Animal Generic Drug User Fee Act Reauthorization Performance Goals and Procedures – Fiscal Years 2024 Through 2028

The goals and procedures of the Food and Drug Administration (FDA or the Agency) as agreed to under the "[placeholder: Animal Generic Drug User Fee Amendments of 2023]" are summarized as follows:

Application/Submission Goals

Beginning October 1, 2023, all applications and submissions under the Federal Food, Drug, and Cosmetic Act (FD&C Act) section 512(b) must be created using the eSubmitter tool and submitted to the Agency through the FDA Center for Veterinary Medicine (CVM) Electronic Submission System (ESS).

1. Original Abbreviated New Animal Drug Applications (ANADAs) and Reactivations

Review and act on 90 percent of original ANADAs within 240 days[1] 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. If the Agency determines that the deficiencies are not substantial, the Agency will review and act on 90 percent of reactivated applications within 120 days after the reactivated ANADA submission date. This shorter review time for reactivated ANADAs 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. If the Agency determines that the deficiencies are substantial or new substantial information is provided, the Agency will review and act on 90 percent of reactivated applications within 240 days after the reactivated ANADA submission date.

2. Administrative ANADAs

Review and act on 90 percent of administrative ANADAs (ANADAs submitted after all scientific decisions have been made in the generic investigational new animal drug (JINAD) process, i.e., prior to the submission of the ANADA) within 60 days after the submission date. Paragraph IV certification applications (FD&C Act section 512(n)(1)(H)(iv)) submitted as administrative ANADAs will be excluded from the administrative ANADA cohort.

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

3. Prior Approval Manufacturing Supplemental ANADAs and Reactivations

Review and act on 90 percent of Prior Approval manufacturing supplemental ANADAs within 180 days after the submission date. A Prior Approval manufacturing supplemental ANADA includes: one or more major manufacturing changes according to 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 270 days review goal (see "Supplement-Changes Being Effected Manufacturing Supplemental ANADAs 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 270 days after the re-submission 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 180 days after the re-submission date of a complete submission.

4. Supplement–Changes Being Effected Manufacturing Supplemental ANADAs and Reactivations

Review and act on 90 percent of "Supplement- Changes Being Effected" manufacturing supplemental ANADAs 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)(iv), within 270 days after the submission date.

5. Generic Investigational New Animal Drug (JINAD) Study Submissions

Review and act on 90 percent of JINAD study submissions within 180 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 study submission and

reach a decision on the issue(s) presented in the submission. If the Agency determines that the deficiencies are not substantial, the Agency will review and act on 90 percent of resubmitted JINAD study submissions within 60 days after the receipt date of a complete study submission. This shorter review time for resubmitted JINAD study submissions is not intended to prevent the use of minor amendments during Agency review of a study submission. If the Agency determines that the deficiencies are substantial or new substantial information is provided, the Agency will review and act on 90 percent of resubmitted JINAD study submissions within 180 days after the receipt date of a complete study submission.

6. JINAD Protocols

Review and act on 90 percent of JINAD 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 ANADA or supplemental ANADA, within 75 days after the submission date.

Allow comparability protocols as described in 21 CFR 514.8(b)(2)(v) to be submitted as protocols without substantial data in a JINAD file. The Agency will review and act on 90 percent of JINAD submissions consisting of protocols without substantial data within 75 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.

7. Request to Establish a JINAD File

Review and act on 90 percent of original submissions requesting establishment of a JINAD file, within 100 days after the submission date.

For the application/submission goals above, the term "review and act on" means the issuance of either: (1) a complete action letter that approves an original or supplemental ANADA or notifies a sponsor that a JINAD submission is complete or that a JINAD file has been established; or (2) an “incomplete letter” that sets forth in detail the specific deficiencies in an original or supplemental ANADA or JINAD submission and, where appropriate, the actions necessary to place such an original or supplemental ANADA or JINAD submission in condition for approval, filing, or complete submission. Within 30 days of receipt of the application, FDA shall refuse to file an original or supplemental ANADA, or their reactivation, that 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 receipt of the submission, FDA will refuse to review a JINAD submission that 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.

FDA may request minor amendments to original or supplemental ANADAs and JINAD 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 JINAD submissions.

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 original or supplemental ANADA, 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 new animal drug. 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 design, execution, or analyses unless the Agency issues a written order that a substantiated scientific requirement essential to the assessment of the study appeared after the Agency's protocol assessment, or public (human or animal) health concerns unrecognized at the time of protocol assessment under this process are evident.

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.

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 will be reviewed with the highest possible priority among those pending.

Amending Similar Applications and Submissions

The Agency and regulated industry agree that applications and submissions to the Agency will be complete and of sufficient quality to allow the Agency's complete and timely review. The Agency will refuse to file poor quality and incomplete applications and submissions rather than allowing them to serve as "placeholders" in the review queue that are subsequently amended to add the missing or inadequate portions.

The Agency recognizes that there are circumstances in which a controlled amendment process can make the review of similar, pending submissions more efficient without compromising the sponsor's responsibility for high quality submissions. Thus, if the Agency requests an amendment to a non-administrative original ANADA, manufacturing supplemental ANADA, JINAD study submission, or a JINAD protocol submission (a "CVM-initiated amendment"), or issues an incomplete letter for such an application or submission, a sponsor may request to amend other, similar applications or submissions it has pending with the Agency ("sponsor-initiated amendment(s)") in accordance with the following criteria:

1. The amended information for these similar applications or submissions must be the same as in the CVM-initiated amendment or incomplete letter; and
2. The amended information must not significantly change the similar applications or submissions; and
3. The amended information for these similar applications or submissions must be submitted no later than:
    a. 120 days after the submission date for the similar original ANADA, manufacturing supplemental ANADA; or
    b. 100 days after the submission date for the similar JINAD study submissions; or
    c. 40 days after the submission date for the similar JINAD protocol submissions.

If the Agency determines that the above criteria have been met, it will not change the user fee goal for the similar application or submission that has been amended by a sponsor-initiated amendment. If the above criteria have not been met, the Agency may consider the similar application or submission resubmitted on the date of the sponsor-initiated amendment, thereby resetting the clock to the date FDA received the amendment.

Multiple Data Submissions to the Chemistry, Manufacturing, and Controls Technical Section

The Agency will continue to allow two-phased Chemistry, Manufacturing, and Controls technical section submissions under the JINAD process.

Timely Foreign Pre-Approval 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 abbreviated application, supplemental abbreviated application, or generic investigational file and may be subject to foreign PAIs for the following fiscal year; and 2) a notification 30 days prior to submitting an abbreviated application, a supplemental abbreviated application, or generic investigational file 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 abbreviated 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.

Foreign GMP Inspections

The Agency commits to exploration and implementation of the United States and European Union and the United States and United Kingdom Good Manufacturing Practice Mutual Inspection Agreement and future Mutual Recognition Agreements, with respect to generic new animal drug products subject to review, starting in FY 2024 for establishments manufacturing animal/veterinary drugs. The Agency will provide annual progress updates to the industry.

Timely Meetings with Industry

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

Transparency in the Review Process

<u>Bioequivalence Technical Section meeting process</u>

The Agency will enhance transparency by establishing the Bioequivalence Technical Section (BETS) meeting process. The term "Bioequivalence Technical Section (BETS) meeting" means an optional meeting for a sponsor seeking further discussion with the Agency after their receipt of CVM's response to their submission of bioequivalence study data in support of their ANADA.

The formalized process is the following: Once CVM receives a bioequivalence technical section with study data for review, CVM will schedule the BETS meeting for a date approximately one month after the date CVM's review of the technical section is due. The sponsor is expected to submit a detailed list of questions to CVM by email no later than two weeks prior to the BETS meeting date to facilitate preparation for the

discussion. The BETS meeting will be a virtual meeting and will include the CVM scientific reviewer and CVM team leader to whom the submission has been assigned for review. CVM will not generate any formal documents after a BETS meeting (e.g., a memorandum of conference).

Response to request to establish a JINAD file

When a sponsor submits a request to establish a JINAD file, the Agency will include in its response information describing its current thinking regarding specific elements for inclusion in the the Chemistry, Manufacturing, and Controls technical section for the dosage form proposed. The response will list relevant guidance, regulations, and compendial expectations relevant to that dosage form.

Workload Adjustment

For purposes of calculating the workload adjustment, it has been agreed to reset the base years to a rolling average comprising the most recent 5-year completed fiscal years. For example, beginning October 1, 2024 (FY 2025), the base will comprise Fiscal Years 2019 through 2023. At the start of each fiscal year thereafter, the base will be adjusted upward by one year on the upper and lower ends of the range. There will be no workload adjustment for FY 2024. Workload adjustments are one-time adjustments, and are calculated annually. The percent increase in fees will be made if the amount of the workload adjuster is equal to or greater than one percent (1%). The weighting factor is the percent of direct review time spent on each of the six component submission types over the most recent five-year period.