept registration and listing information in paper  
139 format unless a waiver is granted.

140 FDA intends to update these documents regularly to reflect the evolving technology and user  
141 experience.

142

143 FDA's guidance documents, including this guidance, do not establish legally enforceable  
144 responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should  
145 be viewed only as recommendations, unless specific regulatory or statutory requirements are  
146 cited. The use of the word *should* in Agency guidances means that something is suggested or  
147 recommended, but not required.

148

149

#### 150 II. BACKGROUND

151

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17<sup>1</sup> The Office of Critical Path Programs, Office of the Commissioner, Food and Drug Administration prepared this  
18 guidance document in cooperation with the Center for Drug Evaluation and Research, the Center for Biologics  
19 Evaluation and Research, and the Center for Veterinary Medicine.

20

21<sup>2</sup> SPL standard is a Health Level Seven, Inc. standard for the exchange of product information using extensible  
22 markup language (XML).

152 Requirements for drug establishment registration and drug listing are set forth in section 510 of  
 153 the Federal Food, Drug, and Cosmetic Act (the Act) and section 351 of the Public Health Service  
 154 Act (the PHS Act), and 21 CFR Part 207.<sup>3</sup> Fundamental to FDA's mission to protect the public  
 155 health is the collection of this information, which is used for important activities such as  
 156 postmarket surveillance for serious adverse drug reactions, inspection of drug manufacturing and  
 157 processing facilities, and monitoring of drug products imported into the United States.  
 158 Comprehensive, accurate, and up-to-date information is critical to conducting these activities  
 159 with efficiency and effectiveness.

160

161 Section 510 of the Act and 21 CFR part 207, subject to certain limited exceptions, require  
 162 establishment owners and operators (registrants) upon first engaging in the manufacture,  
 163 preparation, propagation, compounding, or processing of drugs, (including human drugs,  
 164 veterinary drugs, and biological drug products<sup>4</sup>) to register their establishments and submit  
 165 listing information for all drugs and biological drug products in commercial distribution.  
 166 Registrants are also required to submit updates to registration information for their  
 167 establishments annually on or before December 31.<sup>5</sup> At the time of registration, registrants must  
 168 also submit required listing information.<sup>6</sup> Additionally, registrants are required to update listing  
 169 information in June and December of each year to include information for drugs and biological  
 170 drug products that have not been previously listed.<sup>7</sup> Certain changes to information for  
 171 previously listed drugs and biological drug products must also be submitted every June and  
 172 December.<sup>8</sup>

173

174 Changes in the Act, resulting from the Food and Drug Administration Amendments Act of 2007  
 175 (Public Law 110-85) (FDAAA),<sup>9</sup> require that drug establishment registration and drug listing  
 176 information be submitted electronically unless a waiver is granted. Before FDAAA was enacted,  
 177 section 510(p) of the Act expressly provided that drug establishment registration information be  
 178 submitted electronically, based on a finding that electronic receipt was feasible, and section  
 179 510(j) of the Act stipulated that drug listing information be submitted in the form and manner  
 180 prescribed by FDA. Section 224 of FDAAA, which amends section 510(p) of the Act, now  
 181 expressly requires electronic drug listing in addition to drug establishment registration.

---

27<sup>3</sup> This guidance document does not apply to establishment registration and product listing information required  
 28 solely under 21 CFR part 607 (Blood and Blood Products), 21 CFR 807 (Devices), and 21 CFR part 1271 (Human  
 29 Cells, Tissues, and Cellular and Tissue-Based Products).

30

31<sup>4</sup> Under section 351(j) of the PHS Act, the Act and regulations promulgated under the Act apply to biological drug  
 32 products except that new Drug Applications (NDAs) are not required for products licensed under section 351(a) of  
 33 the PHS Act.

34

35<sup>5</sup> Section 510(b)(1) of the Act.

36

37<sup>6</sup> Section 510(j)(1) of the Act.

38

39<sup>7</sup> Section 510(j)(2)(A) of the Act.

40

41<sup>8</sup> Section 510(j)(2) of the Act.

42

43<sup>9</sup> Signed into law on September 27, 2007.

44

182 Paper-based drug establishment registration and drug listing information have, until now, been  
 183 submitted using Form FDA 2656 (Registration of Drug Establishment/Labeler Code  
 184 Assignment), Form FDA 2657 (Drug Product Listing), and Form FDA 2658 (Registered  
 185 Establishments' Report of Private Label Distributors).<sup>10</sup> Moving from a paper-based format to  
 186 an electronic system will improve the timeliness and accuracy of the submissions. FDA is  
 187 providing a transition period until June 1, 2009, to enable industry to begin submitting drug  
 188 establishment registration and drug listing information electronically.

189

190 FDA is adopting the use of extensible markup language (XML) files in a standard SPL format  
 191 for the exchange of drug establishment registration and drug listing information (including  
 192 labeling as specified under 21 CFR 207.25). The automated submission process functions most  
 193 efficiently and effectively when this information is provided in a standardized format with  
 194 defined code sets and codes. This guidance and accompanying technical documents describe  
 195 how to make these submissions using the SPL format, which FDA can process, review, and  
 196 archive.<sup>11</sup> Information in a properly created and complete SPL file can be processed in minutes  
 197 and allows for greater precision and accuracy through the use of coded data fields rather than just  
 198 electronic text. Timely and accurate information will enhance FDA's efforts to help ensure the  
 199 integrity of the drug supply and protect public health.

200

201 Technical specifications are provided in the following technical documents, which can be found  
 202 on the FDA Data Standards Council website: <http://www.fda.gov/oc/datacouncil/spl.html> and are  
 203 discussed in section IV:

- 204 • *Structured Product Labeling Implementation Guide for FDA Drug Establishment*
- 205 *Registration and Drug Listing*
- 206 • *Step-by-Step Instructions for Creating Structured Product labeling (SPL) Files for Drug*
- 207 *Establishment Registration and Drug Listing*
- 208 • *Structured Product Labeling Validation Procedures for Drug Establishment Registration*
- 209 *and Drug Listing*

210

211 FDA issued a proposed rule that would amend 21 CFR part 207 to require electronic submission  
 212 of drug establishment registration and drug listing information, among other provisions such as  
 213 certain changes to the National Drug Code system and requiring the appropriate NDC on the  
 214 drug label (71 FR 51276, August 29, 2006). FDA is considering comments submitted on the  
 215 proposed rule and intends to revise, reissue, or revoke this guidance document as appropriate to  
 216 make it consistent with the final rule, when the rule is issued.

217

218

### 219 III. DRUG ESTABLISHMENT REGISTRATION AND DRUG LISTING

#### 220 INFORMATION FOR ELECTRONIC SUBMISSION

221

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49<sup>10</sup> These forms are currently available at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

50

51<sup>11</sup> When we are ready to receive a particular submission type in electronic format only, we generally identify the  
 52 specific type of document that FDA can adequately process, review, and archive. This information can be found in  
 53 the public docket 92S-0251 at [regulations.gov](http://www.regulations.gov). (21 CFR part 11) See also *Guidance for Industry: Part 11,*  
 54 *Electronic Records; Electronic Signatures -- Scope and Application* (August 2003).

55

222The following information should be submitted to FDA in the SPL file format using the defined  
223code sets and codes as described in section IV of this document.

224

225 **A. Drug Establishment Registration**

226

227 1. *Who must register and when?*

228The owner or operator of an establishment entering into the manufacture, preparation,  
229propagation, compounding, or processing (which includes, among other things, repackaging and  
230relabeling) of a drug or drugs<sup>12</sup> and not exempt under section 510(g) of the Act or subpart B of  
23121 CFR part 207, must register the establishment with FDA within 5 days after beginning the  
232operation (21 CFR 207.21(a)). Alternatively, if the establishment has not previously entered into  
233such an operation, the owner or operator must register within 5 days after submitting a drug  
234application, biological license application, or medicated feed mill license application. Owners or  
235operators must renew their registration information annually (21 CFR 207.21(a)).

236Foreign establishments that engage in the manufacture, preparation, propagation, compounding,  
237or processing (which includes, among other things, repackaging and relabeling) of a drug that is  
238imported or offered for import into the United States (and that are not exempt) must upon first  
239engaging in such activity immediately register and register annually thereafter (see section 510(i)  
240of the Act and 21 CFR 207.40).

241Amendments to drug establishment registration must be submitted in accordance with 21 CFR  
242207.26.

243 2. *What information is required for drug establishment registration?*

244

245Under 21 CFR 207.25, drug establishment registration information has historically been  
246submitted on Form FDA 2656. Section 510 of the Act and 21 CFR Part 207 set forth the  
247registration information required to be submitted by domestic and foreign drug establishments  
248(see sections 510(b), (c), (d), and (i) of the Act and 21 CFR 207.22(a), 207.25(a), 207.26, and  
249207.40).

250

251Under 21 CFR 207.40(c), foreign registrants must provide certain additional information specific  
252to their establishments. For example:

- 253 • The name, address, and phone number of the foreign registrant's United States agent, and
- 254 • Under section 510(i)(1)(A) of the Act, the name of each importer that is known to the
- 255 establishment (this means each U.S. company or individual in the United States that is an
- 256 owner, consignee, or recipient, of the foreign establishment's drug, that is imported into
- 257 the United States. An importer does not include the consumer or patient who ultimately
- 258 purchases, receives, or is administered the drug, unless the foreign establishment ships
- 259 the drug directly to the consumer or patient.); and the name of each person who imports
- 260 or offers for import (this means the name of each agent, broker, or other entity, other than
- 261 a carrier, that the foreign drug establishment uses to facilitate the import of their drug into
- 262 the United States).

263

---

60<sup>12</sup> Means both human, including biological drug products, and animal drugs.



264 To facilitate correspondence between registrants and FDA, foreign registrants should submit the  
 265 email address for the U.S. agent, and the telephone number(s) and email address for the importer  
 266 and person who imports or offers for import described in section III.A.2 of this document.

267

268 Section 510(p) of the Act, as amended by FDAAA, now requires drug establishment  
 269 registrations to be submitted electronically unless a waiver is granted. Therefore, the  
 270 information previously submitted using Form FDA 2656 and the information required under 21  
 271 CFR 207.40(c) is now submitted electronically using SPL files with coded data fields.

272

273 Failure to register in accordance with section 510 of the Act is a prohibited act under section  
 274 301(p) of the Act. Failure to comply with section 510 of the Act renders drugs misbranded under  
 275 section 502(o) of the Act.

276

277 *3. What additional information is recommended?*

278

279 Registrants have also voluntarily submitted additional drug establishment registration  
 280 information on Form FDA 2656. For electronic submission, registrants are encouraged to also  
 281 submit the following information in their SPL file:

- 282 • Official contact's name, mailing address, telephone number(s), and email address;
- 283 • Each registered establishment's telephone number(s); and
- 284 • The type of operation(s) performed at each registered establishment.

285

## 286 **B. Drug Listing**

287

288 *1. Who must list and when?*

289

290 Registrants, which do not include those exempt under 21 CFR 207.10, must submit the initial  
 291 listing information for all drugs<sup>13</sup> in commercial distribution at the time of their initial  
 292 registration of their establishment(s) (21 CFR 207.21(a)).

293

294 Although FDA does not accept drug establishment registration information from private label  
 295 distributors, private label distributors may request their own NDC Labeler Code and elect to  
 296 submit drug listing information to FDA (21 CFR 207.20(b)). In such instances, at the time of  
 297 submitting or updating drug listing information, private label distributors must certify to the  
 298 registered establishment(s) that manufactured, prepared, propagated, compounded or processed  
 299 (which includes, among other things, repackaging and relabeling) the listed drug(s) that the drug  
 300 listing submission was made (21 CFR 207.20(b)). The certification to the registered  
 301 establishment by the private label distributor may be satisfied using paper forms.

302

303 Registrants (and, if applicable, private label distributors) must update their drug listing  
 304 information, and include drugs that have been introduced for commercial distribution and have  
 305 not previously been listed.<sup>14</sup> Any updates must be submitted every June and December.<sup>15</sup>

65<sup>13</sup> Includes combination products and their constituents (see 21 CFR part 3).

66

67<sup>14</sup> Section 510(j)(2) of the Act.

68

69<sup>15</sup> Section 510(j)(2) of the Act.

306 However, registrants (and, if applicable, private label distributors) are encouraged to submit  
 307 updates through the registration and listing system more frequently as a change occurs, including  
 308 updates to labeling required to be submitted. (21 CFR 207.21(b), 207.22(b), 207.25, and 207.30)  
 309

310 2. *What information is required for drug listing?*

311

312 Under 21 CFR 207.25, listing information has historically been submitted on Forms FDA 2657  
 313 and FDA 2658. Section 510 of the Act and 21 CFR Part 207 set forth the drug listing  
 314 information required to be submitted by domestic and foreign drug establishments (see section  
 315 510(j) of the Act and 21 CFR 207.25(b) and (c), 207.30, 207.31, and 207.40). However, if the  
 316 carton and container labels required under 21 CFR 207.25(b) and 207.40 are submitted with a  
 317 marketing<sup>16</sup> application, it is not necessary to resubmit the carton and container labels when  
 318 listing a human prescription drug.

319

320 Section 510(p) of the Act, as amended by FDAAA, now requires drug listing, including updates,  
 321 to be submitted electronically unless a waiver is granted. Therefore, the information previously  
 322 submitted using Form FDA 2657 and FDA 2658 is now submitted electronically using SPL files  
 323 with coded data fields.

324

325 Registrants and private label distributors can consult the National Drug Code Directory for all  
 326 drug products listed with FDA. The registrant and private label distributor must provide  
 327 complete and accurate information to be listed in the directory. If the drug product does not  
 328 appear in the directory, FDA will not consider the drug product listed. This directory is available  
 329 at the Data Standards Council website.

330

331 3. *What additional information is recommended?*

332

333 a. *Additional information on Form FDA 2657*

334

335 Registrants and, if applicable, private label distributors have also voluntarily submitted  
 336 additional drug listing information on Form FDA 2657 and Form FDA 2658. For electronic  
 337 submission, registrants are encouraged to submit the following information in their SPL file:

- 338 • Name of establishment(s) manufacturing or processing the listed drug and the type of
- 339 operation(s) performed;
- 340 • DEA schedule;
- 341 • Route(s) of administration;
- 342 • Inactive ingredients and strength or amount;
- 343 • Marketing information (e.g., category, start/stop date);
- 344 • Information related to the application or OTC monograph citation number (e.g., type and
- 345 year of approval); and
- 346 • Package size and type.

347

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74

75<sup>16</sup> New Drug Application (NDA), Biologics License Application (BLA), Abbreviated New Drug Application  
 76 (ANDA), New Animal Drug Application (NADA), and Abbreviated New Animal Drug Application (ANADA).

79

***Contains Nonbinding Recommendations***

80

348           b.       Manufacturer’s Information for Voluntary Reporting of Adverse Drug  
349                       Reactions

350

351 In providing the labeling as specified under 21 CFR 207.25, FDA recommends for  
352 manufacturers with a Web site for voluntary reporting of adverse drug reactions that the  
353 registrant provide the manufacturer’s telephone number and URL address that appears on the  
354 label (21 CFR 201.57(a)(11)).

355

356           c.       Site-specific D-U-N-S® Number<sup>17</sup>

357

358 FDA recommends that the D-U-N-S® Number (as described in section V.B.2 of this document)  
359 should be submitted for each site-specific entity (e.g., the registrant, establishments, U.S. agent,  
360 importer). Submitting the site-specific D-U-N-S® Number for an entity would provide by  
361 reference to the number certain business information for that entity, e.g., trade names used by the  
362 entity, addresses, additional ownership information, such as the name of each partner or the  
363 name of each corporate officer and director, and the state of incorporation otherwise required for  
364 drug establishment registration.

365

366           d.       NDC Product Code for a Source Drug Repacked or Relabeled

367

368 Repackers and relabelers may submit the NDC Product Code for the source drug that is repacked  
369 or relabeled to reference previously submitted manufacturing establishment information.

370

371           e.       Reference Drug

372

373 In rare situations, the strength of the drug is based on a reference drug. In such cases, the  
374 registrant (and, if applicable, private label distributor) are encouraged to include the reference  
375 drug used as a basis for the strength of the listed drug to avoid confusion.

376

377           g.       Distinctive Characteristics of Certain Listed Drugs

378

379 Registrants are encouraged to provide the following characteristics for the listed drug, when  
380 applicable. Registrants have previously provided these characteristics voluntarily as helpful  
381 information to the public for the safe and effective use of their products.

382

383                       •   Flavor

384

385 When applicable, the registrants (and, if applicable, private label distributor) may provide the  
386 flavor as a unique distinguishing characteristic of the listed drug. (Registrants have previously  
387 provided this information on Form FDA 2657 as an ingredient.)

388

389                       •   Color

390

---

81<sup>17</sup> D-U-N-S® Numbers are proprietary to and controlled by Dun & Bradstreet (D&B). D&B grants a customer a  
82 non-exclusive, perpetual, limited license to use D-U-N-S® Numbers solely for identification purposes and only for  
83 the customer’s internal business use. Where practicable, the customer will refer to the number as a “D-U-N-S®  
84 Number” and state that D-U-N-S is a registered trademark of D&B.

391For liquid dosage forms, the registrant (and, if applicable, private label distributor) may provide  
392the color as a unique distinguishing characteristic. This may be useful when the color of a  
393solution is confused for contamination or a change in color may indicate contamination.

394

395

- Image

396

397For solid oral dosage forms, the registrant (and, if applicable, private label distributor) may  
398submit an image of the actual dosage form. This information is helpful to the consumer in  
399determining the correctly dispensed drug. The registrant should obtain instructions on obtaining  
400the image and the proper format in the SPL file by following the instructions for technical  
401assistance in section V.D of this document.

402

403

- h. Confidentiality Flag

404

405Registrants (and, if applicable, private label distributor) may identify an inactive ingredient or  
406the registrant's business relationship with an establishment that they view as confidential when  
407submitting registration and listing information. Pursuant to a Freedom of Information Act  
408request or on our own initiative, FDA will ultimately make determinations as to whether drug  
409establishment registration and drug listing information can be disclosed to the public pursuant to  
410the Trade Secrets Act, the Freedom of Information Act, and other applicable law (e.g., section  
411510(f) of the Act and 21 CFR 207.37).

412

413

414

#### 415**IV. CREATING THE DRUG ESTABLISHMENT REGISTRATION AND DRUG** 416**LISTING FILE FOR ELECTRONIC SUBMISSION**

417

418

##### **A. Structured Product Labeling**

419

420SPL is the standard that is used for the exchange of drug establishment registration and drug  
421listing information and is based on the Health Level Seven (HL7) version 3 Reference  
422Information Model (RIM) and the Clinical Document Architecture (CDA).

423

424FDA is using SPL release 4 (SPLr4) for electronic submissions of drug establishment  
425registration and drug listing information. The technical details on using SPLr4 for registration  
426and listing are available in the document *Structured Product Labeling Implementation Guide for*  
427*FDA Drug Establishment Registration and Drug Listing* (SPL Implementation Guide).

428

429FDA has been accepting SPL files for certain product information since 2004, and vendors have  
430provided solutions for creating SPL files ranging from basic software tools to comprehensive  
431information management systems. Additionally, FDA has collaborated with GlobalSubmit on  
432software to create SPL files based on XForms technology. Information on using the XForms is  
433available in the document *Step-by-Step Instructions for Creating Structured Product Labeling*  
434*(SPL) Files for Drug Establishment Registration and Drug Listing*.

435

436These documents are on the FDA Data Standards Council website.

438 **B. Code Sets and Codes**

440As previously described, code sets and codes are used as a language that is recognized by a  
 441computer system. FDA has been working with a number of organizations to develop and  
 442maintain such code sets and codes used for submitting drug establishment registration and drug  
 443listing information electronically. Although many code sets and codes are already available at  
 44421 CFR 207.3 and the Data Standards Council website, FDA is continuously updating these  
 445codes sets and adding additional codes. Information on the organizations that maintain the code  
 446sets for submitting drug establishment registration and drug listing information electronically and  
 447how to obtain the code sets and codes used for electronic drug registration and listing follows.

449 *1. Unique Identifiers (UNII)*

451UNII is the defined code FDA uses for ingredients. FDA along with United States Pharmacopeia  
 452(USP) maintains the UNII using the FDA Substance Registration System. These names and  
 453identifiers are accessible through USP website at <http://www.usp.org> and publications, the Data  
 454Standards Council website and the NCI Thesaurus website at <http://evs.nci.nih.gov>. Additional  
 455ingredient identifiers may be requested through FDA by sending a request to [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov).  
 456In submitting your request, identify in the subject line of the email the Center responsible for  
 457regulating the listed drug, i.e., Center for Drug Evaluation and Research, Center for Biologics  
 458Evaluation and Research, or the Center for Veterinary Medicine.

460 *2. Data Universal Numbering System (D-U-N-S®) Number*

462Dun & Bradstreet assigns and maintains a database of the D-U-N-S® Numbers, which serve as  
 463unique identifiers (code) of business entities. Upon application, each business entity (e.g.,  
 464registrant, establishment, importer, US agent) is assigned a distinct site-specific 9-digit D-U-N-  
 465S® Number. If the D-U-N-S® Number for a location has not been assigned, a business may  
 466obtain one for no cost directly from Dun & Bradstreet (<http://www.dnb.com>).

468 *3. Other code sets*

470FDA collaborates with the National Cancer Institute Enterprise Vocabulary Services (NCI EVS)  
 471to maintain code sets for dosage form, routes of administration, package types, DEA schedule,  
 472product color, product shape, flavors, business operations, marketing categories and equivalence  
 473codes. These code sets are located in the NCI Thesaurus and may be accessed through the NCI  
 474EVS website at <http://evs.nci.nih.gov> and the Data Standards Council website. Additional code  
 475sets and codes for use in registration and listing may be requested though FDA by sending a  
 476request to [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov).

478The Regenstrief Institute<sup>18</sup> maintains a number of different code sets used in electronic drug  
 479establishment registration and drug listing including: document types, section headings, and units  
 480of measure. These code sets are located in the Logical Observation Identifiers Names and Codes

---

93<sup>18</sup> The Regenstrief Institute is an internationally recognized informatics and healthcare research organization.

481(LOINC) and Unified Codes for Units of Measure (UCUM) systems. Both of these  
 482terminologies are available at <http://www.regenstrief.org> and at other locations. Additional code  
 483sets and codes may be requested through FDA by sending a request to [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov)  
 484following the instructions in section IV.D of this document.

485

486 **C. Submission and FDA Validation of Electronic Drug Establishment**  
 487 **Registration and Drug Listing Information**

488

489The SPL file should be created following the technical specifications in the SPL Implementation  
 490Guide and other information found in this document. Other resources for creating the SPL file,  
 491including a link to a user-friendly software tool (XForms), are also available.<sup>19</sup> Once the SPL  
 492file is created, it can then be submitted (uploaded) by following the instructions for the FDA  
 493Electronic Submissions Gateway (ESG), including digital certification.<sup>20</sup>

494

495FDA uses a computer system for processing the SPL files using controlled code sets and codes.  
 496The computer system automatically checks the SPL files for certain errors, mistakes and  
 497omissions prior to entering the information into FDA systems. FDA will work with companies  
 498to help correct identified problems in order to complete the registration and listing process.  
 499Information on the details used in checking SPL files for electronic drug establishment  
 500registration and drug listing are in the document *FDA's Structured Product Labeling Validation*  
 501*Procedures for Electronic Drug Establishment Registration and Drug Listing*.<sup>21</sup> This document  
 502is on the Data Standards Council website.

503

504 **D. Technical Assistance**

505

506For technical problems or questions, or technical assistance with creating SPL files, send an  
 507email to [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov). In submitting a request, identify in the subject line of the email the  
 508Center responsible for regulating the listed drug, i.e., Center for Drug Evaluation and Research,  
 509Center for Biologics Evaluation and Research, or Center for Veterinary Medicine.

510

511

512**V. IMPLEMENTATION**

513

514During the transition period, i.e., until June 1, 2009, FDA intends to continue to accept paper  
 515forms. During the transition period, the registrant should submit the drug establishment  
 516registration and drug listing information either electronically or using the Forms FDA 2656,  
 517FDA 2657, and FDA 2658, but not both.

518

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99<sup>19</sup> See <http://www.fda.gov/oc/datacouncil/spl.html> for additional resources, terminology, and data standards  
 100regarding the SPL files. See <http://www.fda.gov/oc/datacouncil/xforms.html> for information on the user-friendly  
 101software tool.

102

103<sup>20</sup> See <http://www.fda.gov/esg/default.htm> for information on other resources and using the FDA ESG.

104

105<sup>21</sup> This document is used by FDA and describes FDA's computer instructions for automating the validation of  
 106submitted SPL files containing registration and listing information.

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110

*Contains Nonbinding Recommendations*

111

519

**520VI. WAIVER REQUEST**

521

522 Under section 510(p) of the Act, registrations and listings (including the submission of updated  
523 information) must be submitted electronically unless FDA grants a waiver of such requirement  
524 because use of electronic means is not reasonable for the person requesting such waiver. FDA  
525 does not anticipate many instances in which electronic submission of registration and listing  
526 information will not be reasonable for the person requesting the waiver. If you are granted a  
527 waiver, you will be instructed as to how to submit the registration and listing information.

528

529 To apply for a waiver, submit a written request with a complete explanation of why you cannot  
530 submit your registration and listing information electronically to:

531

532 SPL Coordinator

533 U.S. Food and Drug Administration (HF-18)

534 5600 Fishers Lane

535 Rockville, MD 20857-0001

536

537 Phone: 1-888-463-6332

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540

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***Contains Nonbinding Recommendations***

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542/home/ec2-user/sec/disk/omb/icr/201203-0910-007/doc/31374801

543

544Revised: McKeever 10/15/08

545Comments: Levin, Smith 10/18/08

546Revised: McKeever 10/20/08

547Comments: Behrman 10/28/08

548Edited: Falvey 10/29/08

549Comments: CDER, CBER, CVM 1/21/08

550