Draft Guidance for Industry and Food and Drug Administration Staff

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eCopy Program for Medical Device Submissions

DRAFT GUIDANCE

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You should submit comments and suggestions regarding this draft document within 30 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact the Premarket Notification (510(k)) Section or the Premarket Approval Section of CDRH at 301-796-5640 or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

Preface

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 301-827-8149 to receive a hard copy. Please use the document number (1797) to identify the guidance you are requesting.

Additional copies of this guidance document are also available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm.

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Guidance for Industry and Food and Drug Administration Staff

eCopy Program for Medical Device Submissions

1. Introduction

The purpose of this guidance is to explain the new electronic copy (eCopy) Program for medical device submissions. At this time, submission of an eCopy of a medical device submission is voluntary. However, section 745A(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), added by section 1136 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112-144), requires the submission of eCopies after this guidance is finalized. This draft guidance describes how the Food and Drug Administration (FDA) plans to implement the eCopy Program under section 745A(b) of the FD&C Act. The inclusion of an eCopy is expected to improve the efficiency of the review process by allowing for the immediate availability of an electronic version for review rather than relying solely on the paper version.

This draft guidance provides, among other things, the standards for a valid eCopy under section 745A(b)(2)(A) of the FD&C Act. In accordance with section 745A(b), following the issuance of a final guidance on this topic, submission types identified in the final guidance must include an eCopy in accordance with the standards provided by this guidance for the submission to be processed and accepted for review by FDA. Submissions submitted without an eCopy and eCopy submissions that do not meet the standards provided in this guidance will be placed on hold until a valid eCopy is submitted to FDA and verified to meet the standards, unless a waiver or exemption has been granted. While the submission is on hold, the review clock will not begin.

In Section 745A(b), Congress granted explicit statutory authorization to FDA to implement the statutory eCopy requirement by providing standards, criteria for waivers, and exemptions in guidance. Accordingly, to the extent that this document provides such requirements under section 745A(b) of the FD&C Act (i.e., standards, criteria for waivers, and exemptions), indicated by the use of the words *must* or *required*, this document is not subject to the usual restrictions in FDA's good guidance practice (GGP) regulations, such as the requirement that guidances not establish legally enforceable responsibilities. See 21 CFR 10.115(d).

However, this document also provides guidance on FDA's interpretation of the statutory eCopy requirement and the Agency's current thinking on the best means for implementing other aspects of the eCopy program. Therefore, to the extent that this document includes provisions that are not "standards," "criteria for waivers," or "exemptions" under section 745A(b)(2), this document does not create or confer any rights for or on any person and does not operate to bind FDA or the public, but will represent the Agency's current thinking on this topic when finalized. The use of the word *should* in such parts of this guidance means that something is suggested or recommended, but not required. You can use an alternative approach if the approach satisfies

the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

To comply with the GGP regulations and make sure that regulated entities and the public understand that guidance documents are nonbinding, FDA guidances ordinarily contain standard language explaining that guidances should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. FDA is not including this standard language in this draft guidance because it is not an accurate description of all of the effects of this guidance, when finalized. This guidance, when finalized, will contain both binding and nonbinding provisions. Insofar as this guidance, when finalized, provides "standards," "criteria for waivers," and "exemptions" pursuant to section 745A(b) of the FD&C Act, it will have binding effect. For these reasons, FDA is not including the standard guidance language in this draft guidance.

The eCopy Program is not intended to impact (reduce or increase) the type or amount of data the applicant[1] includes in a submission to support clearance or approval. Please refer to other FDA device or program-specific guidance documents from CDRH (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm) and CBER http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/ucm214106.htm) for the appropriate contents for submissions.

2. What is an eCopy?

An electronic copy (eCopy) is defined as an exact duplicate of the paper submission, created and submitted on a compact disc (CD), digital video disc (DVD), or in another electronic media format that FDA has agreed to accept, accompanied by a copy of the signed cover letter and the complete original paper submission.[2]

3. Are differences between the contents of an eCopy and paper submission acceptable?

While an eCopy is defined as an exact duplicate of the paper copy, there are limited cases in which differences between the eCopy and the paper copy may be justified because a paper copy is not practical or appropriate for analysis purposes (e.g., raw data and statistical analysis programs,[3] data line listings to facilitate a bioresearch monitoring review) or is not feasible (e.g., videos, x-rays). The critical attribute of an eCopy is that it must include in electronic form all

[1] For the purposes of this guidance, applicant includes "submitter," "sponsor," or "holder."
[2] An eCopy is not considered to be an electronic submission. For information on eSubmissions, refer to "FDA eSubmitter" (http://www.fda.gov/ForIndustry/FDAeSubmitter/default.htm) and "Regulatory Submissions in Electronic Format for Biologic Products" (http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm163685.htm).
[3] For information on electronically submitted data, refer to "Clinical Data for Premarket Submissions" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm).

data required for that submission type.[4] In other words, the eCopy must include all of the required information for FDA review, whereas the paper copy can include a page cross-referencing the location of certain information in the eCopy.

The cover letter must contain the eCopy statement described in Attachment 1 and describe any differences between the paper version and the eCopy. The paper version must also have a placeholder (e.g., a piece of paper printed with the appropriate section title or a divider appropriately cross-labeled to the table of contents) that cross-references the eCopy to indicate that there are additional data/information in the eCopy and where in the eCopy that information is located.

FDA will consider the eCopy loaded into the appropriate Center's official document repository to be the official record. Any undisclosed differences between the eCopy and the paper version may need to be rectified and could delay the review of the submission.

4. For what submission types is an eCopy required?

Once FDA finalizes this guidance, section 745A(b) of the FD&C Act, as added by section 1136 of FDASIA, will require an eCopy for the following submission types[5]:

- Premarket notification submissions (510(k)s), including third party 510(k)s;
- Evaluation of automatic class III designation petitions (de novos);
- Premarket approval applications (PMAs)[6];
- Modular PMAs;
- Transitional PMAs;
- Product development protocols (PDPs);
- Investigational device exemptions (IDEs);
- Humanitarian device exemptions (HDEs), including Humanitarian Use Device designation requests (HUDs);
- Certain investigational new drug applications (INDs)[7];
- Certain biologics license applications (BLAs)[8]; and
- Pre-Submissions[9].

[4] For example, the content requirements for a 510(k) submission are found in 21 CFR 870.87 and 807.92; those for original PMA submissions are found in 21 CFR 814.20.

[5] Although not subject to the eCopy legislation, FDA accepts and strongly encourages eCopies for Master Access Files ("MAF" submissions), 513(g) Requests for Classification ("C" submissions), and Clinical Laboratory Improvement Act (CLIA) Categorization – Exempt Device submissions ("X" submissions). If you choose to submit an eCopy, it must meet the standards outlined in Attachment 1.

[6] This includes all PMA submission types, including, but not limited to, original PMAs, panel-track supplements, 180-day supplements, manufacturing site change supplements, and post-approval study supplements.

[7] Applicable only to those devices regulated by CBER that are also biologics under section 351 of the Public Health Service (PHS) Act and that also require submission of an IND prior to submission of a BLA. Such devices are generally those intended for use in screening donated blood for transfusion transmissible diseases.

[8] Applicable only to those devices regulated by CBER that are also biologics under Section 351 of the PHS Act, including those that do not require submission of an IND prior to the submission of the BLA. Such devices generally include those reagents used in determining donor/recipient compatibility in transfusion medicine in addition to those for use in screening blood for transfusion transmissible diseases.

[9] Refer to the draft guidance entitled, "Medical Devices: The Pre-Submission Program and Meetings with FDA Staff" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm310375.htm).

eCopies for all subsequent submissions to an original submission, including amendments, supplements, and reports[10] to the submission types identified above would also be required even if the original was submitted to FDA prior to implementation of the eCopy requirement.

5. What submission types does FDA consider exempt from submission of an eCopy?

Due to the potential urgent nature of the following types of submissions, FDA considers these to be exempt from the requirement for an eCopy:

- Compassionate use IDE submissions;
- Emergency use IDE submissions[11]; and
- Emergency Use Authorizations (EUAs)[12].

However, we encourage you to submit eCopies of these submissions, when feasible, in order to facilitate the review process. In addition, this exemption would not preclude you from sending in pertinent electronic information, such as imaging data, as supporting information for these submission types when an eCopy is not submitted.

6. What submission types or applicants are eligible for an eCopy waiver?

FDA believes that, given the widespread availability of software to enable the creation of an acceptable eCopy at little to no cost, all applicants should have the ability to provide an eCopy. Therefore, at this time, FDA does not anticipate the need for waivers, except as described in Section 9.

7. How many copies of a submission are needed?

The eCopy Program would not change the overall number of copies to submit to FDA. Upon finalization of this guidance document, an eCopy (with a signed cover letter) will serve as one of the required number of copies for the various submission types. (See Table 1 below.) FDA will accept additional eCopies (each with a signed cover letter) in lieu of additional paper copies as long as at least one paper copy is submitted along with the eCopy and the total number of required copies remains the same.

[10] Reports include all reports submitted to an applicable submission type, including annual/periodic and post-approval reports. Section 745A(b) of the FD&C Act does not apply to Medical Device Reports submitted under 21 CFR Part 803 .

[11] Please refer to CDRH's device advice page entitled "IDE Early/Expanded Access" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#compassionateuse) and FDA's "Guidance on IDE Policies and Procedures" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm) for additional details on compassionate and emergency use IDE submissions.

[12] Refer to the guidance entitled, "Emergency Use Authorization of Medical Products" (http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm) for more information on EUAs.

For submission types for which only two copies are required to be submitted, one must be an eCopy and the other must be a paper copy. For submission types requiring more than two copies, this policy would allow additional flexibility in how the application is submitted. For example, for an original PMA, you would submit: (1) one eCopy and five paper copies; (2) five eCopies and one paper copy; or (3) any other combination that results in six total copies as long as there is at least one eCopy and one paper copy.

Table 1, provides the total number of copies to be submitted to FDA. As explained above, you must submit at least one eCopy and one paper submission. The format for the remaining copies (i.e., eCopy or paper) is your choice.

Table 1 – Number of Copies for Submission

Submission Type	Total Number of Copies
510(k)s	2[13]
Third Party 510(k)s	2[13]
Original PMAs and Panel-Track Supplements	6[14]
Other PMA supplement types	3[15]
PMA reports	2
Modular PMAs	3
HDEs	Same as PMAs,[16] except for HUD designation requests, which require two.[17]
PDPs	Same as PMAs
IDEs	3[18]
INDs	3[19]
BLAs	3
Pre-Submissions	3

8. What are the processing steps for an eCopy?

Below are the processing steps for the submission and acceptance of an eCopy.

a. What are the standards for an eCopy?

With regard to the standards for an eCopy submitted to FDA, please refer to Attachment 1. Because an eCopy cannot be accepted by our eCopy loading system if it does not meet the standards, you should carefully review this information.

[13] See 21 CFR 807.90(a)(3)(c).
[14] See 21 CFR 814.20(b)(2).
[15] See 21 CFR 814.39(c).
[16] See 21 CFR 814.104(b)(4).
[17] See 21 CFR 814.102(d).
[18] See 21 CFR 812.20(a)(3).
[19] See 21 CFR 312.23(d).

b. How do I know before submission whether my eCopy meets FDA's standards for acceptance?

To confirm that your eCopy will meet FDA's standards, we strongly encourage you to use the new free eSubmitter-eCopies tool available on FDA's website at http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm317334.htm. One of the benefits of utilizing the eSubmitter-eCopies tool is that it creates an eCopy in real-time that is consistent with the standards. Use of the eSubmitter-eCopies tool is intended to prevent delays in review of your submission due to the need to resolve technical issues. Although it is highly encouraged, you will not be required to utilize the eSubmitter-eCopies tool and may choose to skip the eSubmitter step.

Should you have any technical questions when generating your eCopy, please contact cdrhesub@cdrh.fda.gov prior to submission of the eCopy to FDA.

c. What if there is another processing party involved?

In the case that another party (e.g., law firm, consultant) submits a submission on behalf of an applicant, the eCopy must still meet the standards for an eCopy in order to be successfully processed whether accomplished by you (the applicant) or the submitting party. While the applicant may or may not include their own cover letter as part of the eCopy, our standards require that the submitting party include a signed cover letter with an eCopy statement, as described in Attachment 1.

In the case of Third Party 510(k)s, two separate CDs comprise the eCopy. The first CD includes the applicant's submission and should be clearly marked as such. The contents of the CD must include a cover letter with an eCopy statement, as described in Attachment 1, that the applicant has provided. The second CD includes the Accredited Person's review records and should be clearly marked as such. The Accredited Person is responsible for ensuring that the CDs meet the standards in Attachment 1 for an eCopy. In addition, the Accredited Person is responsible for providing a signed cover letter that includes an eCopy statement, as described in Attachment 1, that speaks to both: (1) the Accredited Person's portion of the eCopy and (2) the presence of the eCopy statement provided by the applicant. It is not sufficient for the Accredited Person to address only one of these two eCopy statement issues in their cover letter.

d. How do you submit an eCopy to FDA?

An eCopy is submitted simultaneously with the paper submission(s). First, attach the signed cover letter with the eCopy statement to your eCopy. Then attach this eCopy package to the paper submission(s) and send them to CDRH's or CBER's Document Control Center[20] (DCC). An eCopy that is sent to the DCC without a cover letter and accompanying paper submission(s) will be placed on hold.

If more than one eCopy is to be submitted, then you must attach a signed cover letter as described above to each additional eCopy.

[20] Refer to 21 CFR 807.90 for the DCC addresses for CDRH and CBER.

e. How does FDA process an eCopy?

If an eCopy passes the validation check, the cover letter and eCopy contents will be loaded into the appropriate Center's official submission repository.

If an eCopy fails the validation check (i.e., is rejected), we will notify you in writing (e.g., by email or fax) of the reason(s). The notification will describe the logistics for submitting a replacement eCopy, including how to properly mark it as a replacement eCopy, the address to which to send it, and the submission number to write on it. It is important that you follow these directions to avoid delays in processing the replacement eCopy. The submission will be placed on hold until a valid replacement eCopy is submitted to FDA and verified to meet the standards.

9. What if your device is regulated by CBER?

a. Will the new eCopy Requirement apply?

Yes, unless your submission is an entirely electronic submission exempted under this guidance, as described below. Upon implementation of the statutory requirement, all medical device submission types listed in Section 4 must be accompanied by an eCopy regardless of the Center in FDA in which the submission will be reviewed unless the requirement is waived or exempted. Accordingly, submissions for devices subject to review under the FD&C Act and submitted by filing paper copies with CBER's DCC must be accompanied by an eCopy, except where exempted as described below.

While many submissions made to CBER are still in paper format and require submission of multiple copies, CBER is also currently able to receive and manage submissions that are entirely electronic.

Submissions for devices that are subject to licensure under the Public Health Service (PHS) Act, including biologics license applications and supplements, investigational new drug applications, and EUAs and pre-submissions for these devices, may be submitted as entirely electronic submissions as detailed in sections 9b and 9c below. FDA will exempt such entirely electronic submissions from the eCopy requirement.

FDA additionally waives the eCopy requirement to submit paper copies of any entirely electronic submission made to CBER. Accordingly, entirely electronic submissions that comply with CBER guidance identified in Section 9.c. below do not need to be accompanied by paper copies.

b. Can you submit an electronic submission instead?

Yes, and there are several advantages for both industry and for CBER staff when you choose to make submissions electronically.

The main advantage to you is in the financial savings that will likely result. The costs associated with printing, binding, labeling, and shipping multiple paper copies can be significant, especially for submissions that contain a great deal of supporting

documentation. Likewise, we anticipate that FDA will recognize financial savings in that FDA avoids the costs associated with tracking, routing, and storing large amounts of paper when you choose to submit electronically.

Another advantage with the use of the electronic submission process is that all parties involved in the submission and review are referencing the same document – the electronic one. There is no question about whether the paper copy is an exact copy of the eCopy. Electronic submissions may also reduce the need for reviewers to request re-submission of previously submitted information due to an inability to read or interpret the information on the paper copy, as sometimes occurs when documents are photocopied.

c. How do you prepare and submit an electronic submission to CBER?

CBER has several resources available to applicants who choose to submit electronic submissions as outlined in the document "Regulatory Submissions in Electronic Format for Biologic Products." (http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm163685.htm). Thus, specific details are available in the cited references and will not be repeated in this guidance.

For devices that are regulated under the PHS Act and require the submission of a BLA, consult the guidance document entitled "Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format - Biologics Marketing Applications" (http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM192413.pdf) for details on preparing your electronic submission. Note that certain sections of this guidance, for example, those on pharmacology and toxicology, are generally not pertinent to licensed devices.

For guidance on preparing electronic submissions for other device submissions (e.g., 510(k)s, PMAs) sent to CBER, please see "Guidance for Industry: Providing Regulatory Submissions in Electronic Format - General Considerations" (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072390.pdf) and "CBER SOPP 8110: Submission of Paper Regulatory Applications to CBER" (http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079467.htm), which includes information about providing electronic copies to CBER.

We are currently developing additional, updated guidance for other electronic submissions sent to CBER and have issued a revised, updated draft guidance document for comment entitled, "Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format-General Considerations" (http://www.fda.gov/RegulatoryInformation/Guidances/ucm124737.htm). When finalized, this document will provide an additional resource for applicants preparing electronic submissions.

You can submit questions pertaining to the preparation of submissions in electronic format for submission to CBER at ESUBPREP@fda.hhs.gov.

You may also contact CBER at CBER.CDISC@fda.hhs.gov to discuss the potential for submission of data in CDISC format (http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm209137.htm).

CBER will accept electronic submissions via electronic transmission (i.e., through the Electronic Submissions Gateway[21,22]) or on physical media through CBER's Document Control Center.

[21] Refer to "Food and Drug Administration Electronic Submissions Gateway (Federal Register Notice) - 8/9/2006" (http://www.gpo.gov/fdsys/pkg/FR-2006-08-08/html/E6-12808.htm).
[22] Refer to "Electronic Submissions Gateway" (http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm).

Attachment 1 –Standards for eCopies

Upon implementation of the eCopy statutory provision, below are the proposed standards that will be written into the FDA eCopy software coding. If an eCopy does not meet all of the required standards identified below, then the eCopy will not pass FDA's eCopy validation process.

Table 1 summarizes the specifications that are required in order for the eCopy to be validated by FDA, as well as some recommended specifications. The table also cross-references the section within this attachment where additional information is located.

Table 1: Overview of eCopy Standards and Recommendations

Technical Features That Will be Required by FDA's eCopy Software	**Sec.**
eCopy statement in the cover letter	A
Volume versus non-volume structure; no subfolders	B
Folder naming convention for volume-based submissions	C
Acrobat Portable Document Format (PDF) files that meet certain specifications	D
All non-PDFs files are in zip files in "STATISTICAL DATA" and "MISC FILES" folders	E
PDF file naming convention	F
PDF file size ≤ 50MB	G
Recommended Technical Features	
Recommendations for creating PDF files from source document	H
Bookmarks and hyperlinks within PDF files	I
Recommendations for PDFs created from scanning paper documents	J

NOTE: If an eCopy does not meet all of the required standards, the eCopy will fail the loading process.

A. Cover Letter that accompanies an eCopy

In addition to the required signature,[23] to meet the standards of the eCopy program, the cover letter must also include one of the following eCopy statements:[24]

- the eCopy is an exact duplicate of the paper copy; or
- the eCopy is an exact duplicate of the paper copy except [specify all differences].

We expect the vast majority of the submissions to include the first statement. However, as described in Section 3 above, for those submissions that contain certain clinical datasets, or other types of data/information that is not feasible or practical to put in paper form, the second statement would apply.

[23] You may also choose to include an electronic version of the cover letter in the eCopy; however, this should not be in lieu of the attached cover letter with a signature.

[24] The eCopy statement in the cover letter for a Third Party 510(k) speaks to both the Third Party eCopy and applicant's eCopy portions as described in Section 8.c. above.

If you include the second statement, you must specify the differences between the eCopy and paper submissions (e.g., "The eCopy is an exact duplicate of the paper copy except that in Volume 4 of the eCopy, we included a .zip file of statistical data that was not included in the paper copy."). In addition, you must include a placeholder in the paper submission referring to the eCopy for that specific information.

Please also note that it is FDA's preference that responses to deficiencies identified during submission review not be incorporated into the cover letter, for ease of processing and to minimize the paper scanning involved with the cover letter.

B. Volume versus non-volume structure

The structure of an eCopy is highly dependent on the overall file size of the submission and can be organized using files and folders in one of the ways below.

- **Volume-based submission** (generally recommended for large or complex submissions) - create either multiple volumes on one or more CDs/DVDs organized into folders containing each volume's associated files or create one PDF document for each volume. The allowable folders are as follows:
  - **Content organized by volume.** Only volume-based submissions can use folders. The folders are named as follows: Vol_001 through Vol_999 or Vol_001 Description through Vol_999 Description. The volumes of any individual submission must be sequentially numbered.[25]
  - **"STATISTICAL DATA"** folder as described in Section D below.
  - **"MISC FILES"** folder as described in Section D below.

  NOTE: Subfolders are not allowed by our system. **If you incorporate subfolders, the eCopy will fail the loading process.**

- **Non-volume-based submission** (generally recommended for only small submissions) - create either one PDF document for each table of contents entry or create a single PDF.

Figures are presented below to illustrate how to name and structure a submission. Figure 1 provides an example of an IDE with volumes. Figure 2 provides an example of a submission that contains multiple PDF files, as in the case of a 510(k) submission.

[25] The volumes of any supplement to an existing application should also be numbered sequentially, but only within that submission, i.e., the supplement volumes should start at Vol_001.

Figure 1: Investigational Device Exemption (IDE) with Volumes

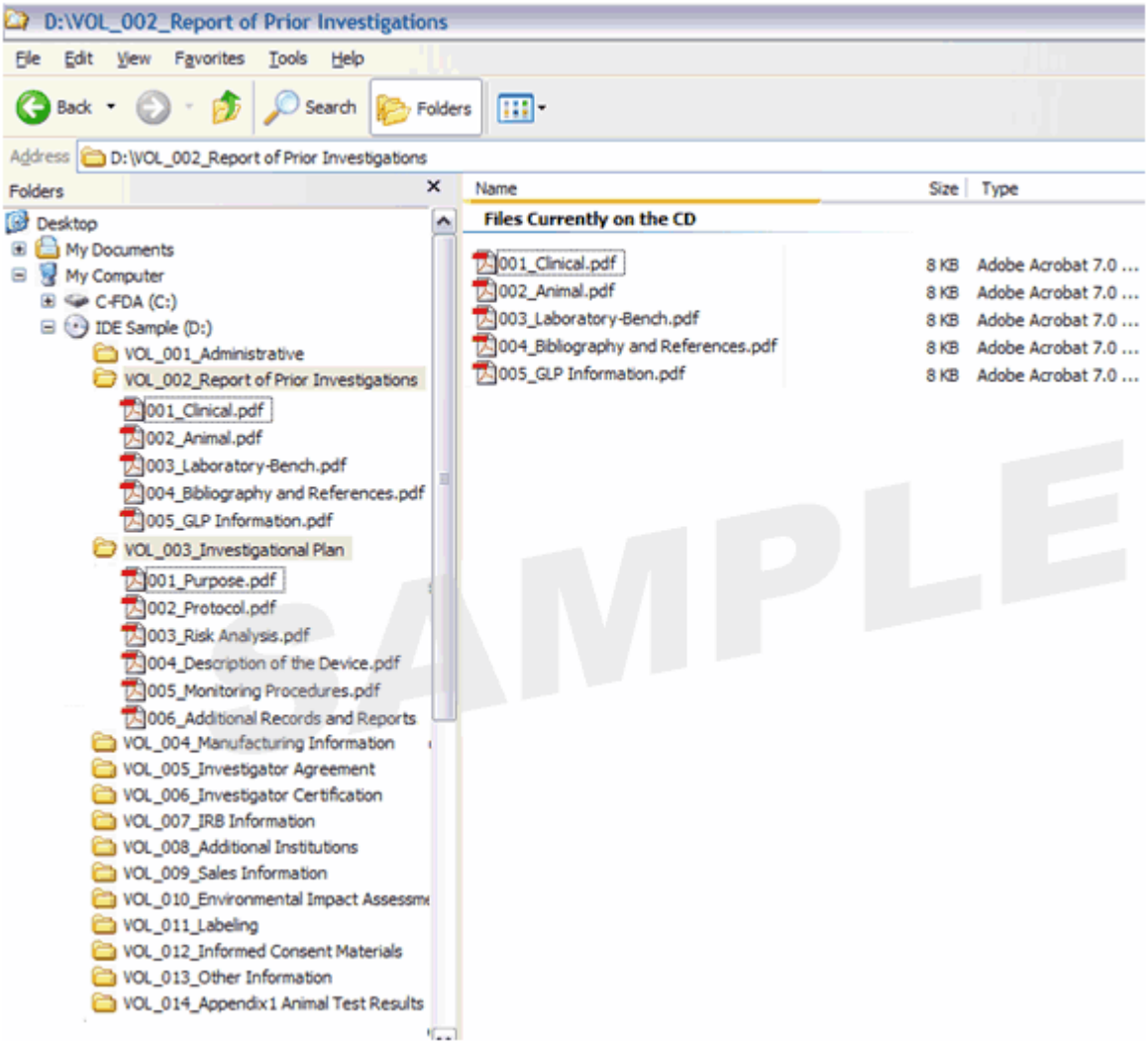
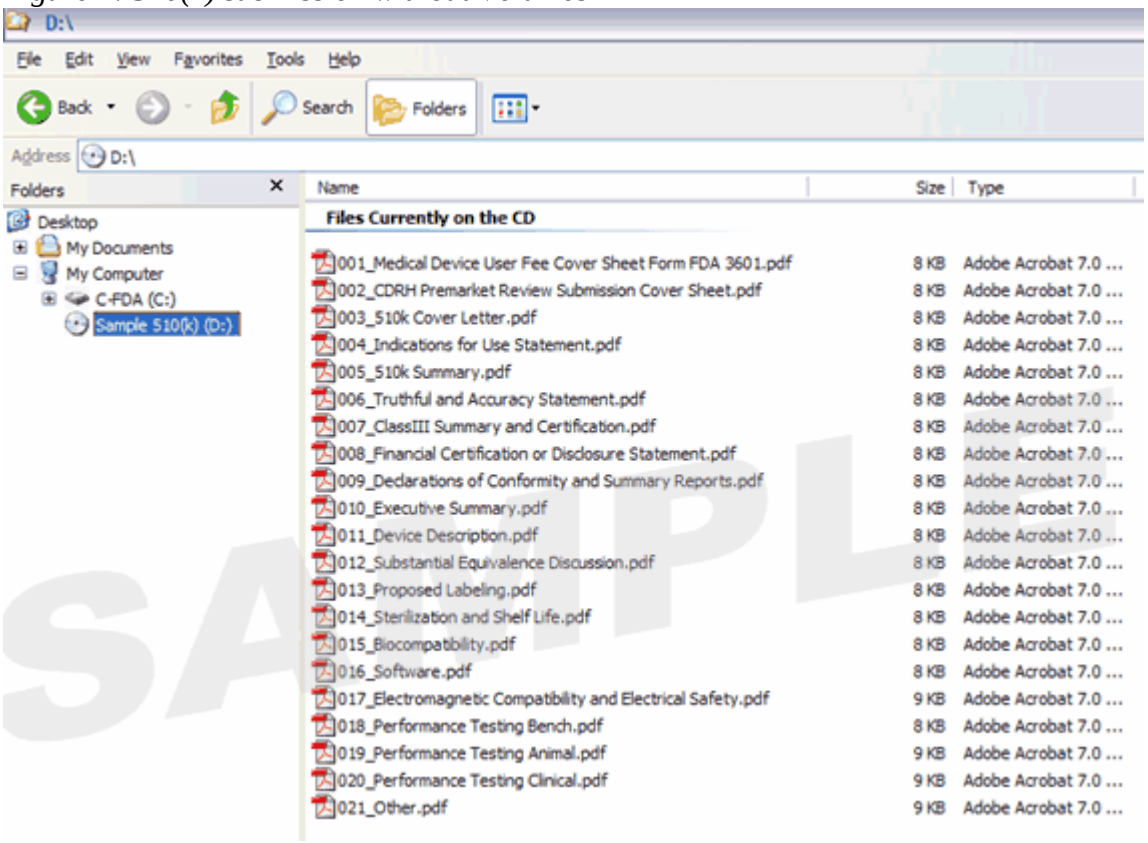


Figure 2: 510(k) submission without Volumes



The eCopy structure must match that of the paper version in order to facilitate the review of the submission. For example, if your paper submission has two volumes, each with 10 files, then the eCopy must have 2 volumes with the 10 files in each volume.

C. Folder naming convention for volume-based submissions that house PDF files

A naming convention is required in order to assure that the system can create a sort order of the folders that matches that of your paper submission. Each volume must be a folder with the following naming convention for the folder: **Vol_001 through Vol_999 or Vol_001_Descriptive Name through Vol_999_Descriptive Name (e.g., Vol_005_Patient Study Data)**. The volume numbering in a submission must be non-repeating consecutive numbers (e.g., 001, 002, 003). The limit for volumes is 999.

If a descriptive name is used for a folder, the folder name should be descriptive of its content and meaningful to the reviewer. The descriptive name can be up to 250 characters but must not contain special characters (e.g., tilde (~), asterisk (*), forward slash (/), backward slash (\), colon (:), question mark (?), single quotation mark (‘), double quotation mark (“), less than sign (<), greater than sign (>) or vertical bar (|)).

NOTE: If this folder naming convention is not followed for volume-based submissions, the eCopy will fail the loading process.

D. Adobe Acrobat PDF file format

The primary file format for an eCopy is Acrobat PDF because it ensures that no inadvertent changes occur to the submission. Use of Acrobat PDF also ensures that what a reviewer sees on the screen is the same as what has been submitted on paper. Choose a method for creating PDF documents that produces the best replication of a paper document. You can ensure that the paper copy is an exact duplicate of the eCopy by using a content rendering software to convert the Word document to a PDF version of the file. Once you have the final PDF version, simply print the PDF version for submission as the original paper copy.

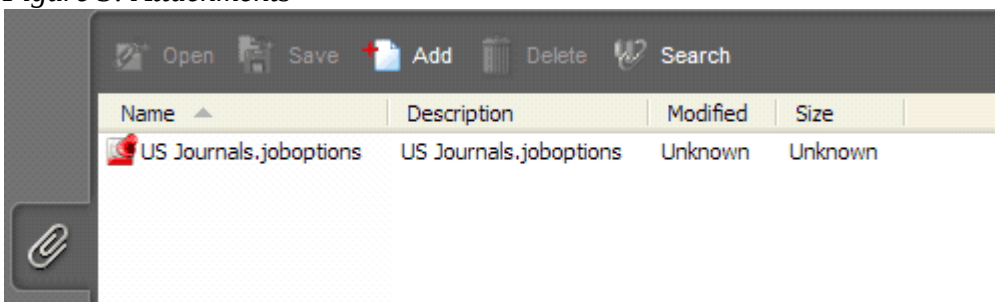
1. Adobe Acrobat PDF Version

Only eCopies submitted using Adobe Acrobat 10.0 or below will be accepted. Furthermore, security settings, attachments, embedded files, and plug-ins within Adobe Acrobat are not allowed and will cause the eCopy to fail the loading process.

2. No Attachments

eCopies submitted with attachments to the PDF files will not be accepted. Attachments must be removed before submittal. Many Acrobat PDF files created by a third party vendor, such as journal articles, user guides, and product labels, contain attachments which are embedded during the creation process. For example, see Figure 3 below, in which an attachment named "…joboptions" has been included. To detect attachments, open the Acrobat PDF and click the paper-clip icon in the lower left-hand corner of the Navigation Panel as shown in Figure 3 below.

Figure 3: Attachments



To remove the attachment:

- contact the vendor directly and ask that they create the Acrobat PDF without appending any attachments like the one shown above; or
- print the file selecting Adobe PDF as the Printer Name (see Figure 6). The file will be printed to a new Acrobat PDF file without the attachment.

Manually deleting this file will not delete the attachment attribute from the file entirely. Attachments will still be detected and cannot be processed by FDA systems.

3. No Security Settings

eCopies submitted with security settings will not be accepted. PDF files are stored as original documents and will not be altered from their original form. Remove any security settings, including read-only and password protection used on the files.

Refer to Section G. below for more details on creating PDF files.

E. Non-PDF file formats

In addition to PDF files, an eCopy may also include non-PDF files as described below. The inclusion of a "STATISTICAL DATA" and/or "MISC FILES" folder is optional for an eCopy.

1. Statistical Raw Data and Statistical Analysis Programs

Statistical information, including metadata[26] and data line listings, may be included in the eCopy in their native formats, such as, but not limited to: SAS; XPORT; XML; SGML; S-Plus; R files; ASCII; Molfiles; and Excel. **You must place all statistical and metadata files in a zip file(s) within a "STATISTICAL DATA" folder as shown in Figure 4 below. This folder must be spelled exactly as shown or it will cause the eCopy to fail the loading process.**

Figure 4: STATISTICAL DATA Folder

2. MISC FILES

Some submissions may require miscellaneous files (e.g., videos, x-rays, machine readable software source code) that cannot be submitted (or should not be submitted) in PDF format and are not statistical in nature. These miscellaneous files may be included in the eCopy in their native formats, such as, but not limited to: .gif; .tif; .jpg; .avi; .mpeg; .wmv; and .txt.

In addition, for the purposes of streamlining the review process, FDA encourages you to also include Word copies of certain documents or pieces of information provided in the main body of the PDF eCopy. Examples of documents or information that would be helpful to be provided in Word, in addition to the PDF format, include:

- Labeling for any submission;

[26] Metadata includes data dictionaries and terminologies, formats, annotated case report forms, statistical analysis details, and any other information that contributes to understanding and using the data.

- Predicate device comparison table for 510(k)s;
- 510(k) Summary;
- Summary of Safety and Effectiveness Data (SSED) for PMAs; and
- Summary of Safety and Probable Benefit (SSPB) for HDEs.

You must place all files in a zip file(s) within a "MISC FILES" folder as shown in Figure 5 below. This folder must be spelled exactly as shown or it will cause the eCopy to fail the loading process.

Figure 5: MISC FILES Folder

F. PDF file naming convention

A naming convention is required in order to assure that the system can create a sort order of PDF files, whether or not part of a volume-based submission, which matches that of your paper submission. You must use the following naming convention for all files (including files organized by volumes):

- Filenames must be named (begin with) with a three digit sequential number to ensure files are loaded and viewed in the proper order: **XXX_ descriptive file name.file extension**. The XXX represents a numeric sequence (e.g., 001, 002, 003) for which the files must be sequentially ordered in the table of contents.

- It is important to follow the file naming convention because it is used to order the submission in the correct sequence in each Center's official document repository. Therefore, a file name must not be repeated or deviate from the sequential order by using decimals.

- An example of a file name is as follows: XXX_descriptive file name.file extension (e.g., 013_Proposed Labeling.pdf).

- An **underscore** separates the sequential number from the descriptive file name.

- The descriptive file name can be up to 250 characters but **must not** contain special characters (e.g., tilde (~), asterisk (*), forward slash (/), backward slash (\), colon (:),

question mark (?), single quotation marks (‘), double quotation marks (“), less than sign (<), greater than sign (>) or vertical bar (|)). When possible, the file name should be descriptive of its content and meaningful to the reviewers.

- When appropriate, you may include the page numbers in the name of the file. This will assist the reviewer when one file cross-references another in a large set of files.

- For files that are organized as volumes, the file name is as follows: XXX_Vol X Name.file extension (e.g., 001_Vol 001 Administrative.pdf).

NOTE: If this file naming convention is not used for PDF files, the eCopy will fail the loading process.

G. PDF file size limit

An eCopy CD/DVD can have one or multiple files. There is not a limitation of the total size of the submission, but each PDF file must be limited to 50MB in file size. If a file size is greater than 50MB, then you must split the contents into multiple files and use the next number in the naming sequence.

NOTE: If this PDF file size limit is exceeded, the eCopy will fail the loading process.

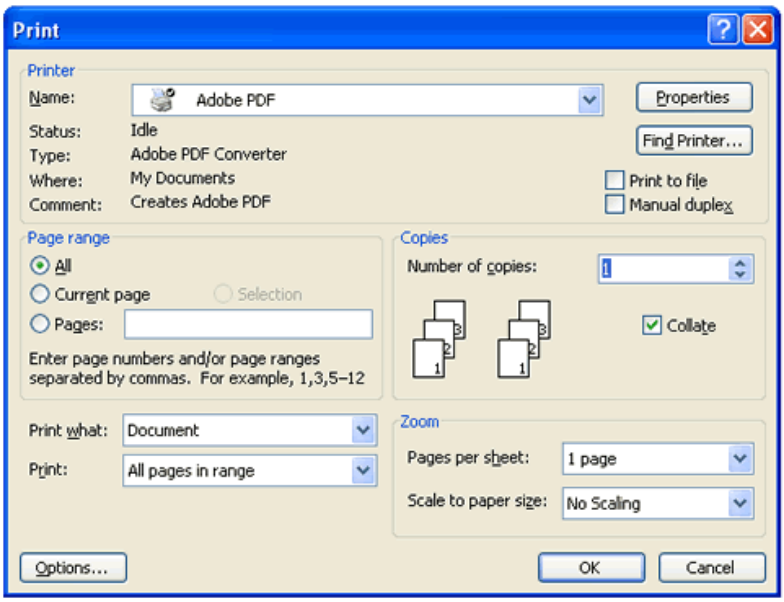
Please note that FDA is able to accept zip files that are larger than 50MB; however, we still recommend that the zip files included under the “STATISTICAL DATA” and “MISC FILES” folders be limited in size to 50MB or less in order to prevent potential problems, such as time delays when uploading the files.

H. Creating a PDF version from the source document

1. Example of Converting a MS Word Document to PDF

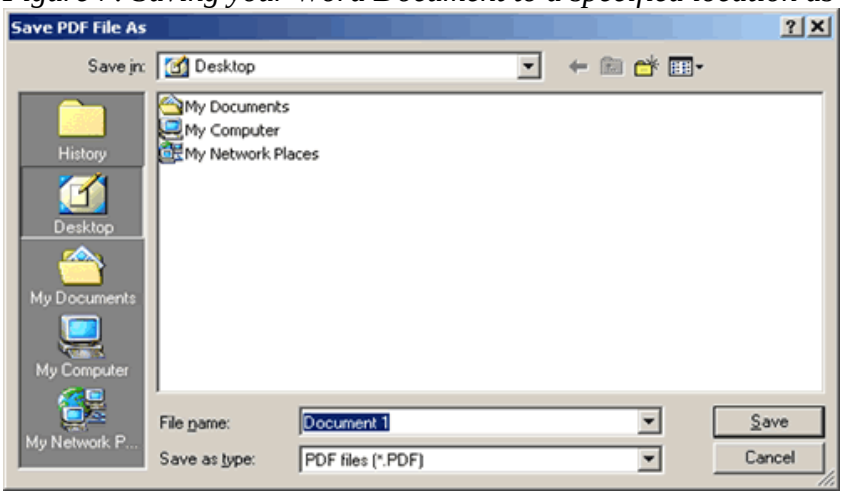
After you have completed your Word document (.doc format), you can easily create a PDF file using the same process you use to print documents. In Microsoft Word, instead of printing your document to a printer, you can select the Adobe PDF printer option from the drop down print menu, and create a new file. (See Figure 6.) Note that all figures in this section are using Adobe Acrobat 6.0; if you are using another version of Adobe Acrobat, the figures may be slightly different. The same basic steps can be used for files of other native formats. You may also use other PDF creation or PDF conversion options that are freely available on the web.

Figure 6: Selecting the Adobe PDF option under the Print Function



After you select Adobe PDF and press OK, you are prompted to save your document as a .pdf file and to select a location to save it. (See Figure 7.) Remember to use the correct naming convention. The PDF document will be stored in the location in which it was saved.

Figure 7: Saving your Word Document to a specified location as a PDF file



2. *Fonts*

PDF viewing software automatically substitutes a font to display text if the font used to create the text is unavailable on the reviewer's computer. Font substitution can affect a document's appearance and structure, and in some cases it can affect the information conveyed by a document. We cannot guarantee the availability of any one font. Therefore, you must embed all fonts you are using in the PDF files to ensure that those fonts will always be available to the reviewer. When embedding fonts, all characters for the font must be embedded (not just a subset of the fonts being used in the document). One problem associated with embedding fonts is that embedding requires additional computer storage space. Three techniques help to limit the

storage space taken by embedding fonts: (1) limit the number of fonts used in each document; (2) use only True Type or Adobe Type 1 fonts; and (3) avoid customized fonts.

Resizing a document because the contents are too small to read is inefficient. We believe that Times New Roman, 12-point font, is adequate in size for reading narrative text and we prefer this font. Although sometimes tempting for use in tables and charts, fonts smaller than 12 points should be avoided whenever possible. We recommend the use of a black font color. Blue font may be used for hypertext links. If a font color other than black is used, avoid light colors that do not print well on grayscale printers. It is advised that you test the color reproduction prior to submission by printing sample pages from the document using a grayscale printer. In addition to font colors, keep formatting simple in tables. When extracting a table from the PDF document, the use of light or white font color will not allow the transfer of text back into a Word document.

3. Page Orientation

Pages should be properly oriented. For example, you should set the page orientation of landscape pages to landscape prior to saving the PDF document in final form to ensure correct page presentation. Landscape pages (including tables) should be oriented such that the header of the document aligns with the left edge of the page and the footer of the document aligns with the right edge of the page.

4. Page Size and Margins

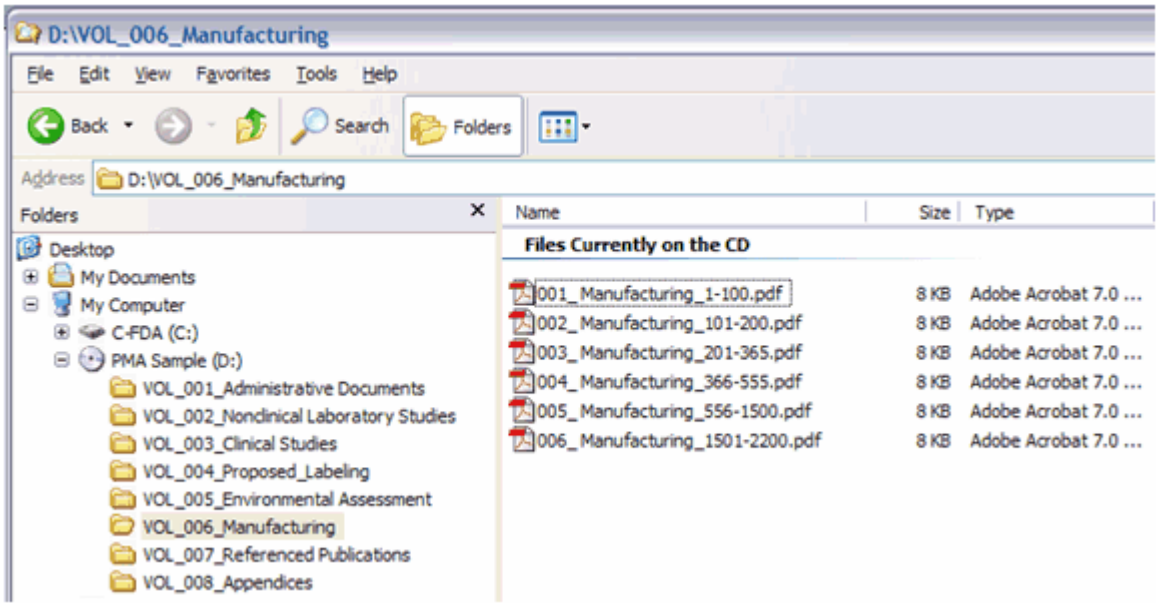
The print area for pages must fit on a sheet of paper that is 8.5 inches by 11 inches. You should allow a margin of at least 1 inch on all sides to avoid obscuring information if the pages are subsequently printed and bound.

5. Page Numbering

If a submission includes files divided into more than one PDF document, such files must have continuous pagination. To simplify navigation, make page numbers for the paper document and the PDF file the same. In order to ensure that the reviewer can locate information by using the page numbers as a reference (see Figure 8), when possible file names should reflects the pages involved (e.g., 001_Manufacturing_1-100.pdf must precede a file named 002_Manufacturing_101-200.pdf).

This format will also ensure that the pagination is consistent throughout the submission. For submissions organized in volumes, it is suggested that each volume be independently paginated, starting at page 1.

Figure 8: Example of a PMA submission with volumes and using page numbers in the file names



I. Bookmarks and hypertext links within PDFs

Bookmarks and hyperlinks within a single PDF file should be used to assist the reviewers in navigating through the content of the submission. If you use either bookmarks or hypertext links, consider the following:

- Bookmark references can be created for the heading of a section, subsection, or title of figures and tables within a single PDF file. In general, including a meaningful bookmark to the main table of contents for a submission or item is helpful, and will aid the reviewer in locating information and navigating the submission.

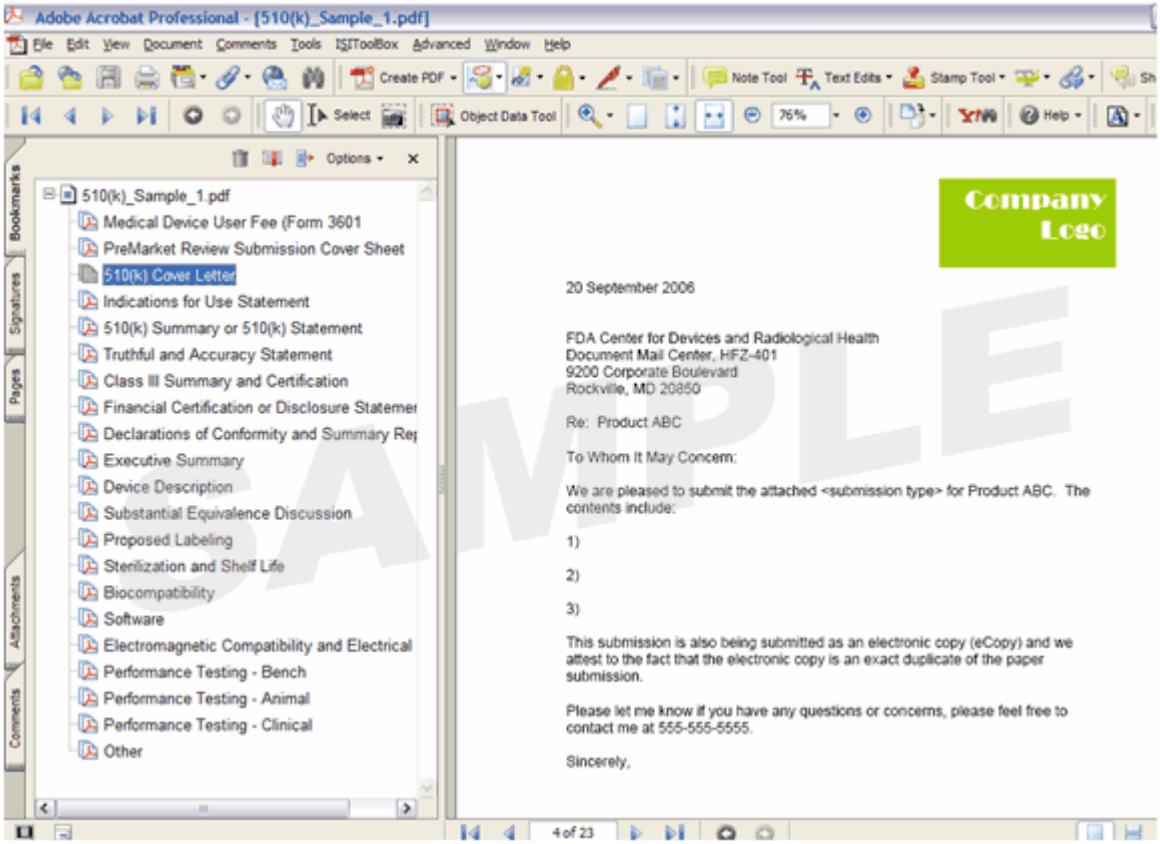
- Hyperlinks are used to improve navigation through individual PDF documents and are encouraged. Hyperlinks can be designated by rectangles using thin lines or by blue text or you can use invisible rectangles for hypertext links in a table of contents to avoid obscuring text. Hyperlinks throughout the body of the document to supporting annotations, related sections, references, appendices, tables, or figures that are not located on the same page are helpful and improve navigation efficiency.

  NOTE: Hyperlinks to other sections within an individual PDF document are permitted and maintained within a given PDF file when added to a Center's official document repository. However, hyperlinks from one PDF to another PDF file (or across other file types) are not supported and will not work.

- When creating bookmarks and hyperlinks, the magnification setting should be set to Inherit Zoom so that the destination page displays at the same magnification level that the reviewer is using for the rest of the document.

Figure 9 provides an example of a 510(k) structured in one PDF document with bookmarks.

Figure 9: Sample of a 510(k) structured in one PDF file with Bookmarks



J. PDFs created from scanning paper documents

The applicant should create all PDF versions directly from the source documents whenever feasible rather than by scanning. PDF documents produced by scanning paper documents are usually inferior to those produced from an electronic source document, such as MS Word. Scanned documents, particularly tables and graphs, are more difficult to read and do not allow the reviewers to search or copy and paste text for editing. **The use of scanned documents should be avoided if at all possible.** If scanning cannot be avoided, the following is highly recommended:

- Perform optical character recognition (OCR) on all scanned documents so that the text is searchable. Check to see that the content has been correctly converted by: (1) highlight an area of text and (2) search for a word or phrase. If the word or phrase is not returned in the search, then the OCR did not recognize the text.

- If the source document is only available on paper, it must be scanned at resolutions that will ensure the pages are legible both on the computer screen and when printed. At the same time, remember to limit the file size to be less than 50MB. We recommend scanning at a resolution of 300 dots per inch (dpi) to balance legibility and file size. We discourage the use of grayscale or color because of file size. After scanning, avoid re-sampling to a lower resolution.

- When creating PDF files containing images, you must not resample images. Re-sampling does not preserve all of the pixels in the original. For photographs, the image must be obtained with a resolution of 600 dpi. If black and white photos are submitted, consider 8-bit gray scale images. If color photos are submitted, consider 24-bit RGB Color Model images. A captured image should not be subjected to non-uniform scaling (e.g., sizing).

- Files with scanned images and photographs tend to be large in file size, so be careful not to exceed 50MB for a single file. Consider multiple files for these types of documents.

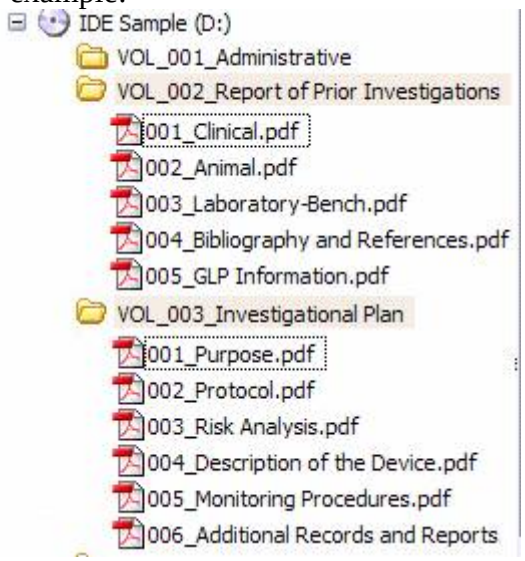
- Paper documents containing handwritten notes must be scanned at 300 dpi. These handwritten notes should be made in black ink for clarity.

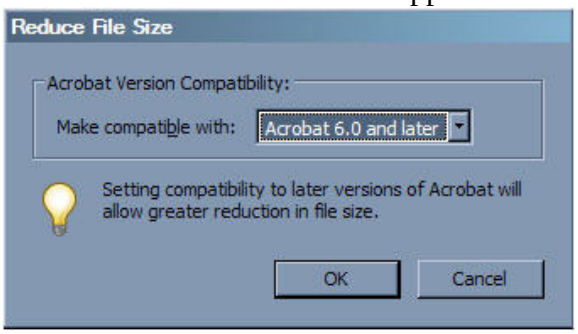
K. Common mistakes in creating an eCopy

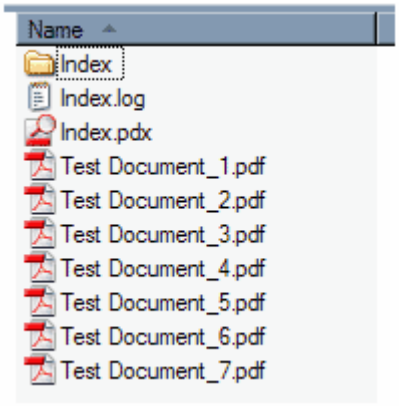
Many of the voluntary eCopies received to date have not been validated. Table 2, below, summarizes some of the common mistakes and suggested solutions.

Table 2: Common Mistakes in Creating an eCopy and Suggested Solutions

Common mistakes	Suggested solution
Cover letter does not include one of the required eCopy statements.	Provide a revised cover letter that includes one of the eCopy statements described in Section A of Attachment 1 above.
PDF Filenames do not follow the numbering convention. For example: • No numbering convention is used for the files and folders • The numbering deviates from the XXX numeric sequence order • Use of decimals in the numbering prefix (e.g., 004.4_Table of contents)	PDF Filenames should be named with the following convention: XXX_ plus name extension. The XXX represents a numeric sequence (e.g., 001, 002, 003) for which the files should be ordered in the table of contents. For example: • 001_Medical Device User Fee Cover Sheet FDA Form 3601.pdf • 002_Premarket Review Submission Cover Sheet.pdf • 003_Table of Contents.pdf • 004_Summary of Safety and Effectiveness.pdf • 005_Device Description.pdf Keep all files in sequential order; do not use decimals to organize the content. Create a new file and use the next number in the sequence.
Files contain security settings	Remove all Security settings on the PDF document(s).

Common mistakes	Suggested solution
Inappropriate use and naming of folders. For example: • Creation of subfolders • Creating subsections of a volume • Deviation from correct naming convention (e.g., Volume 1, Volume I) • Placement of one file in a folder to create a volume • Misspelling of "MISC FILES" and "STATISTICAL DATA" folders	Folders should be placed at the root (in the example below that is "IDE Sample") of the CD/DVD. **Content Volume Folders:** VOL_XXX. The XXX represents a numeric sequence (e.g., 001, 002, 003) for which the folders should be ordered in the table of contents. For example:  If only one file exists for a volume, it is suggested that you do not use volumes to organize your submission. For the **STATISTICAL DATA** and **MISC FILES** folders, there must not be any additional labels placed on this folder.
Subfolders within the volume folders, "STATISTICAL DATA" folder, and/or "MISC FILES" folders	Subfolders are not to be placed within a volume for any reason. If you believe a section requires further organization, consider creating a new volume for that section.

Common mistakes	Suggested solution
File sizes greater than 50MB (e.g., 250MB)	The submission content should be organized in volumes or by logical headings to reduce the overall size of each file. Always check file size before submitting your eCopy. To reduce the file size on a PDF document, complete the following steps: • Select **File | Reduce File Size** • The Reduce File Size window appears.  • • Click the **OK** button • The file size will be reduced, if possible. The reduction in file size varies from document to document. If this does not reduce the file size to less than 50MB, then the content in the document must be split into multiple PDF files.
Use of unsupported Adobe Acrobat functionality, specifically the packaging of multiple files in one PDF  	Our systems do not support attachments or embedded files within an Adobe Acrobat document. Please refrain from using this type of document packaging. The CD/DVD must contain individual files at the root level of the CD/DVD unless you are using the Volume folders.

Common mistakes	Suggested solution
Index Files are provided on the CD/DVD and linked to PDF documents, see below: 	FDA systems do not support the storage of index files and linkages within PDF documents. Please remove all Adobe Acrobat index folders and files, which are packaged as follows: • Index folder • Log file (.log) • Catalog Index File (.pdx)
Unallocated Space Files are placed on the CD/DVD	FDA systems do not support the processing of eCopies that have "unallocated space" files. This may be a byproduct of CD/DVD burning software. Please do not configure your CD/DVD burning software to consume the additional disk space on the CD/DVD.

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