



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-D-2648]

Heritable Intentional Genomic Alterations in Animals: The Approval Process; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing the availability of a draft guidance for industry (GFI) #187B entitled “Heritable Intentional Genomic Alterations in Animals: The Approval Process.” This draft guidance is intended to clarify FDA’s requirements and recommendations for developers of intentional genomic alterations (IGA) in animals. The draft guidance is being issued as one of two companion documents. “Heritable Intentional Genomic Alterations in Animals: The Approval Process” describes how the FDA approval process applies to heritable IGAs in animals. FDA is issuing GFI #187B as a draft guidance to solicit comments that will enable the Agency to update, and make as efficient as possible, the approval process for IGAs in animals. In addition, FDA requests comments on questions that it intends to address in the final version of this guidance document. The companion final guidance, GFI #187A entitled “Heritable Intentional Genomic Alterations in Animals: Risk-Based Approach,” describes FDA’s risk-based regulatory approach to the oversight of heritable IGAs in animals. This means that, for people or companies developing certain types of IGAs in animals, FDA may not expect them to submit an application or get approval before marketing their product.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure

that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2019-D-2648 for “Heritable Intentional Genomic Alterations in Animals: The Approval Process.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the guidance to the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Adam Moyer, Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-796-2319, Adam.Moyer@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

In the *Federal Register* of January 19, 2017 (82 FR 6561), FDA published the notice of availability for a draft GFI #187 entitled “Regulation of Intentionally Altered Genomic DNA in Animals” giving interested persons until April 19, 2017, to comment on the draft guidance. On April 13, 2017, we published a notice announcing the extension of the comment period to June 19, 2017 (82 FR 17844). FDA received numerous comments on the draft guidance GFI #187 and those comments were considered as the guidance was revised. As noted, this draft guidance, GFI #187B, is intended to explain how FDA’s approval process applies in the context of products related to heritable IGAs in animals.

The draft guidance is being issued as one of two companion documents. Draft GFI #187B, “Heritable Intentional Genomic Alterations in Animals: The Approval Process,” describes how the FDA approval process applies to heritable IGAs in animals. Final GFI #187A, “Heritable Intentional Genomic Alterations in Animals: Risk-Based Approach,” whose notice of availability is published elsewhere in this edition of the *Federal Register*, describes FDA’s risk-based approach to the oversight of IGAs in animals.

FDA received and reviewed comments on the draft guidance that came from industry (companies that produce IGAs and trade associations), individual consumers, academics, non-governmental organizations (consumer, environmental), other Federal and State government agencies, and individual developers of IGAs in animals. Among the changes made to the draft guidance, we have:

- Indicated our willingness to consider multiple heritable IGAs or a single IGA in multiple lines or breeds of animals of the same species under a single application;
- Clarified that FDA’s review of applications is subject to specific timeframes;
- Acknowledged that it may not be feasible to gather data on multiple generations and encourage developers of heritable IGAs in animals to contact FDA to discuss alternative approaches of demonstrating durability;
- Indicated that alternative disposition methods for investigational animals may be acceptable if the sponsor contacts FDA’s Center for Veterinary Medicine;
- Further described post-market records and reports requirements and clarified who they apply to; and
- Provided additional information on establishment registration requirements, including explaining that, as a general matter, pet stores, farms, or other animal production facilities do not have to register or list with FDA and can engage in ordinary activities (e.g., breeding, growing, etc.) without contacting FDA.

FDA is issuing this draft guidance to solicit public comment that will further improve it. To help inform our thinking as we begin the process of further updating the guidance, we invite comment on the following questions:

1. What are some alternative strategies for providing data that would support approval of heritable IGAs in animals?

- a. How can a developer demonstrate the durability of a heritable IGA over time in situations where collection of data on multiple generations of animals is difficult or not possible?
 - b. What are possible strategies a developer could utilize to address the approval requirements for multiple heritable IGAs (e.g., multiple iterations of the same alteration resulting in the same intended phenotype or multiple alterations resulting in more than one intended phenotype) under a single approval?
2. What areas of current good manufacturing practices and good laboratory practices specific to the production of heritable IGAs in animals do you believe need clarification through the publication of additional guidance?
 3. Are there process improvements (e.g., combining steps of the approval process) (see page 16, section IV.C. Recommended Process for Completing Pre-approval Assessments for IGAs in Animals, of the guidance) that you believe would make the approval process easier to navigate?

This level 1 draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Heritable Intentional Genomic Alterations in Animals: The Approval Process." 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.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 25 have been approved under OMB control number 0910-0322; the collections of

information in 21 CFR part 58 have been approved under OMB control number 0910-0119; the collections of information in 21 CFR part 207 have been approved under OMB control number 0910-0045; the collections of information in 21 CFR part 211 have been approved under OMB control number 0910-0139; the collections of information in 21 CFR part 511 have been approved under OMB control number 0910-0117; the collections of information in 21 CFR part 514 have been approved under OMB control number 0910-0284; and the collections of information in 21 CFR 558.6(a)(4) have been approved under OMB control number 0910-0363.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at <https://www.fda.gov/animal-veterinary/guidance-regulations/guidance-industry>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: April 25, 2024.

Lauren K. Roth,

Associate Commissioner for Policy.

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