ADUFA Reauthorization Performance Goals and Procedures – FYs 2019 thru 2023

The goals and procedures of the FDA Center for Veterinary Medicine (CVM) as agreed to under the "Animal Drug User Fee Amendments of 2018" are summarized as follows:

I. Definitions

1. For the application/submission goals below, the term "review and act on" is understood to mean the issuance of a complete action letter after the complete review of an animal drug application, supplemental animal drug application, or investigational animal drug submission which either (1) approves an animal drug application or supplemental application or notifies a sponsor that an investigational animal drug submission is complete or (2) sets forth in detail the specific deficiencies in such animal drug application, supplemental animal drug application, or investigational animal drug submission and, where appropriate, the actions necessary to place such an application, supplemental application, or submission in condition for approval. Within 30 days[1] of submission, FDA shall refuse to file an animal drug application, supplemental animal drug application, or their reactivation, which is determined to be insufficient on its face or otherwise of unacceptable quality for review upon initial inspection as per 21 CFR 514.110. Thus, the Agency will refuse to file an application containing numbers or types of errors, or flaws in the development plan, sufficient to cause the quality of the entire submission to be questioned to the extent that it cannot reasonably be reviewed. Within 60 days of submission, FDA will refuse to review an investigational animal drug submission which is determined to be insufficient on its face or otherwise of unacceptable quality upon initial inspection using criteria and procedures similar to those found in 21 CFR 514.110. A decision to refuse to file an application or to refuse to review a submission as described above will result in the application or submission not being entered into the cohort upon which the relevant user fee goal is based. The Agency will keep a record of the numbers and types of such refusals and include them in its annual performance report.
2. A minor amendment is understood to mean information requested by FDA during the review of the application or investigational submission. FDA may request minor amendments to animal drug applications, supplemental animal drug applications, and investigational animal drug submissions during its review of the application or submission. At its

[1] All references to “days” in this document are to calendar days, unless otherwise specified.

discretion, the Agency may extend an internal due date (but not a user fee goal) to allow for the complete review of an application or submission for which a minor amendment is requested. If a pending application is amended with significant changes, the amended application may be considered resubmitted, thereby effectively resetting the clock to the date FDA received the amendment. The same policy applies for investigational animal drug submissions.

3. The term "submission date" means the date the FDA Center for Veterinary Medicine (CVM) Electronic Submission System (ESS) receives an application or submission. Upon receipt of an application or submission, the CVM ESS creates an electronic receipt that contains the date of receipt and is sent to the submitter.
4. The term "labeling supplement" is understood to mean certain applications as described in 21 CFR 514.8(c)(2)(i)(A) and (D) that require approval of a supplemental application prior to distribution of the drug made using the change.
5. The term "presubmission conference" (PSC) is understood to mean one or more conferences between a potential applicant and FDA as described in 21 CFR 514.5 to reach a binding agreement establishing a submission or investigational requirement.
6. The term "dosage characterization" is understood to mean a justification of the dosage (dose or dose range, dosing frequency, and the dosing duration) and a characterization of the critical aspects of the dose-response relationship related to each intended use and associated conditions of use.

II. Application/Submission Goals

Beginning October 1, 2018, all applications and submissions under the Federal Food, Drug, and Cosmetic Act (FD&C Act) section 512(b) and 571 must be created using the eSubmitter tool and submitted to the Agency through CVM's ESS.

1. Original New Animal Drug Applications (NADAs)

Review and act on 90 percent of original NADAs within 180 days after the submission date.

An application is incomplete if it would require additional data or information to enable the Agency to complete a comprehensive review of the application and reach a decision on the issue(s) presented in the application.

The Agency will review and act on 90 percent of reactivated applications:

i Within 180 days after the reactivated NADA submission date if the Agency determines and notifies the sponsor that the deficiencies are substantial;

ii Within 135 days after the reactivated NADA submission date if the Agency determines and notifies the sponsor that the deficiencies are not substantial; and the NADA reactivation must be submitted no more than 120 days after the Agency's dated incomplete letter to qualify for the shorter review time; and

iii Within 180 days after the reactivated NADA submission date if the NADA reactivation is submitted after 120 days of the Agency's dated incomplete letter or new substantial information is provided in the reactivated application.

The Agency will generally favor using the shorter reactivation timeframe of 135 days, where possible. The Agency will state in the incomplete letter the appropriate timeframe for review of the reactivation. Sponsors wishing to discuss the selected timeframe should contact the Agency prior to reactivation of the application. The shorter review time of 135 days for reactivated NADAs for which the deficiencies are determined not to be substantial is not intended to prevent the use of minor amendments during Agency review of an application.

2. Administrative NADAs

Review and act on 90 percent of administrative NADAs (NADAs filed after all scientific decisions already have been made as part of the investigational new animal drug process) within 60 days after the filing date.

3. Non-manufacturing Supplemental Animal Drug Applications

Review and act on 90 percent of non-manufacturing supplemental animal drug applications (i.e. supplemental animal drug applications for which safety or effectiveness data are required) within 180 days after the submission date.

A supplemental application is incomplete if it would require additional data or information to enable the Agency to complete a comprehensive review of the supplement and reach a decision on the issue(s) presented in the supplement.

The Agency will review and act on 90 percent of reactivated supplements:

i Within 180 days after the reactivated supplemental NADA submission date if the Agency determines and notifies the sponsor that the deficiencies are substantial;

ii Within 135 days after the reactivated supplemental NADA submission date if the Agency determines and notifies the sponsor that the deficiencies are not substantial; and the reactivation to the supplemental application must be submitted no more than 120 days after the Agency's dated incomplete letter to qualify for the shorter review time; and

iii Within 180 days after the reactivated supplemental NADA submission date if the reactivation to the supplemental application is submitted after 120 days of the Agency's dated incomplete letter or new substantial information is provided in the reactivated supplement.

The Agency will generally favor using the shorter reactivation timeframe of 135 days, where possible. The Agency will state in the incomplete letter the appropriate timeframe for review of the reactivation. Sponsors wishing to discuss the selected timeframe should contact the Agency prior to the reactivation of the supplement. The shorter review time of 135 days for reactivated supplements for which the deficiencies are determined not to be substantial is not intended to prevent the use of minor amendments during Agency review of a supplemental application.

4. Prior Approval Manufacturing Supplemental NADAs and Reactivations

Review and act on 90 percent of Prior Approval manufacturing supplemental NADAs within 120 days after the submission date. A Prior Approval manufacturing supplemental NADA includes: one or more major manufacturing changes as described in 21 CFR 514.8(b)(2)(ii) and in accordance with Guidance for Industry 83 (Chemistry, Manufacturing, and Controls Changes to an Approved NADA or ANADA); and, changes submitted as "Supplement-Changes Being Effected in 30 Days" that require prior approval according to 21 CFR 514.8(b)(3)(v)(A). If a Prior Approval supplement does not clearly identify any major manufacturing changes, the Prior Approval supplement will be designated by the Agency as a "Supplement-Changes Being Effected" with a 180 days review goal (see "Supplement-Changes Being Effected Manufacturing Supplemental NADAs and Reactivations" below).

A submission is incomplete if it requires additional data or information to enable the Agency to complete a comprehensive review of the submission and reach a decision on the issue(s) presented in the submission. If the Agency determines that the deficiencies are not substantial for manufacturing supplements requiring prior approval, the Agency will allow the manufacturing supplements to be resubmitted as "Supplement-Changes Being Effected in 30 Days" as described in 21 CFR 514.8(b)(3) and the drug made with the change can be distributed 30 days after the

resubmission according to 21 CFR 514.8(b)(3)(iv). The Agency will review and act on 90 percent of these reactivated manufacturing supplements within 180 days after the resubmission date of a complete submission. If the Agency determines that the deficiencies remain substantial or new substantial information is provided, prior-approval is required according to 21 CFR 514.8(b)(3)(v)(A). The Agency will review and act on 90 percent of these reactivated manufacturing supplements within 120 days after the resubmission date of a complete submission.

5. Supplements – Changes Being Effected Manufacturing Supplemental NADAs and Reactivations

Review and act on 90 percent of "Supplement- Changes Being Effected" manufacturing supplemental NADAs and reactivations submitted according to 21 CFR 514.8(b)(3)(vi) and in accordance with Guidance for Industry 83 (Chemistry, Manufacturing, and Controls Changes to an Approved NADA or ANADA), including manufacturing changes not requiring prior approval according to 21 CFR 514.8(b)(3) within 180 days after the submission date.

6. Investigational New Animal Drug (INAD) Study Submissions

Review and act on 90 percent of INAD study submissions within 180 days after the submission date.

An INAD study submission is incomplete if it would require additional data or information to enable the Agency to complete a comprehensive review of the submission and reach a decision on the issue(s) presented in the submission.

The Agency will review and act on 90 percent of resubmissions:

i Within 180 days after the resubmitted INAD study submission date if the Agency determines and notifies the sponsor that the deficiencies are substantial;

ii Within 60 days after the resubmitted INAD study submission date if the Agency determines and notifies the sponsor that the deficiencies are not substantial; and the resubmission must be submitted no more than 120 days after the Agency's dated incomplete letter to qualify for the shorter review time; and

iii Within 180 days after the resubmitted INAD study submission date if the resubmission is submitted after 120 days of the Agency's dated incomplete letter or new substantial information is provided in the resubmission.

The Agency will generally favor using the shorter resubmission timeframe of 60 days, where possible. The Agency will state in the incomplete letter the appropriate timeframe for review of the resubmission. Sponsors wishing to discuss the selected timeframe should contact the Agency prior to resubmitting the application. The shorter review time of 60 days for resubmissions for which the deficiencies are determined not to be substantial is not intended to prevent the use of minor amendments during Agency review of a submission.

Review and act on 90 percent of microbial food safety hazard characterization submissions within 100 days after the submission date.

7. INAD Protocols without Data Submissions

Review and act on 90 percent of INAD submissions consisting of protocols without data, that the Agency and the sponsor consider to be an essential part of the basis for making the decision to approve or not approve an NADA or supplemental NADA, within 50 days after the submission date.

An INAD protocol without data submission is incomplete if it would require additional information to enable the Agency to complete a comprehensive review of the protocol and reach a decision on the issue(s) presented in the protocol.

The Agency will review and act on 90 percent of resubmitted INAD protocol without data submissions:

i Within 50 days after the resubmission date if the Agency determines and notifies the sponsor that the deficiencies are substantial;

ii Within 20 days after the resubmitted INAD protocol without data submission date if the Agency determines and notifies the sponsor that the deficiencies are not substantial; and the resubmission must be submitted no more than 120 days after the Agency's dated non-concurrence letter to qualify for the shorter review time; and

iii Within 50 days after the resubmission date if the resubmission is submitted after 120 days of the Agency's dated non-concurrence letter or new substantial information is provided in the resubmission.

The Agency will generally favor using the shorter resubmission timeframe of 20 days, where possible. The Agency will state in the non-concurrence letter the appropriate timeframe for review of the resubmission. Sponsors wishing to discuss the selected timeframe should contact the Agency prior to resubmission of the protocol without data. The shorter review time of 20 days for resubmitted INAD protocol without data submissions for which

the deficiencies are determined not to be substantial is not intended to prevent the use of minor amendments during Agency review of a submission.

Sponsors are not required to submit study protocols for review. However, for each protocol voluntarily submitted prior to the commencement of the study that the Agency and the sponsor consider to be an essential part of the basis for making the decision to approve or not approve an animal drug application or supplemental animal drug application, the Agency will issue a complete action letter providing comments resulting from a complete review of the protocol. The complete action letter will be as detailed as possible considering the quality and level of detail of the protocol submission; will include a succinct assessment of the protocol; and will state whether the Agency agrees, disagrees, or lacks sufficient information to reach a decision that the protocol design, execution plans, and data analyses are adequate to achieve the objectives of the study.

If the Agency determines that a protocol is acceptable, this represents an agreement that the data generated by the protocol can be used to support a safety or effectiveness decision regarding the subject animal drug. The fundamental agreement is that having agreed to the design, execution, or analyses proposed in protocols reviewed under this process, the Agency will not later alter its perspectives on the issues of design, execution, or analyses unless the Agency by written order determines that a substantiated scientific requirement essential to the assessment of the study appeared after the Agency's protocol assessment, or public or animal health concerns unrecognized at the time of protocol assessment under this process are evident.

The Agency will permit comparability protocols as described in 21 CFR 514.8(b)(2)(v) to be submitted as protocols without substantial data in an INAD file. The Agency will review and act on 90 percent of INAD submissions consisting of protocols without substantial data within 50 days after the submission date of the protocol. For potentially more complex comparability protocols, for example sterile process validation protocols, the sponsor should discuss and have Agency concurrence regarding the appropriate filing strategy.

8. Labeling Supplements

Review and act on 90 percent of qualifying labeling supplements as described in 21 CFR 514.8(c)(2)(i)(A) and (D) within 60 days after the submission date. Qualifying labeling supplements are defined as those for which the sponsor provides and certifies a complete list of label changes made in the application and that CVM can determine upon initial review do not decrease the safety of drug use.

The Agency will review and act on 90 percent of non-qualifying labeling supplements within 180 days after the submission date.

Additional Performance Goals

Work Queue Review Procedures

The Agency will review all submissions in accordance with procedures for working within a queue. An application/submission that is not reviewed within the applicable Application/Submission Goal time frame (noted above) will be reviewed with the highest possible priority among those pending.

III. Pre-Approval Foreign Inspections

The Agency and regulated industry are committed to improving the review and business processes that will facilitate the timely scheduling and conducting of pre-approval inspections (PAIs). To improve the timeliness and predictability of foreign PAIs, sponsors may voluntarily submit 1) at the beginning of the calendar year, a list of foreign manufacturing facilities that are specified in an animal drug application, supplemental animal drug application, or investigational animal drug submission and may be subject to foreign PAIs for the following fiscal year; and 2) a notification 30 days prior to submitting an NADA, a supplemental NADA, or INAD submission that informs the Agency that the application/submission includes a foreign manufacturing facility. Should any changes to the annual list occur after its submission to the Agency, the sponsor may provide the updated information to the Agency.

The Agency will keep a record of the number of foreign PAIs conducted for new animal drug applications, along with the average time for completing the PAIs, and include this information in its annual performance report. The time for completing the PAI is understood to mean the time from the inspection scheduling request through notification to the Center of inspectional findings.

IV. Foreign GMP Inspections

The Agency commits to working to implement the US-EU GMP Inspection Mutual Recognition Agreement starting in FY 2019 for establishments manufacturing animal/veterinary drugs. The Agency will provide annual progress updates to the industry.

1. Supporting Information for Presubmission Conferences and INAD Protocols without Data Submissions

The Agency and the regulated industry agree that data and/or information which uniquely describes the general attributes of the new animal drug (e.g. the known characteristics of the drug that can impact safety,

effectiveness and/or quality) needs to be submitted early in the new animal drug development process in order to enable the parties to reach agreement at a presubmission conference or to begin review of a protocol. The intent of this provision is to avoid the submission of data or information between the presubmission conference and the submission of a protocol. Eligibility both for short justifications in protocols and for concurrent supporting data and protocol review described below is predicated on the sponsor submitting information early in the new animal drug development process.

The Agency will allow for the inclusion of this data and/or information in presubmission conferences; however it would not preclude holding a presubmission conference without such data.

The Agency will allow short justifications within INAD protocols without data submissions that are limited in scope (e.g., no more than ten pages or no more than two (peer-reviewed) journal articles).

The Agency will allow for the concurrent submission of supporting data (INAD H submissions) and protocols (INAD E submissions) provided that the protocol is not submitted until the supporting data has been in the Agency's queue for at least 50 days.

2. Dosage Characterization

The Agency and the regulated industry agree that dosage characterization is part of the effectiveness technical section of an investigational new animal drug file. In instances where data and/or information about the dosage is integral to the review of a protocol, the Agency and the regulated industry agree that this data and/or information should be submitted as supporting data (INAD H submission) well in advance of the protocol submission. Such information may be needed to ensure selection of optimal study time points and would be particularly important for novel drugs and drugs with modified-release characteristics.

3. Animal Drug Availability Act (ADAA) Combination Medicated Feeds Applications

Review and act on 90 percent of qualifying ADAA Combination Medicated Feeds Applications within 60 days after the submission date. An ADAA combination application will qualify for the 60 day review timeframe only if the following criteria are met:

i. The regulatory requirements for an ADAA combination application have been met as outlined in 21 CFR 514.4(c)(2)(ii)

ii. A presubmission conference has been conducted and either:

a. No data are needed (i.e., no tissue residue non-interference study is required) and this is documented in the memorandum of conference for the presubmission conference; or
b. A justification for not conducting a tissue residue non-interference study has been submitted, reviewed and found acceptable under an INAD, prior to the submission of the ADAA combination application; or
c. A tissue residue non-interference study has been submitted, reviewed and found acceptable under an INAD, prior to the submission of the ADAA combination application.

iii. No effectiveness or target animal safety data are required.

iv. No manufacturing data requirements- sponsor can address in meeting assay non-interference, but data submission is not required.

v. All other information is referenced to previous drug experience reports.

vi. Sponsor makes submission and it includes: Bluebird labeling, Veterinary Feed Directive (if applicable).

vii. Includes a request for categorical exclusion from the need to prepare an environmental assessment (EA); i.e., no EA required.

viii. Reference to presubmission conference.

ix. Right of reference (if applicable) to NADA(s) not owned by the filing sponsor of the ADAA combination application has been received by the Agency.

Review and act on 90 percent of ADAA combination applications within 100 days for those applications initially accepted for the 60-day timeframe but subsequently determined to need minor amendments.

If any of the above conditions cannot be met, the ADAA combination application will be given a 180-day review timeframe and placed in the original NADA application cohort.

4. Categorical Exclusions

Review and act on 90 percent of resubmissions of a previously completed Environmental Impact technical section within 60 days after the resubmission date where:

i. A Categorical Exclusion was issued; and

ii. All other technical sections have been submitted; and

iii. Information contained in the other technical sections reveals a change in the conditions of use of the drug that may affect the previous determination of categorical exclusion.

5. Presubmission Conferences

Conduct 90% of qualifying presubmission conferences within a 60-day timeframe when all of the following conditions are met:

i. All background materials, including presentations, have been submitted, and

ii. A complete agenda has been agreed upon by the Agency and the sponsor

A sponsor and the Agency can mutually agree to exclude a particular presubmission conference from this performance goal. If a sponsor accepts a date beyond the 60-day timeframe for their scheduling purposes or is unable to meet with the Agency on Agency available dates, the submission will be excluded from the presubmission conference cohort.

6. Tissue Residue Method

Commence 90% of tissue residue method demonstrations within 120 days of completion of the “3-hour meeting” process or equivalent process milestone where there is a single laboratory validation tissue residue method demonstration.

V. Workload Adjustment

The workload adjustment will continue to be calculated per CVM Program Policy and Procedures Manual 1243.3022, except that, for purposes of calculating the workload adjustment, it has been agreed to reset the base years to FY 2014- FY 2018. There will be no workload adjustment for FY 2019. Workload adjustments are one-time adjustments, and are calculated annually.