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Priority Zoonotic Animal Drug Designation and Review Process

Guidance for Industry

Draft Guidance

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For further information regarding this document, contact Dr. Michelle Hyre, Center for Veterinary Medicine (HFV-133), Food and Drug Administration, 7500 Standish Place, Rockville MD 20855, 240-402-0593, email: michelle.hyre@fda.hhs.gov.

Additional copies of this draft guidance document may be requested from the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville MD 20855, and may be viewed on the Internet at https://www.fda.gov/animal-veterinary, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or http://www.regulations.gov.

U.S. Department of Health and Human Services
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Center for Veterinary Medicine (CVM)
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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. Introduction

This draft guidance is intended to assist sponsors pursuing Priority Zoonotic Animal Drug (PZAD) designation of a new animal drug.[1]

This draft guidance is intended to provide the following:

- the definition of a PZAD,
- eligibility criteria for PZAD designation,
- the process for PZAD designation requests, and
- the process for expedited development and review of PZADs.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Priority Zoonotic Animal Drug

Under section 512A of the Federal Food, Drug, and Cosmetic Act (FD&C Act), a PZAD is defined as a new animal drug, that alone or in combination with one or more other animal drugs, has the potential to prevent or treat a zoonotic disease in animals, including a vector-borne disease, that has the potential to cause serious adverse health consequences for, or serious or life-threatening diseases in, humans.

III. Background – The CARES Act

The Coronavirus Aid, Relief, and Economic Security (CARES) Act,[2] signed into law on March

[1] The scope of this guidance includes products such as intentional genomic alterations in animals and animal cells, tissues, and cell- and tissue-based products.

[2] https://www.congress.gov/116/bills/hr748/BILLS-116hr748enr.pdf

27, 2020, added section 512A *Priority zoonotic animal drugs* to the FD&C Act, which provides for the designation of a new animal drug as a PZAD.[3] Section 512A(a) of the FD&C Act directs FDA to:

> *expedite the development and review of such new animal drug if preliminary clinical evidence indicates that the new animal drug, alone or in combination with 1 or more other animal drugs, has the potential to prevent or treat a zoonotic disease in animals, including a vector borne-disease, that has the potential to cause serious adverse health consequences for, or serious or life-threatening diseases in, humans.*

Section 512A of the FD&C Act identifies actions FDA may pursue for the expedited development and review of the new animal drug applications (NADA) for designated PZADs. These actions include the following:

A) taking steps to ensure that the design of clinical trials is as efficient as practicable, when scientifically appropriate, such as by utilizing novel trial designs or drug development tools (including biomarkers) that may reduce the number of animals needed for studies;

B) providing timely advice to, and interactive communication with, the sponsor (which may include meetings with the sponsor and review team) regarding the development of the new animal drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable;

C) involving senior managers and review staff with experience in zoonotic or vector-borne disease to facilitate collaborative, cross-disciplinary review, including, as appropriate, across agency centers; and

D) implementing additional administrative or process enhancements, as necessary, to facilitate an efficient review and development program.[4]

IV. Priority Zoonotic Animal Drug Designation

A. PZAD Eligibility Criteria

As stated in section 512A(a) of the FD&C Act, among other things, a new animal drug must meet two substantive criteria to be designated as a PZAD:

1. The new animal drug is intended to prevent or treat a zoonotic disease in animals, including a vector-borne disease.

The following are some examples of types of FDA-regulated animal drug products that may meet this criterion:

[3] The PZAD designation is not the same as Minor Use Minor Species (MUMS) designation.

[4] See section 512A(c)(2) of the FD&C Act.

- drug products intended for use in an animal to prevent or treat a specific disease in that animal that has the potential to transfer to humans;

- drug products intended for use in an animal that harbors the zoonotic disease-causing agent that can be transmitted to humans by direct contact with the animal or animal's environment, or by ingestion of or exposure to animal products. These drugs may reduce or eliminate the zoonotic disease-causing agent in the animal or animal's environment;

- drug products intended for use in an animal that harbors a zoonotic disease-causing agent that can be transmitted to humans by insects or other vector species. These drugs may reduce (or eliminate) the vector population, or may reduce or eliminate the zoonotic disease-causing agent in the animal, and so reduce the likelihood of transmission of the zoonotic disease-causing agent from the animal to insects or other vector species;[5]

- drug products intended for use in a vector species that harbors a zoonotic disease-causing agent. These drugs may reduce (or eliminate) the vector population,[6] reduce or eliminate the zoonotic disease-causing agent in the vector, or otherwise decrease the vector's ability to transmit the zoonotic disease-causing agent to humans.

Note that for products proposed to treat or prevent vector-borne diseases, early discussion may be needed between CVM and other regulatory agencies (e.g., United States Environmental Protection Agency,[7] United States Department of Agriculture) to determine which agency should regulate the product.

2. The zoonotic disease the new animal drug is intended to treat or prevent must have the potential to cause serious adverse health consequences for, or serious or life-threatening disease in, humans

The zoonotic disease needs to be recognized as a disease that has the potential to cause serious or life-threatening disease in humans or has the potential to cause serious adverse health consequences for humans.

CVM may consult with other FDA Centers or other agencies to determine if a particular proposed product meets this criterion.

[5] Note that this guidance excludes products EPA regulates, including genetic modifications in pest animals intended for use as a pesticide (such as for mosquito and rodent population control).

[6] See footnote 5.

[7] See footnote 5.

B. Other considerations for PZAD designation

1. For a new animal drug to be eligible for a PZAD designation, there must be at least preliminary clinical evidence to support its proposed indication. (Section 512A(a) of the FD&C Act).

2. A sponsor may seek PZAD designation for a new animal drug that is used alone or that is used in combination with another new animal drug. (Section 512A(a) of the FD&C Act).

3. Only pioneer new animal drug products that may be approved[8] or conditionally approved[9] are eligible for PZAD designation. Generic new animal drugs are not eligible for PZAD designation.

4. The PZAD designation for a new animal drug product will be limited to the zoonotic disease indication, even if the product is previously approved for other uses or is currently being evaluated under the same Investigational New Animal Drug (INAD) file for other indications.

5. The indication for a new animal drug product designated as a PZAD should reflect the primary endpoint used to determine success in the effectiveness study(ies). The indication will not include how the product may prevent or treat zoonotic diseases in humans or that the product may prevent or treat zoonotic disease in animals if the effectiveness study(ies) did not include a prevention or treatment of disease endpoint.

6. PZAD designations can be separately granted to multiple sponsors seeking approval of the same drug for the same or similar zoonotic disease indication(s).

7. If CVM designates the new animal drug as a PZAD, all subsequent submissions to that file that are related to that PZAD designation are afforded the expedited review process described in section VI. *Enhancements to Expedite the PZAD Review Process* below. The expedited review process does not apply to any submissions made to the file prior to the PZAD designation.

8. A PZAD designation does not guarantee the product will be approved or conditionally approved as a new animal drug. PZAD products are still subject to the requirements of the animal drug approval process.

9. A PZAD designation does not provide any marketing incentives (e.g., market exclusivity) for the new animal drug product.

[8] Sections 512(j) and 512(b)(1) of the FD&C Act.

[9] Section 571 of the FD&C Act.

V. Priority Zoonotic Animal Drug Designation Request Process

A request for designation as a PZAD may be made concurrently with, or at any time after, the opening of an INAD file or the filing of an NADA. CVM recommends that PZAD designation requests be submitted to the INAD file. Prior to submission, the sponsor may request a meeting[10] with CVM's Office of New Animal Drug Evaluation (ONADE) to discuss their proposed request for designation. If a drug has multiple indications, only the indication(s) to be evaluated for PZAD designation should be included in the submission.

In the submission, the sponsor should provide information about their proposed conditions of use (i.e., drug identification, indication, species class, and dosage regimen). The submission should address how the new animal drug product meets the criteria for PZAD designation (see section IV.A. *PZAD Eligibility Criteria*) as follows:

a. Provide information on how the drug will be administered.

b. Provide the mechanism of action of the drug (if known).

c. Explain the potential for the new animal drug to prevent or treat a zoonotic disease in animals, including a vector-borne disease.

d. Describe the potential of the zoonotic disease to cause serious adverse health consequences for, or serious or life-threatening disease in, humans.

CVM will issue a letter informing the sponsor whether the drug is designated as a PZAD within 60 calendar days of the request.[11]

VI. Enhancements to Expedite the PZAD Review Process

To fulfill the requirements of the CARES Act for expediting review of PZAD products, CVM aims to increase efficiency in the approval process and thereby reduce the overall time to approval. CVM hopes to achieve this by providing the enhancements to the review process described below, including informal meetings, pre-review feedback upon request, and stopping the review clock under certain circumstances.

CVM's evaluation process for PZADs will follow CVM's new animal drug evaluation phased-review process outlined in GFI #132, "Administrative Applications and the Phased Review Process."[12] Review of PZAD product submissions will be subject to the applicable current Animal Drug User Fee Act (ADUFA) timelines, with the goal of streamlining the process for PZAD products as described below.

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[10] See CVM Program Policy and Procedures Manual 1243.3024 Scheduling and Holding Meetings with Outside Parties (April 2023).

[11] See section 512A(c)(1) of the FD&C Act.

[12] https://www.fda.gov/media/70029/download

A. Informal meetings between CVM and sponsors

Communication is a critical part of the review process that allows both CVM and sponsors to receive timely responses to their questions and allows sponsors to submit appropriate data to ensure efficient evaluation of submissions. To increase communication, once a new animal drug product is designated as a PZAD, CVM will offer recurring informal meetings between the sponsor and the review team without a formal submission. The goal of these meetings is for the sponsor to provide updates on drug development, discuss any changes to data submission timelines, and for CVM to address questions and other issues that may result in minor amendments to technical section submissions. These meetings are not intended to replace presubmission conferences[13] or other formal meetings. CVM encourages the sponsor to contact their CVM project manager (PM) to discuss whether their product may be at the appropriate stage to begin scheduling regular informal meetings. In general, the frequency of these meetings will depend on the stage of the sponsor's drug development and the information planned for submission to CVM.

B. PZAD pre-review feedback

Sponsors pursuing approval or conditional approval of a new animal drug product designated as a PZAD are eligible to receive pre-review feedback from CVM. Pre-review feedback is intended to provide sponsors an opportunity to receive high-level informal feedback from CVM regarding possible deficiencies in draft submissions prior to the formal submission. Possible items that may be addressed under the pre-review feedback option include:

- confirming if information is appropriate for inclusion in a submission and identifying gaps that may need to be addressed;
- answering specific questions regarding the appropriate level of detail to include in a submission; and
- providing examples of data presentation (e.g., data formatting, file format).

Under pre-review feedback, CVM will not review information or data for acceptability, nor will CVM answer specific questions on the overall development plan. Sponsors should contact their CVM PM with questions regarding their overall development plan.

To receive pre-review feedback from CVM, sponsors should submit a meeting request via eSubmitter[14] and include a list of questions for CVM to address. The meeting request should include sufficient supporting information to allow CVM to provide appropriate

[13] See 21 CFR part 514, which describes the procedures to be followed for requesting, conducting, and documenting presubmission conferences, or CVM Program Policy and Procedures Manual 1243.3024 Scheduling and Holding Meetings with Outside Parties (April 2023).

[14] For more information on eSubmitter, see CVM eSubmitter Program for Animal Drugs—Office of New Animal Drug Evaluation | FDA.

recommendations and feedback. In addition, the meeting request should also indicate if sponsors would like a teleconference to discuss their submission prior to receiving written feedback. If a teleconference is requested, CVM will aim to hold it within approximately 25 calendar days of the receipt of the meeting request.

CVM will aim to send sponsors a summary of CVM's pre-review feedback within approximately 35 calendar days of receipt of the meeting request. No memorandum of conference (MOC) or acknowledgement letter will be issued.

Sponsors should contact their PM for questions regarding pre-review feedback and how to request pre-review feedback.

C. PZAD post-review feedback

Sponsors pursuing approval or conditional approval of a new animal drug product designated as a PZAD are eligible to receive post-review feedback from CVM if they wish to discuss a CVM response letter that they have received. The goal of post-review feedback is to facilitate communication between the sponsor and CVM. Post-review feedback allows the sponsor and CVM to informally discuss the comments in CVM's response letter (e.g., Technical Section Incomplete, protocol non-concurrence letter) with the goal of assisting the sponsor in preparing their resubmission. After the sponsor receives CVM's response letter, the sponsor may request an informal meeting and provide a list of clarifying questions to be discussed. CVM's response letter will include the contact information for requesting post-review feedback. CVM will not provide an MOC or acknowledgment letter for the post-review feedback.

D. PZAD stop-the-review-clock

Under user fee performance goals timeframes, CVM uses a "review clock" system under which each major technical section submission that will support an approval has a 180-day review time. Ordinarily, when CVM determines a technical section submission is incomplete, a letter is sent to the sponsor informing them of this determination and the submission is closed out and removed from the queue. When the sponsor responds to the deficiencies noted in the incomplete letter, the 180-day clock starts anew.

The PZAD "stop-the-review-clock" is an optional process that CVM may initiate when additional information is needed to complete a technical section or accept a study. The stop-the-review-clock process provides sponsors preliminary feedback regarding missing or unacceptable elements of the submission without closing out the submission and removing it from the queue, and provides sponsors with an opportunity to submit additional information to address CVM comments prior to completion of review of the P submission. When a sponsor submits this additional information, the review clock resumes. The goal is to decrease the number of review cycles. Stopping the review clock rather than closing out a submission and initiating a new review cycle when this additional information is submitted can shorten the total time to address that technical section in support of approval.

Sponsors are expected to submit high-quality submissions to facilitate review by CVM. The stop-the-review-clock process is intended to address scientific issues (e.g., need for additional data to support conclusions, justifications, alternate data presentations) to facilitate the expedited review of PZAD products; it is not intended to rehabilitate poor-quality submissions (e.g., issues with organization, incomplete submissions, or unclear purpose of the submission).

If CVM utilizes the stop-the-review-clock process for a submission, CVM will send a letter to the sponsor providing a list of comments to address. The sponsor should respond to CVM within 2 weeks of the date of the letter. The sponsor may either: (1) agree to submit an amendment with the requested information within 120 days of the date of the letter; or (2) request that the clock be restarted because the sponsor does not agree to submit additional information. The review clock will be restarted when the sponsor either declines to submit the amendment or when the amendment is received by CVM.