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News Alert

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FDA Issues Draft Guidance Clarifying Authority Over Biotechnology and Mosquito Products

On January 18, 2017, the U.S. Food and Drug Administration (FDA) issued two draft guidance documents that, if adopted, would clarify how FDA intends to regulate biotechnology and mosquito products under the agency's new animal drug (NAD) authority. The first, *Guidance for Industry # 187: Regulation of Intentionally Altered Genomic DNA in Animals*, revises previous FDA guidance that applied solely to genetic modifications achieved using recombinant DNA (rDNA) technology. This revised version ends speculation as to whether and how FDA might regulate emerging biotechnologies like CRISPR-Cas9—FDA intends to regulate a range of technologies that intentionally alter an animal's genome.

The second document, *Guidance for Industry # 236: Regulation of Mosquito-Related Products*, specifies the circumstances under which FDA would regulate products that affect or modify mosquitoes and when FDA will defer to the authority of the U.S. Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Under FDA's proposed approach, EPA will solely regulate technologies intended to control mosquitos populations. Products intended to reduce pathogen loads in mosquitos or prevent mosquito-borne illness will remain regulated by FDA as NADs. If adopted as final FDA guidance, both of these documents potentially resolve significant uncertainty surrounding how FDA intends to use its regulatory authorities.

FDA is seeking comments on both documents. Comments on the draft *Guidance for Industry # 187* are due on April 19, 2017. The public may also comment on FDA's draft mosquito product guidance through February 21, 2017.

Regulation of Genetically Altered Genomic DNA in Animals

FDA's revised draft guidance on genetic alterations of animals brings a range of DNA-modifying technologies into the Federal Food, Drug and Cosmetic Act's (FFDCA) NAD program, under which FDA has already asserted the authority to regulate modifications achieved using rDNA. Thus, the draft guidance expands the universe of technologies that FDA will subject to the FFDCA's pre-market approval requirements for NADs. The remainder of the document largely updates the draft guidance's sections addressing the NAD-approval process to incorporate changes in terminology and technologies covered.

A. Covering "Intentional Alterations"

The revised draft guidance expands the scope of genetic modifications subject to NAD pre-market approval from introduced heritable rDNA constructs to any heritable genomic alteration.[1] Thus, FDA would regulate as an NAD "any portion of an animal's genome that has been intentionally altered." The guidance provides illustrative examples, such as random or targeted DNA sequence changes, or "any other technologies that introduce specific changes to the genome of the animal." Thus, FDA proposes a flexible, but potentially vague, definition of what may be regulated as an NAD.

FDA has further clarified that each individual, specific alteration to the animal genome constitutes a distinct NAD that must be approved. Previously, FDA considered each animal derived from a separate transformation event to be a distinct NAD due to rDNA's propensity to integrate at different sites during different transformation events. The revised draft expands this concept to apply to a range of biotechnologies: each site of alteration now constitutes a regulated article.

The draft revised guidance also anticipates some of the complexities that may arise from making multiple genomic alterations or passing down genetic modifications through conventional breeding. During the investigational phase, a sponsor may open a single investigational new animal drug (INAD) file for multiple alterations. Additionally, NAD approval would cover all animals containing the same alteration from the same event. Consequently, offspring of an altered animal would not require separate NAD approval.

B. Updated Policy on Enforcement Discretion

FDA intends to continue exercising its discretion not to enforce the FFDCA's NAD provisions against nonfood-producing species under certain circumstances. FDA would generally not enforce the NAD requirements against genetic alterations to nonfood-producing species (a) regulated by another agency (*e.g.*, EPA) or (b) raised and used solely in containment. FDA also proposes to continue to reserve its discretion not to enforce against other nonfood-producing species based on an environmental risk assessment.

C. Accommodating a Wider Range of Technologies

The balance of FDA's proposed revisions also update the guidance's sections advising how to navigate the INAD and NAD application processes. Most of the revisions reflect basic changes in terminology—from "GE animal" in the previous version to "animal with an intentionally altered genome." Others reflect the guidance's new breadth, which would cover a variety of gene-altering technologies. As a result, sponsors would need to provide in their applications basic information regarding the type of genomic alteration involved and how it might be identified in altered animals.

Regulation of Mosquito-Related Products

Prompted by increased interest in the control of mosquito populations and mosquito-borne disease, FDA's second draft guidance clarified which mosquito-altering products fall under its jurisdiction. FDA has proposed that drugs subject to the FFDCA would not include "articles intended to function as pesticides by preventing, destroying, repelling or mitigating mosquitoes for population control purposes." Such products would remain subject to EPA's authority under FIFRA. By contrast, products that reduce virus or pathogen loads in mosquitoes or that directly prevent mosquito-borne diseases will remain under FDA's purview. FDA's proposal would bring much-needed clarification to how mosquito control products, including methods of mosquito control that use biotechnology, would be regulated.

Beveridge & Diamond's reputation for excellence in agricultural biotechnology law and regulation is based on forty years of working with U.S. and international clients who research, develop, obtain government approvals for, manufacture, promote, and use conventional pesticides, pesticides produced through biotechnology, and other chemical and biotechnology products. We represent both large and small companies, as well as task forces of companies, with an emphasis on entities that invest in research to discover, develop, and defend new technology. We work with each client to identify its business objectives, and

[1] FDA intends the guidance to address primarily heritable, rather than non-heritable, genome alterations. FDA also carves out from the scope of biotechnologies regulated as NADs technologies intended to control mosquito populations. As explained below, EPA would defer to EPA's authority to regulate these technologies as pesticides under FIFRA.

then to establish and implement the most effective regulatory, commercial, litigation, and legislative strategies to achieve or exceed those objectives. To learn more, please contact Kathy Szmuszkovicz (kes@bdlaw.com, (202) 789-6037), Alan Sachs (asachs@bdlaw.com, (212) 702-5445), or any member of our Pesticides and Biotechnology practice groups.