OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

ACCEPTABILITY OF SUBMISSIONS CONTAINING FOREIGN DATA TO SUPPORT SAFETY AND EFFECTIVENESS

I. PURPOSE

This document provides the general criteria used to determine whether data developed in foreign countries are acceptable and are in the proper format for submission.

II. SUBMISSION OF DATA

Section 569B of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as modified by the Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012, codifies FDA's longstanding practice of accepting foreign clinical data to support applications, provided the applicant demonstrates that the data are "adequate under applicable standards to support approval." CVM is committed to supporting global approvals in order to enhance animal drug development, facilitate the use of foreign data, and minimize the need to conduct duplicative studies. CVM also supports international harmonization activities that help leverage work and expertise from other expert authorities. All foreign data pertinent to evaluation of both safety and effectiveness must be submitted in the new animal drug application (NADA) as provided for in 21 CFR 514.1(b)(8)(iv), in an application for conditional approval of a new animal drug (CNADA), or to the investigational new animal drug (INAD) file. This requirement also applies to abbreviated new animal drug applications (ANADA) and generic INAD files. Applicants are required to submit data from investigations or commercial marketing outside the United States, if it is available to them, regardless of whether it is favorable or unfavorable.

CVM considers foreign data to be data generated outside of the United States both by entities based within or outside of the United States.

III. DETERMINING ACCEPTABILITY OF DATA FOR REVIEW

A. Is the Data Acceptable for Filing

The reviewer assigned the submission or the designated person will check that all foreign data submitted are in their original form and in English. All units of measurements should be consistent with the Imperial system of measurement (e.g., inches, pounds, and ounces/gallon), with the International System of units (SI Units) or acceptable SI derivatives (e.g., centimeters, kilograms, and

milligrams per milliliter), or a combination of both as appropriate (e.g., milligrams per pound.).[1] Raw data should be submitted as recorded (e.g., in kilograms, grams, pounds, etc.); however, all data for a specific variable should be converted to the same unit of measure for evaluation and documentation in the final study report (FSR). Unit conversion details should be provided in the FSR.

If the data do not meet these criteria, you may choose to refuse to file or refuse to review the submission.[2]

B. Evaluate Foreign Data Used to Support Safety and Effectiveness for the Following Criteria:

To consider the use of foreign investigational studies to support the effectiveness of a new animal drug, the studies should have the same data qualities and study integrity standards as expected from domestic studies. As with any study submitted to FDA, data is generally assessed by evaluating several factors including, but not limited to, those outlined below.

1. Non-clinical laboratory studies (safety): If we determine the foreign studies are satisfactory, they may be used to complete full NADA or ANADA requirements for non-clinical data for safety, and in the case of an ANADA, bioequivalence. Non-clinical laboratory studies submitted to support safety of a new animal drug must comply with good laboratory practice (GLP) regulations (21 CFR Part 58). Studies conducted under the Organization for Economic Co-operation and Development (OECD) GLP Guidelines (European GLPs) may be acceptable. There should be a statement accompanying the data that the study was conducted in compliance with GLP regulations, or if the study was not conducted in compliance with these regulations, a statement of the reason for noncompliance and its impact on the study. (See 21 CFR 514.1(b)(12)(iii)).

2. Effectiveness studies (conducted in the field): These studies must be conducted by personnel qualified by scientific training and experience to conduct such tests and include all the information required by 21 CFR 514.1(b)(8). Evaluate the data using the recommendations in the Good Clinical Practices guidance (CVM Guidance for Industry #85, VICH GL9).

3. Effectiveness studies (conducted in a laboratory): These studies may include dose confirmation studies or model studies submitted by the sponsor to support the effectiveness of a new animal drug. Although the GLP regulations in 21 CFR Part 58 do not apply to such studies, good clinical practices (GCP) principles are applicable to the conduct of these studies.

NOTE: Review any available inspection history in CVM's BIMO database for the foreign investigators and sites used in the study. If you cannot make a

[1] See ONADE Policy: Frequently Asked Questions about SI Units 12.16.14
Internal information redacted.

[2] See P&P 1243.2050

determination of validity, consider issuing an inspection request prior to accepting the data.[3]

C. Specific Considerations Regarding Foreign Effectiveness Field Studies

Because of differences in animal breeds, nutrition, husbandry practices, and disease, foreign field studies may not be acceptable to fulfill complete NADA requirements for effectiveness. The foreign data may, be used as a portion or all of the basis of approval, if the sponsor can show that the conditions of use are representative of those in the U.S. The sponsor should have justified or included a justification in the submission with the data addressing similarities and differences in the following areas between the U.S. and each foreign site.

- Conditions of use of the investigational drug product;
- The standard of practice of veterinary medicine with respect to any differences that may impact the study;
- Management and husbandry practices;
- Species, breeds, or classes used in the study;
- Bacterial strains, including target pathogen virulence, and target pathogen susceptibility to the investigational antimicrobial;
- Parasitic strains, including source, age, and susceptibility (if applicable); and
- Any other practices or conditions (if applicable) that could impact the study conduct or results.

If there are differences, the justification should address the impact of those differences on the study conduct or on an animal's response to the drug.

NOTE: For anthelmintics and antimicrobials, susceptibility, strains, and husbandry practices will likely vary across geographic locations, which may impact the acceptability of the data. For more information on anthelmintics, see Guidance for Industry #90.

IV. COMMUNICATING OUR FINDINGS WITH THE SPONSOR

Section 569B of the FD&C Act requires FDA to accept clinical data from foreign studies provided that those studies comply with applicable U.S. standards. There are many submission types that may contain foreign data. So, any determinations we make regarding the acceptability of the foreign data will be conveyed in the letter we issue in response to the submission received that contains that foreign data. It may be in the form of an acknowledgement letter, a technical section complete or incomplete letter, or some other formal piece of correspondence. If there is a template for the correspondence, you will use that to template.

[3] See P&P 1243.8220

V. REFERENCES

Federal Food, Drug, and Cosmetic Act

Section 569B

Code of Federal Regulations (Title 21)

Part 58 – Good Laboratory Practice for Nonclinical Laboratory Studies

Part 514 – New Animal Drug Applications

§ 514.1, Applications

CVM Guidance for Industry

85 – Good Clinical Practices, VICH GL 9

90 – Effectiveness of Anthelmintics: General Recommendations, VICH GL7

265 – Use of Data from Foreign Investigational Studies to Support Effectiveness of New Animal Drugs

CVM Program Policies and Procedure Manual

1243.2050 – Refuse to File and Refuse to Review

1243.8220 – Requesting a Bioresearch Monitoring (BIMO) Status Check

VI. VERSION HISTORY

January 26, 2009 –Original version of 1243.4068 prepared by the ONADE Policy and Procedures Maintenance Working Group. This original version replaces an older policy and procedure document titled 1240.3102 Use of foreign clinical and non-clinical data in an NADA.

May 9, 2018 – revised to include information about meeting our obligations under FDASIA and to be clear we will be communicating our findings regarding foreign studies submitted to support a technical section and approval. Also, reorganized some existing information in the P&P.

July 14, 2020 – revised to align with the recent publication of draft GFI #265 Use of Data from Foreign Investigational Studies to Support Effectiveness of New Animal Drugs