

Guidance for Industry

How to Submit a Protocol without Data in Electronic Format to CVM

**(THIS VERSION OF THE GUIDANCE REPLACES THE VERSION MADE
AVAILABLE IN JUNE 2007)**

This guidance document describes how to submit protocols without data in electronic format for studies in support of New Animal Drug Applications to the Center for Veterinary Medicine (CVM). The guidance was revised to update the phone number for the Electronic Document Control Unit and to replace the web site to submit electronic comments.

Comments and suggestions regarding this document should be sent to 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>. All comments should be identified with the exact title of the document. Please note that on January 15, 2008, the FDA Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic submissions will be accepted by FDA through FDMS only.

For questions regarding this document, contact Margaret Zabriski, Center for Veterinary Medicine, (HFV-010), Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 240-276-9143, E-mail: margaret.zabriski@fda.hhs.gov.

According to the Paperwork Reduction Act of 1995, a collection of information should display a valid OMB control number. The valid OMB control number for this information collection is 0910-0524. The time required to complete this information collection is estimated to vary between 5 and 20 minutes per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection.

Table of Contents

I.	INTRODUCTION	3
II.	ORGANIZATION AND FORMAT OF PROTOCOL SUBMISSIONS	4
A.	Smart Form	4
B.	Cover Letter	4
C.	Protocol and Appendices	4
D.	Electronic format of PDF file	5
1.	Version	5
2.	Fonts.....	5
3.	Page Setup.....	5
4.	Hypertext Linking and Bookmarks.....	5
5.	Security	6
6.	Searching PDF Files	6
E.	Protocol Evaluation by CVM	6
III.	PROTOCOL FORM.....	6
IV.	CHECKLIST FOR SUBMITTING A PROTOCOL USING FORM FDA 3536.....	6

GUIDANCE FOR INDUSTRY¹

HOW TO SUBMIT A PROTOCOL WITHOUT DATA IN ELECTRONIC FORMAT TO CVM

This guidance represents the Agency's current thinking on how to submit a protocol without data in electronic format. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statute 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.

I. INTRODUCTION

This guidance provides advice to industry regarding the procedures to submit a protocol without data for non-clinical laboratory and effectiveness studies in electronic format to the Office of New Animal Drug Evaluation.

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

Protocols for non-clinical laboratory studies (safety studies) are required under 21 CFR 58.120. Protocols for adequate and well-controlled effectiveness studies are required under 21 CFR 514.117(b). Applicants may request that CVM review protocols for safety and effectiveness studies of new animal drugs. The review of protocols facilitates the drug review and approval processes.

Currently, CVM receives protocols in paper. CVM is publishing this guidance to give applicants the option to electronically submit a protocol without data to CVM.

Electronic submissions that follow this guidance will be compatible with CVM's current information technology capabilities. This will help ensure the confidentiality, integrity, security, and authenticity of data submitted to the Center. If a regulated applicant or

¹ This guidance has been prepared by CVM at FDA. For additional copies, access the document on the CVM Home Page (<http://www.fda.gov/cvm>), or send a request to the Communications Staff, HFV-12, 7519 Standish Place, Rockville, MD 20855.

CONTAINS NON-BINDING RECOMMENDATIONS

person wishes to use an electronic approach other than that set forth in this guidance document, the Center will, on request, discuss alternative methods of submitting information.

The electronic submission of protocols is part of the Center's ongoing initiative to provide a method for paperless submissions.

This document reflects the principles behind the Government Paperwork Elimination Act, Pub. L. No. 105-277, 112 Stat. 2681 (1998), which requires that executive agencies, by October 21, 2003, provide: (1) for the option of the electronic maintenance, submission, or disclosure of information, if practicable, as a substitute for paper; and (2) for the use and acceptance of electronic signatures when practicable.

This document contains specific instructions for submitting protocols electronically. **Guidance #108, "How to Submit Information in Electronic Format to CVM using the FDA Electronic Submission Gateway"**, contains general instructions and specifications on submitting information electronically to CVM. It is available on the CVM Home Page (<http://www.fda.gov/cvm>).

II. ORGANIZATION AND FORMAT OF PROTOCOL SUBMISSIONS

The protocol submission will contain a SMART FORM, cover letter, protocol, and any appendices. The cover letter, protocol and any appendices should be contained in one Portable Document Format (PDF) file (protocol file).

A. Smart Form

All applicable fields of the "Protocol for Non-clinical Laboratory and Effectiveness Studies" form (FORM FDA 3536) (SMART FORM) should be filled out. The form cannot be transmitted until all required fields are completed. The use of this SMART FORM allows for quality control of the information about the protocol and reduces the chance incomplete information will be submitted. The information requested on the form also allows the submitted material to be automatically logged into the Center's tracking system (Submission Tracking and Reporting System, known as STARS).

B. Cover Letter

If the applicant chooses to include a cover letter, it should be submitted as part of the PDF file in the order specified in step 2 of the Section III, "Checklist for Submitting a Protocol using form FDA 3536." The cover letter should be the first page of the protocol file.

C. Protocol and Appendices

The protocol must contain the elements described in 21 CFR 58.120 for safety studies and 21 CFR 514.117(b) for adequate and well-controlled effectiveness studies. Additional guidance for protocols for effectiveness studies is contained in

CONTAINS NON-BINDING RECOMMENDATIONS

Guidance for Industry: Good Clinical Practices: VICH GL9, Final Guidance, May 5, 2001.

D. Electronic format of PDF file

The following recommendations are intended to assist applicants in creating PDF files that are compatible with CVM's current information technology capabilities and to ensure the confidentiality, integrity, security, and authenticity of data submitted to the Center.

1. Version

CVM is currently using version 7.0 of Adobe[®] Acrobat[®] for review of electronic submissions. All PDF files submitted to CVM should be created using software that permits the Center to read, search, copy, and paste information from the PDF file into a word processing document using version 6.0 of Adobe[®] Acrobat[®].

2. Fonts

All fonts should be embedded in the PDF file to ensure that those fonts will always be available to the reviewer. Font substitution can affect a document's appearance and structure, and in some cases (for example, Greek letters) it can affect the information conveyed by a document. Therefore, all characters for the font and the subset of the characters should be embedded.

CVM recommends that the following settings be used for general text:

- Arial, 12-point font
- Black font color for general text
- [Blue](#) text for hyperlinks

3. Page Setup

The print area for pages should fit on a sheet of paper that is 8.5 inches by 11 inches.

4. Hypertext Linking and Bookmarks

Tools such as bookmarks and hypertext links enable the reviewer to move efficiently through the document.

Bookmarks should be provided for each item listed in the table of contents including all major section headings and subheadings. All tables, figures, publications, references, and appendices should also be bookmarked.

Hypertext links should be used to connect text to supporting annotations, related sections, references, appendices, tables, or figures that are not located on the same page as the text. Hypertext links should be designated by [blue text](#).

CONTAINS NON-BINDING RECOMMENDATIONS

When creating bookmarks and hyperlinks, you should choose the magnification setting *Inherit Zoom*. This allows the destination page to display at the same magnification level that the reviewer is using for the document.

The open dialog box sets the document view when the file is opened. The initial view of the PDF files should be *Bookmarks* and *Page*. You should set the *Magnification* and *Page Layout* to default.

5. Security

No security settings should be selected that would prevent printing, changes to the protocol, or selecting text and graphics. CVM's internal security and archival processes are designed to maintain the integrity of the submitted files.

6. Searching PDF Files

PDF files should be created in a manner that allows CVM to do full text searches. Because scanned images cannot be indexed, they cannot be searched and their use should be kept to a minimum.

E. Protocol Evaluation by CVM

The Center intends to transmit the results of its evaluation of the protocol to the applicant by a signed paper letter. Until the Center sets specific standards for the use of electronic signatures that meet the requirements of 21 CFR 11, all official responses will be in paper format, including letters intended to transmit the results of protocol evaluations.

III. PROTOCOL FORM

A copy of the Protocol for Nonclinical Laboratory and Effectiveness Studies Form (FORM FDA 3536) is available on the CVM Electronic Submission Page at <http://www.fda.gov/cvm/esubstoc.html>.

IV. CHECKLIST FOR SUBMITTING A PROTOCOL USING FORM FDA 3536

This checklist describes the process CVM recommends for creating a Portable Document Format (PDF) file using a word processing program, printing it to the Acrobat[®] Distiller, and submitting the information.

1. You should build the protocol file from source documents. Scanned PDF documents may be used for pages unavailable for word processing such as diagrams and observations forms but should be kept to a minimum.
2. The protocol file should contain in order: a cover letter (if you choose to submit one), the protocol, and any appendices. The cover letter, protocol, and any appendices should be converted into PDF files by printing the word processing documents using Acrobat[®] Distiller. Use the **Documents** → **Insert Pages** in Adobe

CONTAINS NON-BINDING RECOMMENDATIONS

Acrobat[®] to combine several PDF files into one file. After the file is constructed, the PDF file should be saved using **File** → **Save As**. All hyperlinks and bookmarks should be verified after creating the single PDF file. Document Information Fields of the PDF file may be filled out at the applicant's discretion.

3. Open the Protocol FORM FDA 3536.
4. Fill out the pertinent sections in Form FDA 3536. If the protocol has been previously submitted to CVM, provide the correct information in section I.3a and I.3b.
5. Select the "*Insert Comments*" button to add a PDF file containing any comments regarding the form.
6. Select the "*Insert Protocol*" button to add the protocol file created in steps 1 and 2. The form cannot be successfully validated unless a protocol file has been attached.
7. Once the form is completed, select the "*Validate*" button to verify all of the required fields are completed. Those fields that are required will be highlighted and must be completed before the form can be sent to CVM.
8. Select "*Save*" to save all information on the form.
9. Select the "*Signature*" button to digitally sign the form. Once the form is digitally signed, you cannot make any changes because all of the fields will be locked for editing.
10. Follow the steps outlined in **Guidance for Industry #108, Section IV.J – Sending a Submission to FDA CVM using the FDA ESG** to submit your form to CVM.
11. If you have not received a receipt from CVM by the third business day after you have sent the submission, call the Electronic Document Control Unit at 240-276-8584 to report the problem and find out whether your submission was received.