MOU 225-24-010

Memorandum of Understanding between the U.S. Department of Agriculture and the U.S. Department of Health and Human Services Food and Drug Administration

concerning information sharing and regulatory cooperation related to intentional genomic alterations in animals subject to USDA jurisdiction.

I. Purpose

This Memorandum of Understanding (MOU) between the U.S. Department of Agriculture (USDA) and the U.S. Department of Health and Human Services Food and Drug Administration (FDA) (hereinafter the parties): (1) establishes policies and procedures to enhance the exchange of information between USDA agencies and FDA, (2) describes the regulatory roles of FDA and USDA agencies, and (3) promotes coordination of regulatory responsibilities in a manner that will enable an efficient, seamless regulatory process. This MOU applies to the parties' activities as described herein concerning intentional genomic alterations (IGAs) in animals subject to USDA jurisdiction. This includes animals of amenable species [1] for agricultural use (hereinafter "amenable species") and animals of any species that have the potential to pose a livestock pest or disease risk per the Animal Health Protection Act (AHPA; 7 U.S.C 8301, et seq.) or that produce food that may be subject to labeling requirements under the National Bioengineered Food Disclosure Standard (the Standard). 7 U.S.C. 1639b. [2] Animals of any species that have the potential to pose a livestock pest or disease risk per the Animal Health Protection Act or that produce food that may be subject to labeling requirements under the Standard) are hereinafter, "other animals."

II. Background

IGAs in animals are intentional genomic alterations made using modern molecular technologies, which may include random or targeted DNA sequence changes, including nucleotide insertions, substitutions, or deletions, or other technologies that introduce specific changes to the genome of the animal.

IGAs have the potential to contribute to a more resilient and robust food production system, ensure food-producing animals and their environments are healthier and hardier, and deliver consumers more choices in the foods they eat. These products have the potential to be used to prevent and control animal health challenges, such as zoonotic and animal infectious disease threats, leading to healthier animals, communities, and ecosystems. They also can help animal agriculture adapt to and mitigate climate change. FDA and USDA are committed to risk-based regulatory approaches that keep pace with technological innovation and allow safe IGAs to reach the market and achieve their potential benefits.

FDA regulates such alterations in animals to ensure that they are safe to the animal, safe to anyone that eats food derived from the animal, and that they are effective, i.e., that they achieve their intended effect, under the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 301, et seq. Under these provisions, FDA reviews and approves premarket approval applications for IGAs in animals (21 U.S.C. 360b) and reviews IGAs to determine if, based on a review of data and information, FDA intends to exercise enforcement discretion over approval requirements (described in FDA Guidance for Industry #187A, and hereinafter, as Category 2 determination).

USDA's Food Safety and Inspection Service (FSIS) is responsible for implementing and enforcing the Federal Meat Inspection Act (FMIA; 21 U.S.C. 601 et seq.), the Poultry Products Inspection Act (PPIA; 21 U.S.C. 451, et seq.), and the Egg Products Inspection Act (21 U.S.C. 1031, et seq.). Under the FMIA and PPIA, FSIS ensures the safety of food products derived from amenable species and ensures that their labeling is truthful and not misleading. Under the Agricultural Marketing Act (7 U.S.C. 1622, 1624) FSIS provides voluntary inspection of "exotic animals" (reindeer, elk, deer, antelope, water buffalo, bison, and yak), rabbits, and migratory waterfowl or game birds.

USDA's Animal and Plant Health Inspection Service (APHIS) is responsible for implementing and enforcing the Animal Health Protection Act (AHPA; 7 U.S.C 8301, et seq.). Under this statute, the Secretary of Agriculture has the authority to prevent, detect, control, and eradicate diseases and pests of livestock. To accomplish this in part, APHIS establishes permit-based procedures for the importation and interstate movement of organisms and vectors that could cause or transmit animal disease and may prohibit importation or interstate movement of any animal, article, or means of conveyance into the United States if the Secretary of Agriculture determines this is necessary to prevent the introduction or dissemination of any pest or disease of livestock.

USDA's Agricultural Marketing Service (AMS) is responsible for implementation, oversight, and enforcement of the National Bioengineered Food Disclosure Standard (the Standard). 7 U.S.C. 1639b. The Standard requires food manufacturers, importers, and some retailers to disclose when certain bioengineered foods contain detectable genetic material that has been modified through certain techniques and cannot be created through conventional breeding or found in nature.

III. Substance of the Understanding

A. Information Sharing and Safeguards

It is mutually agreed that:

FDA and USDA agencies will exchange records, data, reports, and other information related to pending submissions concerning FDA approval or review of IGAs in amenable species and other animals and USDA review of data or information related to USDA's statutory authorities; and FDA will disclose to USDA, as described below, the opening of an investigational or veterinary master file concerning IGAs in amenable species and other animals. USDA and FDA agree to protect such confidential information from unauthorized public disclosure. See e.g., 21 U.S.C. 331(j); 18 U.S.C. 1905; 21 C.F.R. parts 20 and 21.

Access to the non-public information shared under this MOU shall be restricted to the employees, agents, and officials of the FDA and USDA, who require access to such information to perform their official duties. USDA agrees not to share information about an upcoming FDA regulatory decision with people or entities outside USDA prior to product approval or Category 2 determination unless the developer has agreed in writing to outside communication.

Any unauthorized disclosure of shared confidential information by the agency receiving the information shall be the responsibility of that agency, so long as the agency providing such information conveys the confidential nature of the information to the receiving agency or the receiving agency otherwise has knowledge that such information is confidential. FDA and USDA agree to notify promptly each other of any actual or suspected unauthorized disclosure of any information shared pursuant to this MOU.

If a participant agency that has received information under this MOU receives a Freedom of Information Act (FOIA) request where there are responsive records, which originated with the other participant agency, the agency will refer the FOIA request to the other agency for it to respond directly to the FOIA requestor. In such cases, the participant agency that received the FOIA request will notify the FOIA requestor that it has referred the FOIA request to another agency and that a response will issue directly from that agency. In all other cases, USDA and FDA shall coordinate on the substance of any response.

B. Regulatory Process

FDA is committed to completing review of each submission by an applicant according to the following timeline:

- Determinations of Category 2: No later than 180 days from submission of the Category 2 determination request;
- Approval of specific sections that are part of the application:

- No later than 180 days from the date of submission of each major technical section (molecular characterization, phenotypic characterization, durability assessment and plan, target animal safety, food safety, environmental, and effectiveness);
- No later than 100 days from the submission of minor technical sections (labeling and "all other information"); and
- No later than 60 days from the date of submission of the administrative application, which occurs after all technical sections are complete.

- For a request for Investigational Food Use Authorizations (IFUA): No later than 100 days from submission of the IFUA request.

For each of these submission types, the timeline is based on receipt of a complete submission. If the submission has deficiencies, FDA may close the submission, which ends the timeline. When FDA receives a corrected submission, the applicable timeline will start over from the beginning. However, if the product is enrolled in the Veterinary Innovation Program (VIP), FDA may pause the running of the timeline by sending the product developer a "stop the clock" letter that sets forth the deficiencies of the submission. Upon resubmission, the timeline will continue from where it left off, rather than starting over.

C. Roles and Responsibilities

FDA will:

1. Notify USDA regarding the opening of an investigational or veterinary master file for IGAs in amenable and other animals, including available information about the animal, the IGA and its intended use at the parties' monthly meeting unless a meeting does not occur that month, in which case FDA will notify USDA by email. If USDA identifies a livestock disease risk concern for an IGA in other (non-amenable) animals, the parties will discuss what information USDA requires in order to address its livestock disease concern and FDA will provide that information to USDA APHIS.
2. Notify USDA regarding IGAs in amenable species with pending submissions for FDA review at the parties' first monthly meeting that occurs after the following, unless a meeting does not occur that month, in which case FDA will notify USDA by email:

    a. For product approvals, at the time FDA receives the first technical section submission;

    b. For Category 2 determinations, at the time FDA receives the submission for Category 2 determination;

    c. For IFUA requests, at the time FDA receives the submission; and

d. For all submission types, subsequent to any of the above notifications, at the time FDA sends a "stop the clock" letter and when FDA receives the associated submission in amended form and the clock restarts for:

i. the molecular characterization, target animal safety, durability assessment and plan, food safety, and effectiveness technical sections for an approval; or

ii. a Category 2 determination; or

iii. an IFUA.

e. For all submission types, at the time FDA receives amendments to the initial submission.

3. Provide to USDA as follows:

a. For approval applications for IGAs in amenable species:

i. The target animal safety technical section, the food safety technical section, amendments to any of these sections when requested and any other information for IGAs in amenable species that may affect slaughter, FSIS inspection or product labeling to FSIS within 30 days of FDA receipt of the submission and FDA's preliminary conclusions at the time of the parties' scheduled monthly meeting that occurs 30-60 days before the review deadline for the relevant submission; and

ii. The molecular characterization, target animal safety, durability assessment and plan, and effectiveness technical section(s) and any amendments to these sections when requested to APHIS within 30 days of FDA receipt of the submission and FDA's preliminary conclusions at the time of the parties' scheduled monthly meeting that occurs 30-60 days before the review deadline for the relevant submission.

b. For Category 2 determinations for IGAs in amenable species the Category 2 determination request to FSIS (for amenable species) and APHIS within 30 days of FDA receipt of the request and FDA's preliminary conclusions at the time of the parties' scheduled monthly meeting that occurs 30-60 days before the review deadline for the Category 2 determination; and

c. For IFUAs for animals that will be slaughtered in FSIS-regulated facilities, the authorization request to FSIS within 30 days of FDA's receipt of the authorization request and FDA's preliminary conclusions three weeks prior to FDA's 100-day review deadline.

USDA will:

1. Upon notification from FDA of IGAs in amenable species as described above, determine whether FSIS, APHIS, and/or AMS [3] should be included in consultations that the parties have determined should be held jointly with the developer.
2. For other animals, upon first notification, determine whether USDA needs any technical sections or additional information to evaluate potential impacts on livestock health.
3. Review information addressing food safety and quality for IGAs in amenable species and provide FSIS comments, if any, to FDA within 120 days of original receipt of information from FDA, unless both agencies agree to a longer timeline, for FDA "approval applications" or "Category 2 determinations."
4. Provide FSIS comments/feedback, if any, to FDA within 45 days of original receipt of information from FDA, unless both agencies agree to a longer timeline, for any investigational food use authorization (IFUA) in an animal that will be slaughtered in an FSIS-regulated facility.
5. Notify FDA of any livestock disease concerns from APHIS related to the IGA's introduction, dissemination, or altered disease resistance no later than 30 days in advance of the 180-day review deadline for the following technical section(s): molecular characterization, target animal safety, durability assessment and plan, and effectiveness.
6. Notify FDA if there is a requirement under the AHPA for a developer to obtain any required permit for any animals with IGAs.
7. Share any updates to AMS guidance and information related to compliance with the bioengineered disclosure standard including the current List of Bioengineered Foods with FDA. Notify FDA at least 60 days in advance of any intent to publish notice and comment rulemaking that would add any covered or other animal to the List of Bioengineered Foods.

The FDA and USDA reviewers will schedule a monthly meeting series to discuss the status of pending submissions and any relevant updates (e.g., requests for amendments) for IGAs in amenable species:

1. For approval applications beginning within 30 days of FDA receiving its first technical section submission and additional meetings as warranted based on the pace of developer submissions and progress of reviews;
2. Beginning within 30 days after FDA receipt of a submission requesting a Category 2 determination;
3. If there are multiple IGAs subject to the MOU that are simultaneously under review, the parties may hold monthly meetings to discuss all relevant products in a single meeting, with additional product-specific meetings scheduled as warranted; and

4. If there are no technical sections under review, the parties may suspend meetings until FDA receives the next submission, at which time monthly meetings will resume.

With regard to other USDA components:

1. FDA will inform USDA when, as specified in section IIIA, the trigger has occurred for such notification regarding an upcoming FDA decision regarding IGAs in amenable species and other animals; and
2. At least 60 days before public announcement, FDA and USDA will coordinate any public-facing and other formal or informal domestic and international communications regarding regulatory decisions subject to this agreement.
3. In addition to individual agency outreach, FDA and USDA will jointly engage in public outreach activities such as public meetings or webinars concerning agricultural animal biotechnology.

IV. Limitations

This agreement does not create binding, enforceable obligations against either agency. This agreement does not affect or supersede any existing agreements or arrangements between FDA and USDA or its agencies and does not affect the ability of FDA and USDA or its agencies to enter into other agreements or arrangements. This agreement will be subject to the applicable policies, rules, regulations, and statutes under which FDA and USDA operate. Nothing in this MOU shall obligate FDA or USDA to any current expenditure or future expenditure of resources in advance of the availability of appropriations from Congress.

V. Liaison Officers

To facilitate the activities carried out under this agreement, each agency will establish an agency liaison. Each agency may designate a new liaison, at any time, by notifying the other agency in writing. If, at any time, an individual designated as a liaison under this MOU becomes unavailable to fulfill those functions, the participating agency will name a new liaison and notify the other agency through the designated liaison. The initial liaisons will be:

For FDA:

Adam Moyer, PhD
Team Leader
Animal Biotechnology Team
Center for Veterinary Medicine
Adam.moyer@fda.hhs.gov (mailto: Adam.moyer@fda.hhs.gov)

For USDA:

Jennifer Rowland, PhD
Biotechnology Coordinator
Office of the Chief Economist
Jennifer.rowland@usda.gov (mailto:Jennifer.rowland@usda.gov)

VI. Effective Date, Terms, Termination, and Modification

This MOU will become effective upon signature of the parties. It will continue in effect unless modified or terminated by mutual written consent of the parties upon a 60-day advance written notice to the other agency. The protection of shared information will survive the termination of this MOU. The parties agree to evaluate the terms of this MOU at least once every five years and determine by mutual agreement whether modifications of its terms are necessary. This MOU may only be modified by mutual agreement of the parties.

APPROVED AND ACCEPTED FOR
U.S. DEPARTMENT OF AGRICULTURE:

/s/
Jenny Lester Moffitt
Under Secretary
Marketing and Regulatory Programs
U.S. Department of Agriculture
Date: 04/18/2024

APPROVED AND ACCEPTED FOR THE
FOOD AND DRUG ADMINISTRATION

/s/
Robert M. Califf, M.D.
Commissioner
Food and Drug Administration
Date: 04/18/2024

[1] Amenable species include cattle, sheep, swine, goats, fish of the order Siluriformes, and poultry (i.e., chickens, turkeys, ducks, geese, guineas, ratites, and squabs).

[2] Excluding invertebrates that are subject to APHIS regulation under the Plant Protection Act and are not intended for use as human or animal food. FDA and USDA will consult to determine the appropriate regulatory approach for any invertebrate pest of livestock that is modified using modern molecular technologies.

[3] After consultation with FDA, USDA may include additional experts from other USDA

agencies with a regulatory or research mission as needed. The USDA Biotechnology Coordinator in the Office of the Chief Economist, as the liaison, is included in meetings and communications.