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Raw Data for Safety and Effectiveness Studies

Guidance for Industry

Draft Guidance

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For further information regarding this document, contact Steven Fleischer, Center for Veterinary Medicine (HFV-110), Food and Drug Administration, 7500 Standish Place, Rockville MD 20855, 240-402-0809, email: steven.fleischer@fda.hhs.gov.

Additional copies of this draft guidance document may be requested from the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville MD 20855, and may be viewed on the Internet at either https://www.fda.gov/animal-veterinary, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.regulations.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine (CVM)
April 2024

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I. Introduction

This guidance for industry provides information to animal drug sponsors (sponsors) on the use of raw data in the Center for Veterinary Medicine's (CVM, we) review of safety and effectiveness studies submitted in support of new animal drug applications.[1] This guidance also describes our recommendations for submitting raw data. In this guidance, when we refer to "submitting or submission of raw data," we mean copies of raw data, not the original documents. This guidance does not address documents that we do not consider raw data but expect to be included in a submission (e.g., final study report, protocols, protocol amendments, and contributing scientist reports).

We recommend that sponsors contact CVM's Office of New Animal Drug Evaluation to discuss the raw data they should include in their submission prior to submitting the study for review. We may request additional raw data and study documents if questions arise during review of the study data and final study report.

In general, FDA's guidance documents 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.

II. Background

In general, to legally market a new animal drug for its intended use, a sponsor must obtain approval of an application, a conditional approval of an application, or an index listing for the drug (see section 512(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)). Sponsors that submit an application for a new animal drug under section 512(b)(1)(A) of the FD&C Act should submit "full reports of investigations which have been made to show whether or not such

[1] Because bioequivalence may serve as a surrogate for safety and effectiveness, the principles in this document also apply to bioequivalence studies used for that purpose.

drug is safe and effective for use."[2] Sponsors should include the raw data to support these studies when they submit these full reports.

In this guidance, we use the term "raw data" as it applies to nonclinical (good laboratory practices for nonclinical laboratory studies (GLP)) and clinical (good clinical practice (GCP)) studies.

For GLP studies, 21 CFR 58.3(k) defines raw data as "any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a nonclinical laboratory study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature), the exact copy or exact transcript may be substituted for the original source as raw data. Raw data may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments."

For GCP studies, Guidance for Industry (GFI) #85 (VICH GL9), "Good Clinical Practice," defines raw data as "any original worksheets, calibration data, records, memoranda and notes of first-hand observations and activities of a study that are necessary for the reconstruction and evaluation of the study. Raw data may include, but are not limited to, photographic materials, magnetic, electronic or optical media, information recorded from automated instruments, and hand-recorded datasheets. Facsimile transmissions and transcribed data are not considered raw data."[3]

We consider raw data the first permanent recording of an observation and, whether handwritten or electronic, should be attributable, original, accurate, contemporaneous, and legible. Attributable means the raw data can be traced by signature (or initials) and date to the individual who observed and recorded the data. If more than one individual observes or records the raw data, that fact should be reflected in the data entries. In automated data collection systems, the individual(s) responsible for direct data input should record their name along with the date at the time of data input. Original and accurate means the raw data are the firsthand observations. Contemporaneous means the raw data are recorded at the time of observation. Legible means the raw data are readable and recorded in a permanent medium, e.g., ink for written records or electronic records that are unalterable.

III. Purpose of CVM's Review of Raw Data

Our review of raw data allows us to have confidence in the information upon which we make regulatory decisions. We do not rely solely on summaries of the data in the final study report(s)

[2] Applications for conditional approval are not subject to section 512(b)(1)(A) of the FD&C Act; however, they are subject to section 571(a)(2)(B) of the FD&C Act, which requires full reports of investigations that have been made to show whether or not such drug is safe under section 512(d) of the FD&C Act and there is a reasonable expectation of effectiveness for use. Section 572 of the FD&C Act contains the requirements for requesting that a new animal drug be determined eligible and added to the index listing.

[3] https://www.fda.gov/media/70333/download (May 2001).

because raw data provides support for reconstruction and evaluation of the study. We review the raw data to:

1. Confirm the accuracy of the final study report. The raw data should support the content of the final study report and the final study report should accurately reflect the raw data collected according to the study protocol. The audit trail should also be submitted if raw data were collected by an electronic data capture system.

2. Confirm the study was adequately conducted according to the applicable requirements or standards (i.e., GLP or GCP). Although a study report may include a statement indicating that GCP recommended standards or GLP requirements were followed, CVM will verify the study conduct by evaluating the raw data.

3. Evaluate the quality and integrity of the data collected during the study to ensure that the reported study results are accurate.

IV. How to Submit Raw Data

When submitting raw data in support of safety and effectiveness studies, sponsors should:

1. Submit raw data in electronic format through the eSubmitter platform.[4] If the raw data are first recorded on paper, sponsors should submit electronic scans of the paper records as optical character recognition (OCR) portable data files (PDFs). If the raw data are first recorded in a validated electronic data capture (EDC) system, then a copy of that raw data as one or more eXtensible Markup Language (XML) or SAS transport XPORT (XPT) file(s) is acceptable. In addition, copies of audit trails should be submitted (in XML or XPT). For additional information about file type formatting for raw data and audit trails, see our "Question and Answer Document for the Data Quality Webinar," updated April 2021.[5]

2. Describe how the raw data were collected (e.g., manually, or electronic data capture), including a record of all changes to the raw data, starting from the electronic data files created from transcribed case report forms or from EDC systems to the completed statistical analyses that form the basis for the study's conclusions. For additional information for documenting electronic data files and statistical analyses, see GFI #197, "Documenting Electronic Data Files and Statistical Analysis Programs."[6]

[4] https://www.fda.gov/industry/fda-esubmitter/cvm-esubmitter-programs.

[5] https://cacmap.fda.gov/media/147451/download (April 2021).

[6] https://www.fda.gov/media/75077/download (November 2020).