OFFICE OF NEW ANIMAL PRODUCT EVALUATION AND OFFICE OF GENERIC ANIMAL DRUGS REVIEWER'S CHAPTER

REVIEW OF RAW DATA FOR MARKER RESIDUE DEPLETION STUDIES TO SUPPORT A NEW ANIMAL DRUG APPLICATION

I. PURPOSE

This P&P document describes the raw data that are expected to be submitted with the final study report to the Office of New Animal Product Evaluation (ONAPE) for a marker residue depletion study to support a new animal drug approval. It does not affect what raw data should be generated or collected during the study conduct according to the protocol and the standard of conduct. It also does not affect what raw data CVM may ask sponsors to submit during the review of the study after the initial submission.

II. MARKER RESIDUE DEPLETION STUDIES

Sponsors submit copies of raw data from marker residue depletion studies conducted using the principles of Good Laboratory Practice (GLP) in the human food safety (HFS) technical section submission. Examples of marker residue depletion studies include:

- Tissue marker residue depletion studies
- Milk marker residue depletion studies
- Egg marker residue depletion studies
- Honey marker residue depletion studies

III. RAW DATA FOR MARKER RESIDUE DEPLETION STUDIES

A. Raw Data

Raw data are defined in 21 CFR Part 58.3(k) (Good Laboratory Practice for Nonclinical Laboratory Studies) 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."

CVM expects copies of certain raw data be submitted for evaluation. Copies of raw data include data collected manually on paper forms and data collected electronically via an electronic data capture system. The audit trails of electronic records must be submitted as part of the raw data for those electronic records. The sponsor should demonstrate how the collected data maintained the attributes of being attributable, legible, contemporaneous, original, and accurate (also known as ALCOA) throughout the internal handling of the data files through the submission of the data files to CVM for review.

CVM published a document that provides responses to questions asked by industry regarding data quality, including raw data and submissions to CVM. For additional information, please refer to the Question-and-Answer Document for the Data Quality Webinar held June 4 and 6, 2013 (UPDATED April 2021).[1]

B. Process Used to Determine ONAPE's List of Raw Data

ONAPE used a risk-based approach to determine which copies of raw data should be submitted to the HFS technical section.

In general, copies of raw data listed in Appendix 1 of this document are expected to be submitted with the final study report for a marker residue depletion study. However, situations may arise where additional raw data are required to be submitted to complete the review of the marker residue depletion study.

Reviewers may identify omissions, inconsistencies, or questions related to the raw data that should be addressed by the sponsor before ONAPE can complete the review of the studies and make scientific and regulatory decisions.

IV. REFERENCES

CVM Question and Answer Document for the Data Quality Webinar held June 4 and 6, 2013 (Updated April 2021) at https://www.fda.gov/media/147451/download.

V. VERSION HISTORY

July 30, 2025 – Original version.

[1] CVM Data Quality Webinar Q&A: https://www.fda.gov/media/147451/download

APPENDIX 1. COPIES OF RAW DATA EXPECTED TO BE SUBMITTED WITH THE FINAL STUDY REPORT FOR MARKER RESIDUE DEPLETION STUDIES

Table 1. Marker Residue Depletion study variables

General variable name	Definition
Animal Body Weights	Documentation of the weight of individual animals taken at protocol-defined times during the study using a calibrated scale and weights.
Physical Examinations	Documentation of the physical exam conducted by a veterinarian documenting the health status of an animal, usually conducted prior to assignment to the study to determine eligibility or as dictated by the protocol during the study to identify health problems. The veterinarian or scribe typically records notes on designated form. As needed, exams may be on a form or in the veterinarian's notes.
Clinical Observations	Documentation of original records of animal observations including routine daily observations and post-dosing observations. These are typically more detailed health evaluations than General (Daily) Health Observations and less detailed than physical examinations. These are not typically done by a veterinarian but done by an individual with some medical training such as a technician.
General Health Observations	Documentation of routine health checks for signs of ill health that include assessment of limited physical parameters (e.g., mortality/ moribundity checks).
Test and control article identification and characterization	Certificate of analysis for investigational drugs or a label for approved drugs
Dose Calculation and Preparation	Documentation of how doses were calculated and prepared (e.g., the actual dose calculation table that lists animal ID, body weight, calculated dose, etc.), batch preparation records and drug concentration assays (potency, homogeneity, stability).
Administered Dose	Documentation of how much dose was provided including treatment (e.g., when/where/how it was provided by injection, orally in food or water or as a bolus, applied, or infused, etc.) and data capture form for list of animals and an indication (check box, etc.) that each animal received its assigned dose per treatment group assignment, per body weight. For medicated feed and medicated water studies, documentation should include

	daily feed or water issuance and weighback and daily consumption records. For treatment by injection, documentation should include pre and post syringe weights.
Slaughter Records	Documentation of the slaughter method and time and date after last treatment that slaughter occurred.
Sample Collection	Documentation of time and date that samples were collected, the type of tissues collected including sample description (such as what part of liver tissue was collected), and tissue weights.
Tissue Sample Handling and Transfer	Documentation of chain of custody for sample integrity from collection to analysis: time at which samples are placed in the freezer after collection, temperature during transport, date and time of transport, temperature upon arrival at analytical lab, date and time when samples are placed in the freezer at the analytical lab.
Sample Storage Stability	Documentation of temperature during the storage period and duration of storage.
Sample Processing	Documentation of date and time of sample processing prior to analysis (e.g., when samples are removed from the freezer for processing and analysis). Documentation of the preparation of the final extract (before instrumental analysis) of a sample involving various manipulations (e.g., extraction, dilution, concentration) of the original study sample and any storage of the extract prior to analysis.
Preparation, storage, and stability of standard and fortification solutions	Documentation of the procedure for preparing, storing (including storage duration) and demonstrating stability of standard and fortification solutions and any testing to determine a standard is fit for use should be submitted.
Reference standard receipt and use	Documentation of receipt and use of the standard.
Special tests	Documentation of tests that are based on the individual drug and species, e.g., somatic cell count, equipment cleaning documentation for milk residue study, implant pay-out data.
Chromatograms	All chromatograms and parameters enabling verification of tissue residue values should be submitted. All run summary data tables of accepted and failed analytical runs should be submitted.

Documentation of deviations and amendments with copies of raw data to support the deviations and amendments.	Documentation of departures from the GLP and protocol before or during the conduct of the study including: • The date when an amendment/deviation occurred. • Description/explanation of the amendment/deviation (what happened?) • Was any action taken to address the deviation, if appropriate • Discussion of the impact on the study • Meets the basic standards we expect for all raw data, e.g., attributable, legible, contemporaneous, original, and accurate (ALCOA) Copies of the raw data where the documentation of departures from the GLP and/or protocol occurred during the conduct of the study.
Adverse Events	Documentation with descriptions of any observation in animals that is unfavorable and unintended and occur after the use of an article, whether or not considered to be product related.
Note to File	Documentation of study procedures that occur during the study which may affect study outcome or information relevant for reconstruction of the study.
Communication Records	Documentation of emails, summary of telephone calls, such as communication between the study director and contributing scientists, and Quality Assurance Unit for the study.