Animal Drug User Fee Act Reauthorization Performance Goals and Procedures – Fiscal Years 2014 Through 2018

The goals and procedures of the FDA Center for Veterinary Medicine (CVM) as agreed to under the "Animal Drug User Fee Amendments of 2013" are summarized as follows:

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 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 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 “end-review amendment” is understood to mean an amendment to an animal drug application, supplemental animal drug application, or investigational

animal drug submission that is requested by the Agency after it has completed its review of the submitted information and determines that the submission of additional non-substantial data or information would likely complete the application or submission. This term does not include minor amendments requested by the Agency during review of applications or submissions that do not impact upon the user fee goals, as described in Definitions paragraph 2 above.

4. The term "submission date" is understood to mean the date CVM's Document Control Unit (either electronically through FDA's electronic submissions gateway or via paper) receives an application or submission.
5. 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.
6. The term "presubmission conference" 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.
7. 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.

I. Performance Goals for Fiscal Year 2014

Non-administrative Animal Drug Applications

1. The Agency will review and act on 90 percent of non-administrative animal drug applications and reactivations of such applications within
   i. 180 days after the submission date (Day 180) if the Agency determines that the application is complete or incomplete. An application is incomplete if it would require substantial data or information to enable the Agency to complete a comprehensive review of the application and reach a decision on the approvability of the application; or
   ii. 220 days after the submission date if the Agency determines that the submission of additional non-substantial data or information would likely complete the application and electronically requests an end-review amendment to the application on or before Day 180, but the sponsor fails to file such amendment on or before Day 210. If a sponsor files an amendment after Day 210, then the amendment is ineligible for consideration as an end-review amendment, the extended performance goal (345 days) will not apply, and a complete action letter will be issued by Day 220 for the original application; or
   iii. 345 days after the submission date if the Agency electronically requests an end-review amendment to the application on or before Day 180 and the sponsor files an end-review amendment on or before Day 210.

2. The end-review amendment procedure is not intended to prevent the use of minor amendments as described in Definitions, paragraph 2. above during Agency review of a non-administrative animal drug application.

Non-manufacturing Supplemental Animal Drug Applications

1. The Agency will 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) and reactivations of such supplemental applications within
    i. 180 days after the submission date (Day 180) if the Agency determines that the application is complete or incomplete. An application is incomplete if it would require substantial data or information to enable the Agency to complete a comprehensive review of the application and reach a decision on the approvability of the application; or
    ii. 220 days after the submission date if the Agency determines that the submission of additional non-substantial data or information would likely complete the application and electronically requests an end-review amendment to the application on or before Day 180, but the sponsor fails to file such amendment on or before Day 210. If a sponsor files an amendment after Day 210, then the amendment is ineligible for consideration as an end-review amendment, the extended performance goal (345 days) will not apply, and a complete action letter will be issued by Day 220 for the original application; or
    iii. 345 days after the submission date if the Agency electronically requests an end-review amendment to the application on or before Day 180 and the sponsor files an end-review amendment on or before Day 210.
2. The end-review amendment procedure is not intended to prevent the use of minor amendments during Agency review of a supplemental new animal drug application as described in Definitions, paragraph 2. above.

Investigational Animal Drug Study Submissions

1. The Agency will review and act on 90 percent of investigational animal drug study submissions within
    i. 180 days after the submission date (Day 180) if the Agency determines that the submission is complete or incomplete. A submission is incomplete if it would require substantial data or information to enable the Agency to complete a comprehensive review of the study submission and reach a decision on the issue(s) presented in the submission; or
    ii. 220 days after the submission date if the Agency determines that the submission of additional non-substantial data or information would likely complete the submission and electronically requests an end-review amendment to the submission on or before Day 180, but the sponsor fails to submit such amendment on or before Day 210. If a sponsor submits an amendment after Day 210, then the amendment is ineligible for

consideration as an end-review amendment, the extended performance goal (270 days) will not apply, and a complete action letter will be issued by Day 220 for the original submission; or

iii. 270 days after the submission date if the Agency electronically requests an end-review amendment to the submission on or before Day 180 and the sponsor submits an end-review amendment on or before Day 210.

2. The end-review amendment procedure is not intended to prevent the use of minor amendments as described in Definitions, paragraph 2. above during Agency review of a study submission.

Investigational Animal Drug Protocols without Data Submissions

1. Review and act on 90 percent of investigational animal drug submissions consisting of protocols without substantial 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 animal drug application or supplemental animal drug application, within

i. 60 days after the submission date (Day 60) if the Agency does not request an end-review amendment to the protocol.

(1) If the Agency determines that the protocol is acceptable, the Agency will notify the sponsor of this decision electronically on or before Day 50, followed by a complete action letter; or

(2) If the Agency determines that a protocol is not acceptable, the Agency will notify the sponsor of this decision electronically, providing preliminary broad areas of protocol deficiency, on or before Day 50, with the subsequently issued complete action letter providing the detailed protocol assessment. The sponsor may contact the Agency for a brief clarification of these areas of deficiency prior to the issuance of the complete action letter; or

ii. 75 days after the submission date if the Agency electronically requests an end-review amendment to the protocol on or before Day 50, but the sponsor fails to submit such amendment within 10 days of the amendment request date. If a sponsor files an amendment more than 10 days after the amendment request date, then the amendment is ineligible for consideration as an end-review amendment, the extended performance goal (refer to paragraph 1.iii of this section) will not apply, and a complete action letter will be issued by Day 75 for the original submission; or

iii. the greater of 60 days after the original protocol is received by the Agency or 20 days after the amended protocol is received by the Agency if the Agency electronically requests an end-review amendment on or before Day 50 and the sponsor submits such amendment within 10 days of the date the amendment is requested.

2. Sponsors are not required to submit study protocols for review. However, for each voluntarily submitted protocol for a 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.
3. 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.
4. The end-review amendment procedure is not intended to prevent the use of minor amendments as described in Definitions, paragraph 2.above during Agency review of a protocol without data submission.

II. Performance Goals for Fiscal Years 2015 – 2018

On October 1, 2014, the beginning of fiscal year 2015, the Agency will discontinue end-review amendment procedures and replace them with a process for shorter review times for reactivations and resubmissions as outlined in the Application/Submission goals section of this letter. These new procedures only apply when the sponsor provides submissions for the NADA and INAD through the use of the eSubmitter electronic submission tool. The original application/submission and the reactivation/resubmission must be submitted through the eSubmitter tool to be eligible to take advantage of the new procedures for the shorter review times for qualified reactivations/resubmissions.

Application/Submission Goals

1. Non-administrative New Animal Drug Applications (NADAs)

Review and act on 90 percent of non-administrative 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. Non-manufacturing Supplemental Animal Drug Applications

The Agency will 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 resubmission date if the Agency determines and notifies the sponsor that the deficiencies are substantial.
ii Within 135 days after the resubmission date if the Agency determines and notifies the sponsor that the deficiencies are not substantial; and the resubmission 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 resubmission date if the resubmission to the supplemental application 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 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 resubmitting the supplement. The shorter review time of 135 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 supplemental application.

3. 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 reactivation. 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.

4. 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 animal drug application or supplemental animal drug application, 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 voluntarily submitted protocol for a 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.

5. 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 submitted through the use of the eSubmitter electronic submission tool, 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.

III. Performance Goals for Fiscal Years 2014 – 2018

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.

Timely Meetings with Industry

The Agency and the regulated industry agree that the use of both formal meetings (e.g., presubmission conferences, workshops, etc.) and informal communication by both parties is critical to ensure high submission quality such that the above performance goals can be achieved.

Administrative NADAs

Review and act on 90 percent of administrative NADAs (NADAs submitted after all scientific decisions have been made in the investigational new animal drug process, i.e., prior to the submission of the NADA) within 60 days after the submission date.

Manufacturing Supplemental Animal Drug Applications

Review and act on 90 percent of manufacturing supplemental animal drug applications within 120 days after the submission date.

A 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. If the Agency determines and notifies the sponsor that the deficiencies are not substantial for manufacturing supplements requiring prior approval according to 21 CFR 514.8(b), the Agency will permit the manufacturing supplements to be resubmitted as "Supplement-Changes Being Effected in 30 Days" as described in 21 CFR 514.8(b)(3). The Agency will generally favor permitting prior approval supplements to be resubmitted as "Supplement-Changes Being Effected in 30 Days", where possible. The Agency will state in the incomplete letter whether the reactivation can be submitted as a "Supplement-Changes Being Effected in 30 Days". If the Agency determines and notifies the sponsor that the deficiencies are substantial or new substantial information is provided in the resubmission, the Agency will review and act on 90 percent of reactivated manufacturing supplements within 120 days after the resubmission date.

Comparability Protocols

Permit comparability protocols as described in 21 CFR 514.8(b)(2)(v) to be submitted as protocols without substantial data in a 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.

Multiple Data Submissions to the Chemistry Manufacturing Controls Technical Section

The Agency will develop guidance for a two-phased Chemistry, Manufacturing and Controls (CMC) technical section submission and review process under the INAD file by the end of fiscal year 2014. If sponsors are interested in using a two-phased submission and review process for the CMC technical section before the draft guidance document is issued, they can contact the Agency.

Pre-Approval Foreign Inspections

1. 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 animal drug application, a supplemental animal drug application, or investigational animal drug submission that informs the Agency that the application 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.

2. 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.

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. Presubmission conferences will be held approximately 100 days after the submission of the data supporting the request.

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.

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.

Conditional Approval

Beginning in early FY 2014, the Agency agrees to explore, in concert with industry, the feasibility of pursuing statutory revisions, consistent with the Agency's mission to protect and promote the public health, that may expand the use of conditional approvals to other appropriate categories of new animal drug applications and develop recommendations by September 30, 2015.

ADAA Combinations

Beginning in early FY 2014, the Agency agrees to explore, in concert with affected parties, the feasibility of pursuing statutory revisions, consistent with the Agency's mission to protect and promote the public health, that may modify the current requirement that the use of multiple new animal drugs in the same medicated feed be subject to an approved application and develop recommendations by September 30, 2016.

Workload Adjustment

The proposed amendment to the Animal Drug User Fee Act of 2003, as amended in 2008, requires FDA to annually adjust fee revenues after fiscal year 2014 to reflect changes in review workload utilizing a weighted average of the change in the total number of applications for new animal drugs, non-manufacturing supplemental animal drug applications (i.e. supplemental animal drug applications for which safety or effectiveness data are required), manufacturing supplemental applications for new animal drugs, investigational new animal drug study submissions, and investigational new animal drug protocol submissions. The Agency will use the method detailed below to calculate the workload adjustment, and the percent increase in fees will be made if the amount of the workload adjuster is equal to or greater than one percent (1%). In accordance with the statute, the workload adjustment will not result in fee revenues for a fiscal year that are less than the fee revenues for that fiscal year as specified in the statute.

The term "workload adjuster" applicable to a fiscal year consists of the sum of the percent of change in the total number of each of the five component submission types submitted (comparing the five-year average number of such submissions for fiscal years 2009 – 2013 -- the base years -- to the five-year average for the most recent five-year period ending June 30 before the start of the next fiscal year) times a weighting factor that is the percent of direct review time spent on the each of the five component submission types over the most recent five-year period.