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# **Guidance for Industry**

## **Providing Regulatory Submissions in Electronic Format — General Considerations**

### ***DRAFT GUIDANCE***

**This guidance document is being distributed for comment purposes only.**

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Biologic Evaluation and Research (CBER)  
Center for Drug Evaluation and Research (CDER)  
Center for Devices and Radiological Health (CDRH)  
Center for Food Safety and Applied Nutrition (CFSAN)  
Center for Veterinary Medicine (CVM)**

**October 2003  
Electronic Submissions  
Revision 1**

# Guidance for Industry

## Providing Regulatory Submissions in Electronic Format — General Considerations

*Additional copies are available at:*

<http://www.fda.gov/cder/guidance/index.htm>

or

<http://www.fda.gov/cber/guidelines.htm>

or

<http://www.fda.gov/cvm/guidance/guidance.html>

or

<http://www.cfsan.fda.gov/~dms/guidance.html>

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## TABLE OF CONTENTS

<b>I. INTRODUCTION.....</b>	<b>1</b>
<b>II. BACKGROUND .....</b>	<b>2</b>
<b>III. HOW DO ELECTRONIC SUBMISSIONS RELATE TO 21 CFR PART 11? .....</b>	<b>2</b>
<b>IV. WHAT FILE FORMATS SHOULD I USE FOR ELECTRONIC DOCUMENTS? .....</b>	<b>2</b>
<b>A. Version.....</b>	<b>3</b>
<b>B. Fonts.....</b>	<b>3</b>
<b>C. Page Orientation.....</b>	<b>4</b>
<b>D. Page Size and Margins .....</b>	<b>5</b>
<b>E. Source of Electronic Document.....</b>	<b>5</b>
<b>F. Methods for Creating PDF Documents and Images.....</b>	<b>5</b>
<b>G. Hypertext Linking and Bookmarks .....</b>	<b>6</b>
<b>H. Page Numbering .....</b>	<b>7</b>
<b>I. Document Information Fields .....</b>	<b>8</b>
<b>J. Open Dialog Box.....</b>	<b>8</b>
<b>K. Naming PDF Files.....</b>	<b>8</b>
<b>L. Security.....</b>	<b>8</b>
<b>M. Indexing PDF Documents .....</b>	<b>8</b>
<b>N. Plug Ins .....</b>	<b>9</b>
<b>V. WHAT FILE FORMATS SHOULD I USE FOR ELECTRONIC DATASETS? .....</b>	<b>9</b>
<b>A. SAS System XPORT Transport Format (Version 5 SAS Transport Format).....</b>	<b>9</b>
<b>B. XML.....</b>	<b>11</b>
<b>C. SGML.....</b>	<b>11</b>
<b>D. Molfiles.....</b>	<b>12</b>
<b>VI. WHAT ARE THE PROCEDURES FOR SENDING ELECTRONIC SUBMISSIONS FOR ARCHIVE? .....</b>	<b>12</b>
<b>A. Electronic Transmission.....</b>	<b>12</b>
<b>B. Physical Media.....</b>	<b>13</b>
<b>VII. WHAT IF I HAVE A QUESTION?.....</b>	<b>16</b>
<b>A. CBER .....</b>	<b>16</b>
<b>B. CDER.....</b>	<b>16</b>

C. CDRH.....	16
D. CFSAN.....	16
E. CVM.....	16
<b>APPENDIX A: ADDITIONAL INFORMATION ON PROVIDING ELECTRONIC SUBMISSIONS ON PHYSICAL MEDIA .....</b>	<b>17</b>



## *Contains Nonbinding Recommendations*

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41 cited. The use of the word *should* in Agency guidances means that something is suggested or  
42 recommended, but not required.

43  
44

### 45 **II. BACKGROUND**

46

47 In the *Federal Register* of March 20, 1997 (62 FR 13430), the FDA published the Electronic  
48 Records; Electronic Signatures regulation (21 CFR part 11). This regulation provides, among  
49 other things, for the voluntary submission of parts or all of records in electronic format without  
50 an accompanying paper copy under certain circumstances. In January 1999, the Center for  
51 Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research  
52 (CDER) finalized a joint guidance document on general considerations for electronic  
53 submissions. They also published guidance documents describing how to provide marketing  
54 applications to each center. Following publication of these guidance documents, a working  
55 group was formed with the CBER, CDER, Center for Devices and Radiological Health (CDRH),  
56 the Center for Food Safety and Applied Nutrition (CFSAN), and the Center for Veterinary  
57 Medicine (CVM) to coordinate electronic submission activity. The efforts of this working group  
58 have resulted in this draft guidance, which updates the 1999 general considerations guidance  
59 document.

60

61 The Agency envisions a series of guidance documents on electronic regulatory submissions. As  
62 individual documents are completed, they will be issued first in draft for comment, then finalized  
63 and added to the series. The guidances will be updated regularly to reflect the continuously  
64 evolving nature of the technology and experience of those using this technology.

65

66

### 67 **III. HOW DO ELECTRONIC SUBMISSIONS RELATE TO 21 CFR PART 11?**

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69 FDA's part 11 regulations (21 CFR part 11), among other things, set forth the criteria under  
70 which records submitted to FDA may be submitted in electronic format in place of paper.  
71 Section 11.2(b) states that, for records submitted to the Agency, persons may use electronic  
72 records in lieu of paper records, in whole or part, provided the requirements of part 11 are met  
73 and the documents or parts of documents to be submitted have been identified by the Agency in  
74 public docket No. 92S-0251 as being the type of submission the Agency is prepared to accept in  
75 electronic format.<sup>2</sup>

76

77

### 78 **IV. WHAT FILE FORMATS SHOULD I USE FOR ELECTRONIC DOCUMENTS?**

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80 Documents submitted in electronic format should:

81

- 82 • Enable the user to easily view a clear and legible copy of the information

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<sup>2</sup> For a discussion of the Agency's perspectives on 21 CFR part 11, see the guidance for industry *Part 11, Electronic Records; Electronic Signatures — Scope and Application*, which issued in September 2003.

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- 84 • Enable the user to print each document page by page, as it would have been  
85 provided in paper, maintaining fonts, special orientations, table formats, and page  
86 numbers
- 87
- 88 • Include a well-structured table of contents and allow the user to navigate easily  
89 through the submission
- 90
- 91 • Allow the user to copy text, images and data electronically into other common  
92 software formats.
- 93

94 To achieve the above goals, you should submit all electronic documents in portable document  
95 format (PDF). We are prepared to archive documents provided as PDF files. PDF is an open,  
96 published format created by Adobe Systems Incorporated (<http://www.adobe.com>). You do not  
97 need to use a product from Adobe or from any specific company to produce your PDF  
98 documents. PDF has been accepted as a standard for providing documents in electronic format  
99 by the International Conference on Harmonisation (ICH).

100  
101 The following will help you create PDF files that we can review and archive.

### **A. Version**

102  
103  
104  
105 We should be able to read all PDF files with Acrobat Reader version 4.0, and above, with  
106 the search plug in. We should not need any additional software to read and navigate the  
107 PDF files.

### **B. Fonts**

108  
109  
110  
111 PDF viewing software automatically substitutes a font to display text if the font used to  
112 create the text is unavailable on the reviewer's computer. In some cases, font substitution  
113 can occur even when the fonts are available. For example, Helvetica or Times are  
114 substituted even if available on the reviewer's computer. Font substitution can affect a  
115 document's appearance and structure, and in some cases it can affect the information  
116 conveyed by a document. We cannot guarantee the availability of any one font.

117 Therefore, you should embed all fonts you are using in the PDF files to ensure that those  
118 fonts will always be available to the reviewer. When embedding fonts, all characters for  
119 the font should be embedded, not just a subset of the fonts being used in the document.

120  
121 However, font embedding does not solve the problems that occur when a reviewer tries to  
122 paste text from a PDF document into another software format. If the font is not available  
123 on the reviewer's computer, font substitution results even if the fonts are embedded. For  
124 this reason, we ask that you restrict the fonts used in documents to one of the following  
125 fonts listed in Table 1. We still ask that you embed the fonts so they are available for  
126 printing older archival files.

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**Table 1: List of recommended fonts**

Font type	Font name
San Serif	AdobeSansMM (Adobe Sans Multiple Master)
	Arial BolitaMT (Arial Bold Italic (From Monotype))
	ArialBolMT (Arial Bold Monotype)
	ArialtaMT Arial Italic (Monotype)
	ArialMT Arial (Monotype)
Non proportional	Couri (Courier)
	CouriBol (Courier Bold)
	CourriBolObl (Courier Bold Oblique)
Serif	AdobeSerifMM (Adobe Serif Multiple Masters)
	TimesNewRomPSBolitaMT (Times New Roman Bold Italic)
	TimesNewRomPSBolMT (Times New Roman Bold)
	TimesNewRomPSItaMT (Times New Roman Italic)
	TimesNewRomPSMT (Times New Roman)
	TimesNewRoman
Other	Symbo (Symbol)
	ZapfDin (Zapf Dingbats)

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140

Resizing a submitted document because the contents are too small to read is inefficient. We believe that Times New Roman, 11 or 12-point font (the font used for this document), is adequate in size for reading narrative text. When making point size larger, data comparisons could become problematic because data that normally might appear in one table would now appear in multiple tables. When choosing a point size for tables, a balance should be made between providing sufficient information on a single page that may facilitate data comparisons while still achieving a point size that remains legible. Generally, point sizes 9-10 are recommended for tables; smaller point sizes should be avoided. Ten point fonts are recommended for footnotes.

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We recommend the use of a black font color. Blue font can be used for hypertext links (preferred for submissions to CBER<sup>3</sup> and CFSAN). If a font color other than black is used, you should avoid light colors that do not print well on grayscale printers. You can test the color reproduction prior to submission by printing sample pages from the document using a grayscale printer.

### C. Page Orientation

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<sup>3</sup> The Commissioner has announced a consolidation of the CDER/CBER review functions for therapeutic products. Once the consolidation has been completed, we will review those guidances that have been affected by the transfer of functions for possible revision.



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149 Pages should be properly oriented to reduce the effort of rotating pages. For example,  
150 you should set the page orientation of landscape pages to landscape prior to saving the  
151 PDF document in final form to ensure correct page presentation.  
152

152

### **D. Page Size and Margins**

153

154 The print area for pages should fit on a sheet of paper that is 8.5 inches by 11 inches.  
155 You should allow a margin of at least 1 inch on the left side of page (to avoid obscuring  
156 information when the pages are subsequently printed and bound) and 3/8 of an inch on  
157 the other sides. For pages in landscape orientation, you should allow 3/4 of an inch at the  
158 top to allow more information to be displayed legibly on the page. Header and footer  
159 information can appear within these margins as long as it is not within 3/8 of an inch of  
160 the edge of the 8.5 by 11 inch page, because the text may be lost upon printing or being  
161 bound.  
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### **E. Source of Electronic Document**

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166 PDF documents produced by scanning paper documents are usually inferior to those  
167 produced from an electronic source document. Scanned documents are more difficult to  
168 read and do not allow us to search or copy and paste text for editing in other documents.  
169 They should be avoided if at all possible. If you use optical character recognition  
170 software, you should verify that all imaged text converted by the software is accurate.  
171

172

### **F. Methods for Creating PDF Documents and Images**

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174 You should choose a method for creating PDF documents that produces the best  
175 replication of a paper document. You can ensure that the paper and PDF version of the  
176 document are the same by printing the document from the PDF version.  
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178 Documents that are available only in paper should be scanned at resolutions that will  
179 ensure the pages are legible both on the computer screen and when printed. At the same  
180 time, you should also limit the file size. We recommend scanning at a resolution of 300  
181 dots per inch (dpi) to balance legibility and file size. We discourage the use of grayscale  
182 or color because of file size. But, if you believe their use is necessary, the following  
183 paragraphs provide preliminary recommendations, and specific guidance documents  
184 provide additional details. After scanning, you should avoid resampling to a lower  
185 resolution.  
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187 The optimal image resolution and bit depth depends to a large part on the actual need for  
188 viewing the image. You should not provide images at high resolution and depth without  
189 determining the need. High resolution and depth images result in large files, taking up  
190 valuable storage space. It is better to provide samples to the appropriate center of the  
191 images at various resolutions and depths prior to sending in the actual submissions to  
192 determine the optimal image resolution and depth to meet the review need.  
193

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194 When creating PDF files containing images, you should not resample images.  
195 Resampling does not preserve all of the pixels in the original. For PDF images, you can  
196 use one of the following lossless compression techniques.  
197

- 198 • For lossless compression of color and grayscale images, you should use Zip/Flate  
199 (one technique with two names). This is specified in Internet RFC 1950 and RFC  
200 1951 (<http://info.internet.isi.edu/in-notes/rfc/files/rfc1950.txt>).  
201
- 202 • For lossless compression of black and white images, you should use the CCITT  
203 Group 4 Faxcompression technique. It is specified as CCITT recommendations  
204 T.6 (1988) - *Facsimile coding schemes and coding control functions for Group 4*  
205 *facsimile apparatus*.  
206

207 When submitting medical images to CBER, such as X-ray, CT, ultra sound, PET, and  
208 SPECT, they should not be compressed.  
209

210 *Note: if you use lossless compression, there should not be a change in the label size and*  
211 *format.*  
212

213 Paper documents containing handwritten notes should be scanned at 300 dpi.  
214 Handwritten notes should be done in black ink for clarity.  
215

216 For photographs, the image should be obtained with a resolution of 600 dpi. If black and  
217 white photos are submitted, consider 8-bit gray scale images. If color photos are  
218 submitted, consider 24-bit RGB images. A captured image should not be subjected to  
219 nonuniform scaling (i.e., sizing).  
220

221 Gels and karyotypes should be scanned directly, rather than from photographs. Scanning  
222 should be at 600 dpi and 8-bit grayscale depth.  
223

224 Plotter output graphics should be scanned or captured digitally at 300 dpi.  
225

226 High-pressure liquid chromatography or similar images should be scanned at 300 dpi.  
227

228 When color is important in the review of a file, labeling for example, you should make  
229 sure that the colors are an accurate representation of the actual image. Since color varies  
230 from monitor to monitor, it is difficult to ensure that the reviewer will see exactly the  
231 same color as in the actual image. However, for printing, there is more control over the  
232 color if you use CMYK color model as opposed to the RGB model. Since PDF uses the  
233 color profile provided by CMYK, you can use Pantone Matching and this will ensure  
234 color consistency for printing. PDF also uses the ICC color profile specifications when  
235 PDF documents are printed.  
236

### **G. Hypertext Linking and Bookmarks**

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239 Hypertext links and bookmarks are techniques used to improve navigation through PDF  
240 documents. Hypertext links can be designated by rectangles using thin lines or by blue  
241 text (the latter is preferred by CBER and CFSAN). We recommend you use invisible  
242 rectangles for hypertext links in a table of contents to avoid obscuring text.  
243 Recommendations for hypertext linking and bookmarks are provided in the guidance for  
244 the specific submission type.

245  
246 In general, for documents with a table of contents, you should provide bookmarks and  
247 hypertext links for each item listed in the table of contents including all tables, figures,  
248 publications, other references, and appendices. These bookmarks and hypertext links are  
249 essential for the efficient navigation through documents. Bookmarks to the roadmap  
250 (when applicable), main table of contents, and item table of contents for the section of the  
251 application a reviewer has accessed, at the top of the bookmark hierarchy, are extremely  
252 helpful. The bookmark hierarchy should be identical to the table of contents with  
253 exceptions made for the following three bookmarks – the roadmap (when applicable), the  
254 main table of contents, and the item table of contents being accessed by a reviewer. You  
255 should avoid using bookmark levels in addition to those present in the table of contents.  
256 Each additional level increases the need for space to read the bookmarks. We  
257 recommend using no more than 4 levels in the hierarchy.

258  
259 Hypertext links throughout the body of the document to supporting annotations, related  
260 sections, references, appendices, tables, or figures that are not located on the same page  
261 are helpful and these hypertext links improve navigation efficiency. You should use  
262 relative paths when creating hypertext linking to minimize the loss of hyperlink  
263 functionality when folders are moved between disk drives. Absolute links that reference  
264 specific drives and root directories will no longer work once the submission is loaded  
265 onto our network servers.

266  
267 When creating bookmarks and hyperlinks, you should choose the magnification setting  
268 *Inherit Zoom* so that the destination page displays at the same magnification level that the  
269 reviewer is using for the rest of the document.

### **H. Page Numbering**

270  
271  
272  
273 See guidance for the specific submission type for guidance on page numbering.

274  
275 In general, it is easier to navigate through an electronic document if the page numbers for  
276 the document and the PDF file are the same. The initial page of the document should be  
277 numbered as page one, with two exceptions. One, when a document is split because of  
278 its size (e.g., > 50 MB), the second or subsequent file should be numbered consecutively  
279 to that of the first or preceding file. Two, when several small documents with their own  
280 internal page numberings have been brought together into a single file, it is not necessary  
281 to renumber the documents into one page sequence, although you should provide a  
282 bookmark at the start of each subdocument. For example, if you are adding an original  
283 protocol as an appendix to a study report, you should not add page numbers to the

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284 original protocol so the page numbers are consecutive to the rest of the study report. You  
285 should provide a bookmark to the original protocol.

286

### **I. Document Information Fields**

288

289 Document information fields are used to search for individual documents and to identify  
290 the document when found. Recommendations for the document information fields will  
291 be provided in the guidance for the specific submission type.

292

### **J. Open Dialog Box**

294

295 The open dialog box sets the document view when the file is opened. The initial view of  
296 the PDF files should be set as *Bookmarks* and *Page*. If there are no bookmarks, we  
297 recommend that you set the initial view as *Page* only. You should set the *Magnification*  
298 and *Page Layout* to default.

299

### **K. Naming PDF Files**

301

302 Recommendations on names to use for folders and selected files are provided in the  
303 individual guidances for specific submission types. For uniformity, you should use our  
304 specific naming conventions when they are provided. Reviewers are trained to look for  
305 these folders and files, and using the recommended names should help avoid  
306 misunderstandings, improve communication, and speed the review of a submission.

307

308 When we do not specify a file name, you can use file names up to 32 characters in length  
309 including PDF as the 3-character extension. We recommend that you avoid using  
310 punctuation, dashes, spaces, or other nonalphanumeric symbols (e.g., \ / : \* ? < > | “ % #  
311 +) in file names. Underlines can be used.

312

### **L. Security**

314

315 You should not include any security settings or password protection for PDF files except  
316 when recommended in guidance for a specific submission type. You should allow  
317 printing, changes to the document, selecting text and graphics, and adding or changing  
318 notes and form fields. Our internal security and archival processes will maintain the  
319 integrity of the submitted files. A read-only copy of the files, generated from the  
320 submitted files, will be provided to the reviewer.

321

### **M. Indexing PDF Documents**

323

324 We use full text indexes to help find specific documents and/or search for text within  
325 documents. When a document or group of documents is indexed, all words and numbers  
326 in the file and all information stored in the document information fields are stored in  
327 special index files that are functionally accessible using the search tools available in  
328 Acrobat. Portions of a document that are imaged are not indexed. Even if the document

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329 only contains images, the text in the Document Information fields of the file will be  
330 indexed.

331  
332 These full text indexes should not be confused with a table of contents. Adobe Acrobat  
333 Catalog is one example of a tool that can be used to index PDF documents. Indexes  
334 should not require extensions or additions to the off-the-shelf Acrobat Reader.

335  
336 With many submissions, we ask that you associate the table of contents file for a section  
337 with the corresponding full text index file. By *associate*, we mean that when the table of  
338 contents file is opened, the index file is automatically added to the available index list and  
339 is ready to be used.

340  
341 Further recommendations for full text indexes will be provided in individual guidances  
342 for the specific submission types.

### **N. Plug Ins**

343  
344  
345  
346 You can use plug ins to assist in the creation of a submission. However, the review of the  
347 submission should not require the use of any plug ins, in addition to those provided with  
348 the latest Acrobat Reader because we are not prepared to archive additional plug-in  
349 functionality.

## **V. WHAT FILE FORMATS SHOULD I USE FOR ELECTRONIC DATASETS?**

350  
351  
352  
353 You should provide data subsets in certain formats. Currently, we are able to accept and archive  
354 datasets in SAS System XPORT transport format (Version 5 SAS transport file). In  
355 circumstances when data are moved directly to a database or special review tool, tagged ASCII  
356 file, specifically, standard generalized markup language (SGML) and extensible markup  
357 language (XML), may be the appropriate file format. At times, delimited ASCII files are also  
358 acceptable. See the individual guidance for the specific submission type for the appropriate  
359 dataset format.

### **A. SAS System XPORT Transport Format (Version 5 SAS Transport Format)**

360  
361  
362  
363 SAS XPORT transport format, also called Version 5 SAS transport format, is an open  
364 format published by the SAS Institute. The description of this SAS transport file format is  
365 in the public domain. Data can be translated to and from this SAS transport format to  
366 other commonly used formats without the use of programs from SAS Institute or any  
367 specific vendor.

368  
369  
370 You should follow the recommendations in this section to create SAS transport files that  
371 we can review and archive.

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### *1. Version*

In SAS, SAS XPORT transport files are created by PROC XCOPY in Version 5 of SAS software and by the XPORT engine in Version 6 and higher of SAS Software. We are unable to archive SAS Transport files processed by the CPORT engine.

You can find the record layout for SAS XPORT transport files in SAS technical support TS-140. This document and additional information about the SAS Transport file layout can be found on the SAS World Wide Web page at <http://www.sas.com/fda-esub>.

### *2. Transformation of Datasets*

We use a variety of software tools to analyze the datasets. Stat/Transfer from Circle Systems and DBMS/copy from Conceptual Software Inc., are two programs used to convert data to various formats used for analysis. SAS Viewer version 7 or higher is used to open SAS transport files directly.

### *3. Naming SAS Transport Files*

All SAS transport files should use *xpt* as the file extension.

### *4. Compression of SAS Transport Files*

SAS transport files should not be compressed. There should be one transport file per dataset.

### *5. Content of Datasets and Organization*

You should provide a single transport file for each dataset. Many of the software tools used by the reviewers require datasets to be loaded into random access memory (RAM) prior to opening the file. Therefore, dataset files should be organized so that their size is generally less than 50 MB per file. Datasets divided to meet the maximum size restrictions should contain the same variable presentation so they can be easily merged, joined, and concatenated. The datasets should be accompanied by data definition tables that include metadata such as the variable name, a description of the variable, the type of variable (e.g., number, character, date), and codes used in the dataset. Variable names should be limited to 8 characters. You should include a descriptive name up to 40 characters in the label header. Further recommendations for content of SAS Transport files are provided in guidance for each specific submission type.

We recommend that you discuss the content of the datasets with the review division prior to submission.

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### **B. XML**

Extensible markup language (XML) was developed by a working group at the World Wide Web Consortium (W3C). It is a nonproprietary language developed to improve on previous mark up languages including standard generalized markup language (SGML) and hypertext markup language (HTML). XML is not as complicated to use as SGML and is more flexible than HTML.

Information in an XML file is divided into specific pieces. These pieces are called objects or elements types. The element type identifies the piece of information. For example, the NDA application number might be identified with the element type <appNum>. All element type names are bracketed using the special characters <>. Inside the XML document, the element type name is placed just prior to the piece of information and after the information. This is called tagging. So, in the XML file, the application number for NDA 123456 would be tagged as follows <appNum>123456</appNum>. The / prior to the element type denotes that this is the end of the information about the appNum.

By using a hierarchial structure, XML allows you to relate two or more elements. This is accomplished by nesting one element within another.

Additional information about the element type is provided by attributes. Attributes are placed within the element types and are surrounded by “ ”. For example, if you wanted to identify the type of the application number as an NDA, you could add this piece of information as an attribute. This could be represented in the XML file as <appNum type="NDA">123456</appNum>.

Internet browsers read XML files. Style sheets provide the browser with the information necessary to create tables, fonts, and colors for display in the XML file.

The specific names of the element types and attributes as well as the valid syntax, structure and format for defining the XML elements are included in a file called document type declaration (DTD). If the XML document does not follow the DTD, the file might not be used properly.

We currently use XML version 1.0 recommended by the World Wide Web Consortium (W3C). We will be evaluating additional uses for XML as enhancements for data exchange evolve and extensions are developed. Additional information can be found at the W3C web site at [www.w3c.org](http://www.w3c.org).

For specific tags and formats see the individual guidance document for the specific submission type.

### **C. SGML**

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463 A working group at the W3C developed standard generalized markup language (SGML).  
464 It is a nonproprietary language developed to organize and transmit information in digital  
465 format. It shares many of the features of XML described above. Additional information  
466 can be found at the W3C web site at [www.w3c.org](http://www.w3c.org).

467

### **D. Molfiles**

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470 The file format called *Molfile* is in the public domain and was developed by Molecular  
471 Design Limited (MDL) in the late 1970's. Currently, the company, now named  
472 Molecular Design Limited Information Systems, is a wholly owned subsidiary of Elsevier  
473 Science. Technical information about the Molfile format can be found at the MDL web  
474 site at <http://www.mdli.com/downloads/literature/ctfile.pdf>.

475

476 Molfiles are generated by chemical structure drawing programs. The most common  
477 drawing programs, ISIS/Draw from MDL and ChemDraw Pro from Cambridge Soft  
478 (<http://www.cambridgesoft.com>), create Molfiles. A free copy of ISIS/DRAW for your  
479 personal use may be obtained from the MDL Web site at  
480 <http://www.mdli.com/downloads/isisdraw.html>.

481

482 Molfiles can be viewed and reformatted using Chime, a free plug in to Microsoft  
483 Internet Explorer and Netscape Communicator from MDL. You can download the plug  
484 in at <http://www.mdli.com/downloads/chime.html>.

485

486 Molfiles can be searched using database programs such as ISIS Base. Additional  
487 Information about this database program can be found at the MDL web site at  
488 <http://www.mdli.com>.

489

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## **VI. WHAT ARE THE PROCEDURES FOR SENDING ELECTRONIC SUBMISSIONS FOR ARCHIVE?**

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492  
493 Electronic submissions should be provided in electronic format, either on physical media or by  
494 acceptable methods of electronic transport. You should refer to the individual guidance for the  
495 specific submission type for the appropriate procedures to use for sending electronic submissions  
496 for archive.

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499

### **A. Electronic Transmission**

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501 Currently, we have identified three methods for sending submissions electronically.  
502 Submissions using electronic data interchange (EDI), web-based transmissions, and  
503 secure email. We will provide additional information on these transmission methods as  
504 they are used for specific submission types. For example, CVM accepts electronic  
505 submission of certain types by attaching encrypted PDF files to e-mail to the Electronic  
506 Document Control Unit at [cvmdcu@cvm.fda.gov](mailto:cvmdcu@cvm.fda.gov). You can get more information at  
507 [www.fda.gov/cvm/fda/TOCs/guideline.html](http://www.fda.gov/cvm/fda/TOCs/guideline.html).



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### **B. Physical Media**

The following information is important when sending electronic submissions on physical media. See Appendix A: Additional information on providing Electronic Submissions on Physical Media for additional information.

#### *1. Where do I send the electronic submission?*

Electronic submissions should be sent directly to the appropriate center involved. See guidance for specific submission type for additional information.

- **CBER**

You should provide a minimum of two copies of the submission. One copy will be used to load the submission into our electronic document room (EDR). This copy will be made available to the Agency's review community upon request. The second copy will be archived for disaster recovery. Additional copies of items of an application, bundled by review discipline, may be requested to facilitate the review offsite. All materials are received centrally within CBER and should be addressed as follows:

Center for Biologics Evaluation and Research  
Document Control Center, HFM-99  
Food and Drug Administration  
1401 Rockville Pike  
Rockville, MD 20852-1448

Submitting organizations should use the above address for regulatory documents and media in support of applications within CBER. This includes regulatory documents and media sent via U.S. Postal Service or via common or private carriers.

- **CDER**

Unless otherwise specified in the specific submission guidance, send one copy of the electronic regulatory submission for archive to the CDER Central Document Room.

- **CDRH**

Contact the appropriate reviewing division prior to making an electronic submission. The division will inform you as to where and how to send submissions. Contacts can be found at <http://www.fda.gov/cdrh/organize.html#ODE>. See individual guidance for specific submission type for additional information.

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- CFSAN

CFSAN’s Office of Nutritional Products, Labeling, and Dietary Supplements (ONPLDS) is working on procedures for submitting new dietary ingredient notifications and applications for temporary marketing permits. Unless otherwise specified in the specific submission guidance, send one copy of the electronic regulatory submission for ONPLDS to the following address:

Office of Nutritional Products, Labeling, and Dietary Supplements  
Center for Food Safety and Applied Nutrition  
5100 Paint Branch Parkway, HFS-800  
College Park, MD 20740

Currently, CFSAN’s Office of Food Additive Safety (OFAS) accepts a submission provided only on physical media. All submissions should be sent directly to OFAS. The procedure for handling paper submissions is unchanged from the past.

You should send electronic and paper submissions to:

Office of Food Additive Safety  
Center for Food Safety and Applied Nutrition  
Food and Drug Administration  
5100 Paint Branch Parkway  
College Park, MD 20740

You should communicate with OFAS prior to submitting an electronic document, notifying it of your intention to submit an electronic document in advance of the target date for the submission

OFAS will schedule a teleconference or meeting between petitioners and the appropriate OFAS staff. The objective of the teleconference is to convey information relating to the proposed electronic submission’s management paradigm, content, format, and structure. Moreover, OFAS will discuss any issues specific to your submission that may not have been fully addressed in this general considerations guidance. The amount of time that will be needed to ensure that the document is ready for submission will depend on the complexity of the document and experience of the said submitter in preparing petitions and notifications.

- CVM

We are working on procedures for accepting electronic submissions on physical media. See individual guidance for specific submission type for additional information.

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596 2. *What type of media should I use?*

597  
598 We are prepared to accept electronic submissions on CD-ROM and digital tape. In  
599 CDER and CFSAN, you can also use floppy disks. To optimize processing efficiency,  
600 we recommend choosing media with a capacity most appropriate to the size of the  
601 submission. Whenever possible, applicants should choose media capable of holding the  
602 submission on the *fewest* number of units.  
603

Recommendations for Media		
Size of Submission	Media and format	Units
Less than 10MB*	3.5 inch DOS Formatted Floppy Disks	1 to 10
Less than 3.25GB	CD-ROM ISO 9660	1 to 5 CDs
Greater than 3.25GB	Digital Linear Tape (DLT) 35/70, 20/40 and 10/20 GB format using NT server 4.0 with NT backup or backup exec.	No limit

604 \*This is not an option for CBER and CVM

605  
606 3. *How should I prepare the media for electronic submissions?*

607  
608 You should send all electronic media adequately secured in a standard binder marked  
609 clearly on the outside ELECTRONIC REGULATORY SUBMISSION FOR ARCHIVE.  
610 CDs should be packaged carefully to ensure that they arrive in a usable condition.  
611 Particularly vulnerable are diskettes and CD jewel cases shipped in envelopes without  
612 bubble-type protective material or stiff backing. We do not recommend the use of jiffy-  
613 type bags alone to ship media because they may not provide adequate protection.  
614

615 You should provide the following identification information on the media, as appropriate:

- 616
- 617 • Sponsor, applicant or company name
  - 618 • Name of the product, chemical, or ingredient
  - 619 • Appropriate regulatory ID number (e.g., Petition Notification number, NDA,  
620 IND, BLA number, petition or notification number)
  - 621 • Application type (e.g., IND amendment, BLA supplement, title of petition or  
622 notification)
  - 623 • Submission date in the format of dd-mmm-yyyy
  - 624 • Copy number (e.g., original, copy 1, copy 2)
  - 625 • Media series (e.g., "1 of 1," "1 of 2")
  - 626 • When sending CD-ROMs to OFAS, number them from 0.001 through 0.XXX  
627 for the original submission, and 1.001 through 1.XXX for subsequent  
628 submissions to the same files with additional information.
- 629

630  
631 You should include the information directly on the DLT tape cover label. For CDROMs,  
632 you should include the information on the jewel case. The CDROM itself should include,

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633 at a minimum, sufficient identification information so that it can be paired with the jewel  
634 case bearing the complete identification information, in the event that they become  
635 separated. See the individual guidance for the specific submission type for additional  
636 information on labeling physical media.  
637

638

### **VII. WHAT IF I HAVE A QUESTION?**

640

#### **A. CBER**

642

643 You can submit questions pertaining to the preparation of submissions, in electronic  
644 format, for CBER to [ESUBPREP@CBER.fda.gov](mailto:ESUBPREP@CBER.fda.gov).

645

#### **B. CDER**

647

648 We maintain a web site on electronic submissions at  
649 [www.fda.gov/cder/regulatory/ersr/default.htm](http://www.fda.gov/cder/regulatory/ersr/default.htm). You can direct questions regarding the  
650 preparation of submissions in electronic format in CDER to [esub@cder.fda.gov](mailto:esub@cder.fda.gov).

651

#### **C. CDRH**

653

654 You can submit questions about electronic submissions via email to [esub@cdrh.fda.gov](mailto:esub@cdrh.fda.gov).  
655 We also maintain a web site on electronic submissions at  
656 [www.fda.gov/cdrh/elecsub.html](http://www.fda.gov/cdrh/elecsub.html). In addition, you can sign up for email updates on the  
657 CDRH home page at [www.fda.gov/cdrh](http://www.fda.gov/cdrh).

658

#### **D. CFSAN**

660

661 You can direct questions regarding the preparation of submissions in electronic format in  
662 CFSAN to the Electronic Submissions Coordinator email [esubprep@opa.fda.gov](mailto:esubprep@opa.fda.gov).

663

#### **E. CVM**

665

666 You can direct questions regarding the preparation of submissions in electronic format in  
667 CVM to the Electronic Submissions Coordinator, email [cvmstars@cvm.fda.gov](mailto:cvmstars@cvm.fda.gov) or you  
668 can call the Center Hot Line at 301-827-8277. Additional information on electronic  
669 submissions can be found at <http://www.fda.gov/cvm/guidance/guidance.html>.

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**APPENDIX A: ADDITIONAL INFORMATION ON PROVIDING ELECTRONIC SUBMISSIONS ON PHYSICAL MEDIA**

**CBER**

*Processing the electronic submission*

The structure and content of electronic submissions to CBER should be based upon the application (e.g., BLA and IND). Subsequent to the delivery of an electronic application, any additional electronic information (i.e., amendments) will be added to the existing copy of the submission residing in the Electronic Document Room (EDR). BLA supplements are treated as separate submissions, not as continuations of the base application. They will be stored in their own EDR folder. The root directory of an electronic application should contain a roadmap.pdf file to orient the review team to the application as well as subsequent information amending the application.

*Roadmap file*

CBER suggests that a roadmap.pdf file be used to establish hypertext links to an application's or amendment's main table of contents and to the application folders and files. If an application is submitted on multiple CDROMs or DLT tapes, each unit of media should contain the identical roadmap.pdf file, which links to folders and files on all of the media units. This *roadmap* file should be updated and resubmitted when additional information is submitted to amend an application.

The roadmap.pdf file should be placed in the root directory of a submission. This ensures that the outdated roadmap.pdf file is overwritten each time a new amendment is loaded into the EDR. The roadmap file should not contribute in any way to the content of the submission under review. It is a map, intended to facilitate navigation through the contents of an application. The application's roadmap.pdf file should be easily updated or modified, for example, using the Replace File command under the Document menu option in Adobe Exchange. This function will automatically replace the old hypertext links to previously submitted sections of the application, leaving only the task of creating the new links corresponding to newly submitted information.

In addition to providing a navigable guide to the application, the roadmap.pdf file should include the sponsor's submission date in the DD-MMM-YYYY format (e.g., 01-Jan-1999). The contents of the original application and any subsequent amendments to that application should be briefly described in a roadmap.pdf table. The location of these files and folders on the submitted media should be indicated in the roadmap.pdf. Where portions of an application have been submitted only as a paper documents, they should be included in the roadmap and table of contents and tagged as *paper only*.

The following text is a representative example of a roadmap.pdf file.

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### Electronic Roadmap

BLA Submission	Submission Date	Submission Content	CD-ROM	Hypertext link Destination
Sponsor Name	15-Jan-1999	FDA Form 356h .001		../blatoc.pdf
		cover.pdf	.001	
		BLA Table of Contents	.001	
		Item 01-Index	.001	
		Item 02-Labeling	.001	
		Item 03-Summary	.001	
		Item 04-CMC	.001	
		Item 05-Pharmtox	.001	
		Item 06-Cpbio	.001	
		Item 08-Clinical	.002	
		Item 10-Statistical	.002	
		Item 12-Crf	.002	
		Item 15-Estab	.002	
		Others (Items 13-16)	.002	
BLA 123456/5001/1	01-Apr-1999	cover.pdf	.001	..\ 123456/5001/1\ amendtoc.pdf
		confid.pdf	.001	
		CMC	.001	
BLA 123456/5001/2	19-Jun-1999	Cover.pdf	.001	..\ 123456/5001/2\amendtoc.pdf
		Clinstat	.001	
BLA 123456/5001/3	04-Jul-1999	cover.pdf	.001	..\ 123456/5001/3 \amendtoc.pdf
		confid.pdf	.001	
		Clinstat	.001	
		Safety Update	.001	

746

#### 747 *Summary File*

748

749 A summation of the electronic document, using at least 40 key words from the  
750 main document, should be included with all electronic applications delivered to  
751 CBER. This summation should be located in the root directory on the  
752 CDROM or DLT tape. The file containing the key words should be an ASCII  
753 text file entitled *Summary.txt*.

754

#### 755 **CDER**

756

757 In general, when an electronic submission arrives in CDER, we copy the electronic files  
758 to tape to create an archival copy of the submission. We also copy the files to a network  
759 server to create a read-only copy for the reviewer. See specific submission type guidance  
760 for additional details.

761

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762 **CDRH**

763

764 Contact the appropriate reviewing division prior to making an electronic submission.

765 The division will inform you as to where and how to send submissions. Contacts can be

766 found at <http://www.fda.gov/cdrh/organize.html#ODE>. See individual guidance for

767 specific submission type for additional information.

768

769 **CFSAN**

770

771 When an electronic submission arrives in OFAS one copy of the media is archived: the

772 second copy of the submission's media is copied to a network server to create a read-only

773 copy for the reviewer.

774

775 The structure and content of electronic submissions to OFAS should be based upon the

776 application (e.g., Petition, Notification). Subsequent to the delivery of the electronic

777 application, any additional electronic and/or paper information will be added to the

778 existing network copy of the submission and made available to appropriate managers and

779 reviewers. The root directory of an electronic application should contain a roadmap.pdf

780 file to orient the review team to the original application and to any and all subsequent

781 information added to the application.

782

783 OFAS suggests that a roadmap.pdf file be used to establish hypertext links to the

784 application's main table of contents and to the application folders and files. This

785 *roadmap* or *home page* should be updated and resubmitted as additional information to

786 the application.

787

788 The roadmap file should not contribute in any way to the content of what is under review.

789 It is a map, intended to facilitate navigation through the contents of an application. The

790 application's roadmap.pdf file should be easily updated or modified, for example, using

791 the Replace File command under the Document menu option in Adobe Exchange. This

792 function will automatically replace the old hypertext links to previously submitted

793 sections of the application, leaving only the task of creating the new links corresponding

794 to newly submitted information.

795

796 In addition to providing a navigable guide to the application, the roadmap.pdf file should

797 include the sponsor's submission date in the DD-*MMM*-*YYYY* format.<sup>17</sup> (e.g., 01-Jan-

798 2000). The contents of the original application and any subsequent amendments to that

799 application should be briefly described in a roadmap.pdf table. The location of these files

800 and folders on the submitted media should be indicated in the roadmap.pdf. Where

801 portions of an application have been submitted only as paper documents, they should be

802 included in the roadmap and table of contents and tagged as *paper only*.

803

804 A summation of the electronic document, using at least 40 key words from the main

805 document should be included with all electronic applications delivered to OFAS. This

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806 summation should be located in the root directory on the CDROM or DLT tape. The file  
807 containing the key words should be an ASCII text file entitled *Summary.txt*.  
808

### **CVM**

810  
811 We are developing procedures for processing electronic submissions sent on physical  
812 media. See individual guidance for specific submission type for additional information.