

**FDA, JUST SAY NO: WHY USING BETA-AGONIST
DRUGS IN ANIMALS FOR CONSUMPTION
REQUIRES NEW FDA REGULATIONS**

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INTRODUCTION	155
I. BACKGROUND	158
<i>A. The Federal Food, Drug, and Cosmetic Act</i>	158
<i>B. Animal Drug Approval Process</i>	161
<i>C. Types of Animal Drugs</i>	164
1. Antibiotics	164
2. Hormones	165
3. Beta-agonists	166
<i>D. Legal Challenges</i>	168
II. THE CURRENT REGULATORY SCHEME FAILS TO PROTECT HUMAN HEALTH AND ANIMAL HEALTH AND WELFARE	170
<i>A. The FDCA's Language Incorporates the Precautionary Principle</i>	171
<i>B. The FDA Has Failed to Meet its Duties Under the FDCA</i>	174
<i>C. Legal Challenges Are Inadequate to Safeguard Public and Animal Health</i>	178
III. FDA MUST PROMULGATE RULES TO SAFEGUARD PUBLIC HEALTH, ANIMAL HEALTH, AND ANIMAL WELFARE.....	182
IV. THE FDA MUST RESTORE CONSUMER CONFIDENCE IN ITS AGENCY DECISIONS	185
CONCLUSION	187

INTRODUCTION

In 1999, the United States Food and Drug Administration (FDA) approved a beta-agonist drug commonly known as

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ractopamine.¹ Meat producers “use ractopamine to accelerate weight gain and promote . . . leanness in pigs, cattle, and turkeys.”² Today, over 160 countries either restrict or completely ban ractopamine’s use.³ Yet, the United States (U.S.) and 25 other countries still permit its use.⁴ Most countries banned or restricted ractopamine because of animal or human health concerns.⁵ For instance, studies have found that ractopamine affects animal behavior and physiology, making them more susceptible to handling abuse.⁶ Moreover, lawsuits challenging ractopamine have cited that, in farmed animals, it can cause “trembling, lameness, inability to rise or walk, reluctance to move, stiffness, hyperactivity, . . . difficulty breathing, collapse, and death.”⁷ While studies evaluating ractopamine’s effects on humans are limited, its known and unknown health risks have evoked international concern.⁸ Disagreement over the science behind ractopamine’s health effects has led to international trade disputes, including between the U.S. and countries banning the drug, such as China, the United Kingdom, and the European Union.⁹

¹ Lindsay Chichester et al., *Beta-agonists: What are they and should I be concerned?*, UNIV. NEBRASKA–LINCOLN, <https://newsroom.unl.edu/announce/beef/2563/14863> (last visited Dec. 7, 2021).

² *Food Safety Fact Sheet: Ractopamine Factsheet*, CTR. FOR FOOD SAFETY (2013), https://www.centerforfoodsafety.org/files/ractopamine_factsheet_02211.pdf [hereinafter *Factsheet*].

³ Delcianna Winders, *Why are U.S. Factory Farms Feeding Animals A Drug Banned in Most Countries?*, MILLION DOLLAR VEGAN (Mar. 10, 2020), <https://www.milliondollarvegan.com/why-are-u-s-factory-farms-feeding-animals-a-drug-banned-in-most-countries/>.

⁴ *Factsheet*, *supra* note 2.

⁵ *Id.*

⁶ Jeremy N. Marchant-Forde et al., *The Effects of Ractopamine on the Behavior and Physiology of Finishing Pigs*, J. ANIMAL SCI. 416, 419 (2003) (explaining that ractopamine affects “behavior, heart rate, and [the] catecholamine profile of finishing pigs.” These changes made the pigs more susceptible to handling and transport abuse).

⁷ *E.g.*, Complaint for Declaratory and Injunctive Relief ¶ 45, Ctr. for Food Safety v. Hamburg, 142 F. Supp. 3d 898 (N.D. Cal. 2015) (No. 3:14-cv-4932).

⁸ *Factsheet*, *supra* note 2.

⁹ Ben Valsler, *Ractopamine*, CHEMISTRY WORLD (July 17, 2020), <https://www.chemistryworld.com/podcasts/ractopamine/4012161.article>; U.S.-Taiwan Trade Relations, CONG. RSCH. SERV., <https://sgp.fas.org/crs/row/IF10256.pdf> (last updated Dec. 23, 2020); Helena

Many countries took a precautionary approach to reviewing ractopamine because studies have insufficiently demonstrated the drug's safety.¹⁰ The FDA, however, fails to adopt a precautionary approach in approving animal drugs.¹¹ This failure is highly problematic and concerning for meat consumers, animal welfare advocates, environmentalists, and others alike because animal drugs can greatly affect human health, animal health and welfare, and the environment.¹² Even more concerning is that ractopamine is not the only non-essential, beta-agonist drug on the market. The FDA recently approved Experior, which purports to reduce ammonia in cows.¹³ Although this sounds like a good, environmentally conscious idea due to the impending effects of climate change, Experior's known and unknown risks may substantially outweigh any benefits.¹⁴ Thus, the U.S. must proceed with caution when approving drugs that are non-essential and only serve some other—likely economic—purpose.¹⁵

The FDA's current regulatory scheme fails to protect human health, animal health and welfare, and the environment because the

Bottemiller, *Dispute Over Drug in Feed Limiting US Meat Exports*, NBC NEWS (Jan. 25, 2012), <https://www.nbcnews.com/business/markets/dispute-over-drug-feed-limiting-us-meat-exports-flna174014>; Helena Bottemiller, *Escalating Trade Dispute, Russia Bans Turkey Over Ractopamine Residues*, FSN (Feb. 8, 2013), <https://www.foodsafetynews.com/2013/02/escalating-trade-dispute-russia-bans-turkey-over-ractopamine-residues/>; see also *Factsheet*, *supra* note 2.

¹⁰ Valsler, *supra* note 9; see also *Factsheet*, *supra* note 2.

¹¹ Susan A. Schneider, *Beyond the Food We Eat: Animal Drugs in Livestock Production*, 25 DUKE ENV'T. L. & POL'Y F. 227, 255–61 (2015) (questioning the FDA's approval process as it favors the pharmaceutical and agricultural industries).

¹² *Id.* at 274; see also *Factsheet*, *supra* note 2.

¹³ *FDA in Brief: FDA Approves First Animal Drug that Reduces Gas Emissions from an Animal or its Waste*, U.S. FOOD & DRUG ADMIN. (Nov. 6, 2018), <https://www.fda.gov/news-events/fda-brief/fda-brief-fda-approves-first-animal-drug-reduces-gas-emissions-animal-or-its-waste> [hereinafter *FDA in Brief*].

¹⁴ Complaint for Declaratory and Injunctive Relief ¶¶ 1–14, Animal Legal Def. Fund v. Azar, No.3:20-cv-03703 (N.D. Cal. June 4, 2020); see *FDA in Brief*, *supra* note 13 (explaining how ammonia gas emissions contribute to “atmospheric haze and noxious odors,” which can irritate the eyes, nose, and throat in humans and animals. In addition, ammonia gases contribute to eutrophication, which leads to algae blooms).

¹⁵ See Valsler, *supra* note 9 (quoting a 2007 study that showed ractopamine affected farmed animals’ “compositional attributes that are economically relevant to today’s swine producers.”); see also *FDA in Brief*, *supra* note 13.

animal drug approval process shifts the burden onto consumers and organizations to ensure drug safety. The approval process lacks transparency, and the bar for approving non-essential drugs is too low. Though there is the question of whether the FDA *should* ever approve non-essential drugs—drugs that primarily serve an economic, rather than animal or human health benefit—this Note only explores ways the FDA *could* improve its approval process. The FDA could increase transparency and shift the burden back to itself by raising standards for non-essential animal drugs. To do so, the FDA could promulgate regulations for each major animal drug type, addressing the risks associated with each drug. The Federal Food, Drug, and Cosmetic Act provides the FDA with broad authority to regulate animal drugs in this way.

Throughout this Note, ractopamine and Exuperior will serve as beta-agonist drug examples. Part I outlines the current regulatory structure for animal drugs, describes various types of animal drugs, and briefly introduces prior and current legal challenges to beta-agonist drugs. Part II illustrates how the current regulatory scheme fails to protect animal and human health through analyzing legal challenges. Then, Part III dives into the various ways the FDA could promulgate rules to better safeguard human health, animal health and welfare, and the environment. Finally, Part IV discusses how these new rules could restore consumer confidence in the FDA's decisions.

I. BACKGROUND

A. The Federal Food, Drug, and Cosmetic Act

In 1938, Congress passed the Federal Food, Drug, and Cosmetic Act (FDCA) in response to public outcry over unsafe drugs on the market.¹⁶ The FDCA's primary purpose is to protect public

¹⁶ *Part II: 1938, Food, Drug, Cosmetic Act*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/about-fda/fdas-evolving-regulatory-powers/part-ii-1938-food-drug-cosmetic-act#:~:text=FDR%20signed%20the%20Food%2C%20Drug,adequate%20directions%20for%20safe%20use.&text=The%20act%20also%20corrected%20abuses,mandated%20legally%20enforceable%20food%20standards> (last updated Nov. 27, 2018).

health and safety through “preventing deleterious, adulterated, or misbranded articles from entering interstate commerce.”¹⁷ Congress conferred authority to the FDA to regulate these articles, which include animal drugs.¹⁸

The FDCA requires pre-market approval for all new animal drugs.¹⁹ The drug manufacturers must demonstrate a drug’s safety *before* the FDA may approve the drug for sale on the market.²⁰ The FDA must ensure new drugs meet a *safe and effective* standard.²¹ The FDCA defines a new animal drug as:

[A]ny drug intended for use for animals other than man, including any drug intended for use in animal feed but not including such animal feed, — (1) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as *safe and effective* for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . (2) the composition of which is such that such drug, as a result of investigations to determine its *safety and effectiveness* for use under such conditions, has become so recognized but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.²²

¹⁷ See Nicholas Freitag, *Federal Food and Drug Act Violations*, 41 AM. CRIM. L. REV. 647, 648 (2004) (explaining the FDCA’s purpose).

¹⁸ See 21 U.S.C. § 321(g)(1) (defining the term *drug* to include articles intended for animal consumption or use).

¹⁹ *FDA Regulation of Animal Drugs*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/animal-veterinary/resources-you/fda-regulation-animal-drugs#overview> [hereinafter *FDA Regulation*] (last updated Aug. 10, 2021) (explaining “a new animal drug may not be legally introduced into interstate commerce unless it is the subject of either” 21 U.S.C. § 360b, 360ccc, 360ccc-1, or 360bbb-3).

²⁰ See *id.*; see also 21 U.S.C. § 321(v) (describing the FDA requirements for new animal drug approval).

²¹ 21 U.S.C. § 321(v).

²² *Id.* (emphasis added).

The FDCA further defines *drug* as “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals” and as “articles (other than food) intended to affect the structure or any function of the body of man or other animals.”²³ The FDA has authority over any drug that impacts an animal’s “structure or . . . function.”²⁴

Congress amended the FDCA in 1996 to give the FDA more flexibility in approving and regulating new animal drugs to streamline the approval process.²⁵ Congress entitled the amendment the Animal Drug Availability Act (ADAA). The ADAA’s purpose was to improve animal and public health by increasing the number of approved new animal drugs on the market.²⁶ The ADAA amended the FDCA’s definition for *substantial evidence*, which the FDA uses in determining a drug’s efficacy.²⁷ The ADAA’s definition eliminated the requirement for field studies and expanded the types of studies the FDA may consider in finding substantial evidence.²⁸ For example, the FDA may consider published studies, foreign studies, studies using models, laboratory animal studies, in vitro studies, and the drug sponsor’s studies.²⁹ In addition, the FDA only needs to find substantial evidence in at least one “adequate and well-controlled” study to determine the effectiveness of a new animal drug.³⁰ Congress hoped the ADAA would “cut the time needed for the drug approval process by reducing the amount of data that the FDA must review.”³¹ Although Congress stated the ADAA should not compromise the FDA’s mission, this Note

²³ *Id.* §§ 321(g)(1)(B)–(C).

²⁴ *Id.* § 321(g)(1)(C).

²⁵ See Animal Drug Availability Act of 1996, Pub. L. No. 104-250, 110 Stat. 3151 (1996); H.R. REP. NO. 104-823, at 8–9 (1996).

²⁶ See H.R. REP. NO. 104-823, at 10 (1996) (noting the dwindling number of animal drugs receiving FDA approval and the negative impact on the animals’ health due to lack of available FDA-approved animal drugs).

²⁷ Animal Drug Availability Act of 1996, Pub. L. No. 104-250, 110 Stat. 3151, § 2(b)(2)(B) (1996); see also H.R. REP. NO. 104-823, at 2 (1996).

²⁸ Animal Drug Availability Act of 1996, Pub. L. No. 104-250, 110 Stat. 3151, § 2(b)(2)(B) (1996); see also H.R. REP. NO. 104-823, at 2 (1996).

²⁹ 21 C.F.R. §§ 514.4(a), 514.4(b)(3)(ii) (2020).

³⁰ *Id.* § 514.4(a) (2020).

³¹ H. R. REP. NO. 104-823, at 12.

will explain how this amendment's flexibility has increased risks to public health and animal welfare.³²

B. Animal Drug Approval Process

The FDA's Center for Veterinary Medicine (CVM) approves, reviews, and regulates new animal drugs.³³ The Office of New Animal Drug Evaluation (ONADE) is CVM's pre-approval office for reviewing information about new animal drugs.³⁴ A team of CVM personnel, including veterinarians, biostatisticians, chemists, animal scientists, pharmacologists, and toxicologists reviews new animal drug applications to determine whether the drug is safe and effective according to the proposed label's directions.³⁵ The FDA interprets *safe* to include "safety to the animal, safety of food products derived from the animal, and safety to persons [administering the drug or otherwise] associated with the animal."³⁶ The FDA further interprets *effective* to mean that the product will consistently and uniformly do what the label claims it will do.³⁷ The scope of *safe* and *effective* is limited because the terms only address the safety and effectiveness in the *target* animal, leaving out broader risks.³⁸ If the CVM team concludes that the new animal drug is safe and effective, then the team will approve the drug for sale on the market.³⁹

³² *Id.* at 8.

³³ *From an Idea to the Marketplace: The Journey of an Animal Drug through the Approval Process*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/animal-veterinary/animal-health-literacy/idea-marketplace-journey-animal-drug-through-approval-process> [hereinafter *Marketplace*] (last visited Dec. 7, 2021).

³⁴ *Id.*

³⁵ *Id.*

³⁶ *FDA Regulation*, *supra* note 19.

³⁷ *Marketplace*, *supra* note 33.

³⁸ *Id.*; see 21 U.S.C. §§ 321(u)–(v), 360(ccc-1)(d)(2) (limiting *safe* and *effective* to the target animal species, which suggests the broader impacts of an animal drug are ignored); see also Schneider, *supra* note 11, at 244–45, 274 (“There is never any consideration of cumulative multi-drug environmental or food safety effects. Furthermore, there is no apparent thought about the systemic impact of creating a billion tons of contaminated manure and then applying it to cropland or allowing it to enter waterways” which could affect wildlife animals, the environment, and neighboring communities).

³⁹ *Marketplace*, *supra* note 33.

The animal drug approval process begins, however, with a drug sponsor.⁴⁰ The drug sponsor is responsible for collecting all the necessary information regarding the new animal drug.⁴¹ This information includes the results of a pilot study on a target animal species for the drug's intended use.⁴² Once the drug sponsor collects enough information, the sponsor contacts CVM to open an Investigational New Animal Drug (INAD) file.⁴³ The drug sponsor updates CVM through their INAD file.⁴⁴ At this point, CVM and the drug sponsor create a development plan to determine the remaining information needed for CVM to approve the drug.⁴⁵

The development plan requires the drug sponsor to determine an appropriate dosage regimen.⁴⁶ The dosage regimen includes not only the dose's quantity, but also the dose's frequency, duration, and the "route of administration."⁴⁷ Once the sponsor determines a drug dosage that is *safe* and *effective*, the sponsor prepares its New Animal Drug Application (NADA).⁴⁸ The sponsor's NADA must include five technical sections: (1) target animal safety; (2) effectiveness; (3) human food safety; (4) chemistry, manufacturing, and controls; and (5) environmental impact.⁴⁹ In each section, the sponsor must

⁴⁰ See *id.* (defining *drug sponsor* as an "entity responsible for collecting all of the information about a new animal drug and submitting this information to CVM for review"); see also 21 C.F.R. § 511.3 (providing a definition for *drug sponsor*).

⁴¹ *Marketplace*, *supra* note 33.

⁴² *Id.*

⁴³ *Id.*

⁴⁴ *Id.*

⁴⁵ *Id.*

⁴⁶ *Id.*

⁴⁷ *Id.*

⁴⁸ *Id.*

⁴⁹ *Id.* Although, in theory, an environmental impact section should consider the broad implications of an animal drug on the environment, this section only analyzes the target animal's environmental impact. The National Environmental Policy Act (NEPA) requires a more thorough environmental assessment, however, many animal drug approvals are categorically excluded from NEPA analysis. See 21 C.F.R. § 25.21 (stating the FDA requires an environmental assessment in "extraordinary circumstances"); Schneider, *supra* note 11, at 269–71 (explaining the FDA relies on the drug sponsor to adequately assess environmental impacts and that categorical exclusions often apply such that the drug sponsor never completes an assessment).

include information on adverse effects or risks.⁵⁰ Lastly, the CVM reviews the NADA and approves the application if the CVM agrees with the drug sponsor's conclusions on the drug's safety and effectiveness.⁵¹ Drug approvals do not go through notice and comment like other regulations. Instead, the approvals become *immediately* effective as a regulation once the FDA publishes its notice.⁵²

Once an animal drug is on the market, the Office of Surveillance and Compliance (OS&C) monitors adverse events and regulates the drug's advertisements and marketing.⁵³ The OS&C analyzes reported event data to detect safety or effectiveness issues in animal drugs.⁵⁴ Often, these problems arise from misuse of the drug, like exceeding the dosage amount or frequency.⁵⁵ The OS&C also works with the United States Department of Agriculture (USDA) Food Safety and Inspection Service to monitor drug residues in meat, milk, and poultry products.⁵⁶ Additionally, the OS&C reviews the marketing and advertising of animal drugs to ensure promotions "are truthful and not misleading."⁵⁷ Yet, the OS&C does not thoroughly check for animal welfare or cumulative environmental effects from the drug's continued use.⁵⁸ The OS&C only reviews a drug's safety and

⁵⁰ *Animal Drug Approval Process*, DAWN BREAKER (Nov. 2018), <https://mrr.dawnbreaker.com/portals/medical/veterinary-products/animal-drug-approval-process/>.

⁵¹ *Marketplace*, *supra* note 33.

⁵² 21 U.S.C. § 360b(i).

⁵³ *Office of Surveillance and Compliance*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/about-fda/cvm-offices/office-surveillance-and-compliance#:~:text=OS%26C%20is%20responsible%20for%20regulating,they%20are%20on%20the%20market.&text=OS%26C%20is%20responsible%20for%20assuring,safe%20residue%20tolerances%20are%20established> [hereinafter *OS&C*] (last updated Apr. 15, 2021).

⁵⁴ *Id.*

⁵⁵ *Id.*

⁵⁶ *Id.*

⁵⁷ *Id.*

⁵⁸ *See id.* (describing how the OS&C narrowly reviews promotion, advertising, and post-surveillance activities of approved animal drugs). The OS&C does not assess how a drug's continued use impacts *animal welfare* or the *environment*. OS&C only conducts assessments on drugs that have adverse events, which means if there are no adverse events reports, OS&C would never check up on how the drug is doing. *See also* Schneider, *supra* note 11, at 274 (explaining that "[t]here is no systemic analysis

effectiveness when someone reports an adverse event.⁵⁹ Thus, OS&C monitors animal drugs in a limited capacity.

C. Types of Animal Drugs

Although this Note focuses on beta-agonist drugs, a discussion of the various types of animal drugs on the market aids in understanding how these drugs differ. This Part will explain antibiotics, hormones, and beta-agonists.

1. Antibiotics

Producers use antibiotics to treat, control, and prevent disease in animals.⁶⁰ Antibiotics “stop the growth of or kill bacteria.”⁶¹ Antibiotics are given to livestock through their feed or drinking water.⁶² Concentrated Animal Feed Operations (CAFOs) commonly provide antibiotics to farmed animals because the cramped housing conditions and poor sanitization increase the potential for disease-causing bacteria.⁶³ CAFOs use a *sub-therapeutic* dosage—a dosage insufficient to treat an active infection—to prevent disease and promote animal growth.⁶⁴ This practice has become controversial because studies have confirmed the link between the overuse of antibiotics in the livestock industry and antibiotic resistance.⁶⁵ Thus,

of the cumulative effects” in the environment).

⁵⁹ OS&C, *supra* note 53.

⁶⁰ *The Facts About Antibiotics in Livestock & Poultry Production*, N. AM. MEAT INST. 4, <https://www.meatinstitute.org/index.php?ht=a/GetDocumentAction/i/99943> [hereinafter NAMI, *Antibiotics*] (last visited Dec. 8, 2021).

⁶¹ *Factsheet, supra* note 2; *An HSUS Report: Welfare Issues with the Use of Hormones and Antibiotics in Animal Agriculture*, THE HUMANE SOC’Y OF THE U. S. 1 (Jan. 2016), <https://www.humanesociety.org/sites/default/files/docs/hsus-report-issues-with-hormones-welfare.pdf> [hereinafter *HSUS Report*].

⁶² *Id.*

⁶³ *Antibiotics in Our Food System*, FOOD PRINT, <https://foodprint.org/issues/antibiotics-in-our-food-system/#easy-footnote-bottom-15-1322> (last visited Dec. 8, 2021).

⁶⁴ *Id.*

⁶⁵ See NAMI, *Antibiotics, supra* note 60, at 13 (“[T]he ability of bacteria or other microbes to resist the effects of a drug after being exposed to them. This means that

sub-therapeutic dosages raise animal welfare concerns because animals are becoming more susceptible to bacterial diseases.⁶⁶

2. Hormones

The FDA approved the use of steroid hormone drugs for beef, cattle, and sheep in the 1950s.⁶⁷ Producers administer these drugs to livestock to increase their growth rate and feed-conversion ratios—the rate that animals convert feed into weight gain.⁶⁸ Some of these approved drugs use hormones that are naturally occurring and purport to improve meat quality and animal reproduction.⁶⁹ However, the FDA has approved synthetic hormone drugs as well.⁷⁰ Most hormone drugs are administered as implants, which are usually placed under the skin on the back of the animal's ear.⁷¹ The implants then slowly dissolve and do not need to be removed.⁷² The FDA has approved hormone implants for growth purposes in cattle and sheep, but not for swine, poultry, veal calves, or dairy cows.⁷³

Hormone drugs also raise animal welfare concerns. For example, recombinant bovine growth hormone (rBGH) causes the inflammation of dairy cows' mammary glands, a condition known as mastitis.⁷⁴ rBGH appears to be the most controversial of hormone drugs, as others are either widely accepted or lack sufficient data disclosing their effects.⁷⁵

the drug, and similar drugs, will no longer work against those bacteria.”); Schneider, *supra* note 11, at 242.

⁶⁶ *HSUS Report*, *supra* note 61, at 5.

⁶⁷ *Steroid Hormone Implants Used for Growth in Food-Producing Animals*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/animal-veterinary/product-safety-information/steroid-hormone-implants-used-growth-food-producing-animals> [hereinafter *Hormone Implants*] (last updated Apr. 13, 2021).

⁶⁸ *Id.*

⁶⁹ Schneider, *supra* note 11, at 246.

⁷⁰ *See id.* (describing how beef cattle receive daily doses of synthetic hormones).

⁷¹ *Id.*

⁷² *Hormone Implants*, *supra* note 67, at 1.

⁷³ *Id.*

⁷⁴ *HSUS Report*, *supra* note 61, at 3 (noting that rBGH is not an implant but is injected into dairy cows).

⁷⁵ *See id.* at 1–3 (describing different adverse effects of rBGH in cattle); *Factsheet*,

3. Beta-agonists

Beta-adrenergic receptor agonists (beta-agonists) are non-hormonal drugs.⁷⁶ They bind to receptors on various cells in an animal's body to redirect and reduce the metabolism of fat.⁷⁷ As a result, animals produce less fat and produce more lean muscle.⁷⁸ Beta-agonist drugs serve no therapeutic or essential purpose for animals.⁷⁹ Rather, beta-agonist drugs serve an economic purpose because the drugs cause animals to grow more lean muscle for slaughter.⁸⁰ Beta-agonists also raise alarming animal welfare concerns. For instance, beta-agonists lead to health and behavioral changes including, "cardiovascular stress, muscular skeletal tremors, increased aggression, hyperactivity, acute toxicity, and genotoxicity."⁸¹ Studies have further found that beta-agonists increase the number of nonambulatory animals, commonly referred to as *downer animals*.⁸²

supra note 2. See also Rick North, *FACT SHEET Recombinant Bovine Growth Hormone (rBGH or rBST) Its Documented Harm to Cows* (Nov. 2010), https://www.organicconsumers.org/sites/default/files/rbgh_harms_cows_fact_sheet.pdf; Cristina Stella & Cameron Harsh, *America's Secret Drug Problem*, CTR. FOR FOOD SAFETY (Sept. 2015), https://www.centerforfoodsafety.org/files/animal_drug_es_10_26_77814.pdf.

⁷⁶ Anna Dilger, *Beta-Agonists: What Are They and Why Do We Use Them in Livestock Production?*, AM. MEAT ASS'N 2 (2015), https://meatscience.org/docs/default-source/publications-resources/fact-sheets/beta-agonists---dilger-20158d82e7711b766618a3fcff0000a508da.pdf?sfvrsn=69f481b3_0.

⁷⁷ *Id.* at 1.

⁷⁸ *Id.* at 1–2.

⁷⁹ See *Use of Beta-Agonists in Cattle Feed*, PENNSTATE EXTENSION, <https://extension.psu.edu/use-of-beta-agonists-in-cattle-feed#:~:text=Beta%2Dagonists%20are%20a%20class,reduce%20the%20metabolism%20of%20fat.&text=At%20the%20same%20time%20the,the%20size%20of%20muscle%20fibers> (last updated Sept. 7, 2017) (explaining how companies like Tyson Foods previously used beta-agonist drugs for economic purposes. Tyson reported it stopped using beta-agonist drugs because of animal welfare concerns).

⁸⁰ *Id.*

⁸¹ *America's Secret Animal Drug Problem*, CTR. FOR FOOD SAFETY 3 (Sept. 2015), https://www.centerforfoodsafety.org/files/animal_drug_es_10_26_77814.pdf; *HSUS Report*, *supra* note 61, at 3.

⁸² Stella & Harsh, *supra* note 75, at 3–4; *Downer (Animal)*, SCIENCE DIRECT, <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/downer->

Because downer animals cannot stand or walk, they suffer from forceful, inhumane attempts to move them, including with forklifts or electrical prods.⁸³ Despite all these concerns, beta-agonist drugs, like ractopamine, remain on the market in the U.S.⁸⁴

Beta-agonists are different from antibiotics and hormones for two reasons. First, antibiotics stop the growth of and kill bacteria while beta-agonists target cells that metabolize fat.⁸⁵ Overall, beta-agonists do not affect bacteria.⁸⁶ Second, beta-agonists do not affect the hormone status of the animal, even though its effects are hormone-like because beta-agonists promote growth.⁸⁷

This Note frequently refers to two beta-agonist drugs—ractopamine and Exuperior. The FDA approved ractopamine in 1999 and Exuperior in 2018.⁸⁸ Producers use ractopamine to “accelerate weight gain and promote feed efficiency and leanness.”⁸⁹ Exuperior’s purpose is different from ractopamine; its drug sponsor, Elanco, and the FDA assert Exuperior’s purpose is to reduce ammonia gas emissions.⁹⁰ Exuperior is the first drug that the FDA approved to reduce emissions from an animal or its waste.⁹¹ At first glance, Exuperior seems like an innovative way to tackle the environmental harms of ammonia gas emissions within the animal agriculture industry.

animal (last visited Dec. 8, 2021) (defining a downer animal as one that is nonambulatory, meaning unable to walk or stand).

⁸³ *During Transport*, ANIMAL WELFARE INST., <https://awionline.org/content/during-transport> (last visited Dec. 8, 2021) (explaining that while in transport, downer animals often cannot reach food or water and are sometimes left to die without being humanely euthanized to end their suffering); see Kimberly Kindy, *Downed Pigs are Turned into Pork Products. A New Lawsuit Seeks to Stop That*, WASH. POST (Feb. 6, 2020) (explaining that USDA “inspection records show plant workers in recent years have kicked, shocked and dragged downed pigs in an effort to get them to stand upright.”); *Farm Sanctuary v. United States Dep’t of Agric.* (2021) (No. 6:19-CV-06910), WL 2644068 (W.D.N.Y. June 28, 2021) (denying motion to dismiss lawsuit challenging line speeds and treatment of downer animals).

⁸⁴ Winders, *supra* note 3.

⁸⁵ Dilger, *supra* note 76, at 1.

⁸⁶ *Id.*

⁸⁷ *Id.* at 2

⁸⁸ *Factsheet*, *supra* note 2, at 1; *FDA in Brief*, *supra* note 13.

⁸⁹ *Factsheet*, *supra* note 2, at 1.

⁹⁰ *FDA in Brief*, *supra* note 13.

⁹¹ *Id.*

However, this drug's innovation fails to help an unsustainable industry become more sustainable. Rather, it only assists the industry in continuing unsustainable practices. Moreover, Experior raises similar, troublesome animal-welfare concerns to ractopamine.⁹²

D. Legal Challenges

Various groups have unsuccessfully challenged the FDA's approval of ractopamine. In 2015, the Center for Food Safety, the Humane Society of the United States, the Center of Biological Diversity, and the United Farm Workers of America challenged the FDA's approval of 11 new animal drug applications that used ractopamine as the active ingredient.⁹³ The groups asserted the FDA violated the National Environmental Policy Act (NEPA) and the Administrative Procedure Act (APA).⁹⁴ NEPA requires federal agencies to consider the environmental impacts of major federal actions.⁹⁵ The groups stated "the FDA approvals were 'arbitrary and capricious, an abuse of discretion, and otherwise not in accordance with NEPA . . . and must be set aside.'"⁹⁶ However, the U.S. District Court for the Northern District of California found that the groups failed to exhaust all administrative remedies—as the APA requires—before seeking review of the FDA's compliance with NEPA.⁹⁷ The Ninth Circuit Court of Appeals agreed with the district court's decision to deny review, holding the court lacked jurisdiction over the matter.⁹⁸

⁹² Complaint for Declaratory and Injunctive Relief, ¶ 125, *Animal Legal Def. Fund v. Azar*, No. 3:20-cv-03703 (N.D. Cal. June 4, 2020).

⁹³ Carey Gillam, *U.S. Food, Animal Health Groups Petition FDA on Ractopamine*, REUTERS (Dec. 20, 2012), <https://www.reuters.com/article/usa-meat-hormones-idUSL1E8NK72M20121220>; *Ctr. for Food Safety v. Hamburg*, 142 F. Supp. 3d 898, 900 (N.D. Cal. 2015), *vacated and remanded*, 696 F. App'x 302 (9th Cir. 2017); P.J. Huffstutter, *Environmental, Public Health Groups Sue FDA Over Feed Additive*, REUTERS (Nov. 6, 2014), <https://www.reuters.com/article/us-usa-fda-ractopamine-lawsuit/environmental-public-health-groups-sue-fda-over-feed-additive-idUSKBN0IQ2E520141106>.

⁹⁴ *Ctr. for Food Safety*, 696 F. App'x 302.

⁹⁵ National Environmental Policy Act of 1969, 42 U.S.C. § 4332.

⁹⁶ *Ctr. for Food Safety*, 142 F. Supp. 3d at 901.

⁹⁷ *Id.* at 910.

⁹⁸ *Ctr. for Food Safety*, 696 F. App'x at 302–04.

The Ninth Circuit then stayed any further proceedings to allow the groups an opportunity to exhaust all administrative remedies, therefore, requiring the groups to file a citizen petition with the FDA.⁹⁹ Instead of filing a citizen petition, the groups decided to dismiss the lawsuit in part because they disagreed with the court's opinion and believed that the court should have resolved the case on the merits.¹⁰⁰

More recently, the Animal Legal Defense Fund (ALDF), Food & Water Watch, and Food Animal Concerns Trust filed a complaint against the FDA for approving Experior.¹⁰¹ The groups are challenging the FDA's denial of a petition to stay the drug's approval.¹⁰² The groups asserted the FDA approved Experior in violation of NEPA, the APA, and the FDCA.¹⁰³ These groups expressed concern over animal welfare, the environment, and public health because Experior's effects are largely unknown.¹⁰⁴ The complaint explained that "though the negative effects of beta-agonist drugs are widely known and well established, the beta-agonist subtype to which Experior belongs is the least-studied of all beta-agonist drugs; the specific mechanism of the drug is not yet understood, even by the drug's sponsor."¹⁰⁵ The complaint thoroughly detailed Experior's potential harm to animals,

⁹⁹ *Id.*

¹⁰⁰ The groups believed the court had jurisdiction to decide the case on the merits. In addition, the groups believed the court had no authority to stay the case after determining it lacked jurisdiction. Moreover, the groups argued that requiring a citizen petition would only further insulate the FDA from judicial review. *See Pebble Ltd. Partnership v. U.S. EPA*, 604 F. App'x. 623, 625–26 (9th Cir. 2015); *League of United Latin American Citizens v. Wheeler*, 899 F.3d 814, 826 (9th Cir. 2018); *Conn. Dep't of Children & Youth Servs. v. United States*, 16 Cl. Ct. 102, 105 (1989) ("[I]t is not possible for this court to work within a jurisdictional vacuum . . . without the requisite jurisdiction, this court in these circumstances has no authority to grant a stay of proceedings."). The groups further argued the FDA's citizen petition rule is not the type of adequate exhaustion requirement contemplated in the APA. Brief of Petitioner-Appellant for Rehearing En Banc at 10, *Ctr. for Food Safety*, 696 F. App'x. 302 (2017) (No. 15-17510).

¹⁰¹ Complaint for Declaratory and Injunctive Relief ¶ 1, *Animal Legal Def. Fund v. Azar*, No. 3:20-cv-03703 (N.D. Cal. June 4, 2020).

¹⁰² *Id.* ¶ 34 ("An interested person can, within 30 days of the approval, request that FDA stay a particular approval pending further review. 21 C.F.R. § 10.35(b).").

¹⁰³ *Id.* ¶ 14.

¹⁰⁴ *Id.* ¶ 10.

¹⁰⁵ *Id.* ¶ 4.

such as “trembling, lameness, inability to rise or walk, reluctance to move, stiffness, hyperactivity, hoof disorders and total hoof deterioration, difficulty breathing, cardiomyopathy and other heart issues, collapse, and death.”¹⁰⁶ Despite the compelling reasons detailed in the complaint, challenging FDA approvals of animal drugs is difficult due to the flexible and discretionary regulatory regime. Therefore, this Note proposes amendments to the FDCA that would raise the threshold for non-therapeutic new animal drug approvals.

II. THE CURRENT REGULATORY SCHEME FAILS TO PROTECT HUMAN HEALTH AND ANIMAL HEALTH AND WELFARE

The FDCA requires the FDA to adopt a precautionary approach to drug approvals, however, the FDA has failed to embrace such an approach in approving animal drugs. The FDA’s failure to adopt a precautionary approach has led to the approval of drugs with unknown and known human health, animal health and welfare, and environmental risks. Although scholars define the precautionary principle in various ways, the simplest understanding is that it requires a “better safe than sorry” approach to regulation.¹⁰⁷ This Part first argues the FDA has failed to meet its duties under the FDCA. Then, this Part argues legal challenges to the FDA’s approval are not enough and that new regulations are required to effectuate change in the animal drug approval process.

¹⁰⁶ *Id.* ¶ 125.

¹⁰⁷ DAVID B. FIRESTONE ET AL., ENVIRONMENTAL LAW FOR NON-LAWYERS 111 (5th ed. 2014) (explaining that the precautionary principle states regulations should air on the side of caution and depend on scientific information rather than political or philosophical ideals); see also *The Precautionary Principle & Animal Agriculture*, NAT’L. INST. FOR ANIMAL AGRIC. 4 (2014), https://www.animalagriculture.org/wp-content/uploads/2021/01/FINAL_May-16-2014_Precautionary-Principle-White-Paper.pdf (“A precautionary approach is when regulators, not knowing in advance the full extent of risk associated with an innovation, are cautious and seek more information about the product.”); Bernard D. Goldstein, *The Precautionary Principle Also Applies to Public Health Actions*, 91 AM. J. PUBLIC HEALTH 1351, 1358 (2001) (“The precautionary principle asserts that the burden of proof for potentially harmful actions by industry or government rests on the assurance of safety and that when there are threats of serious damage, scientific uncertainty must be resolved in favor of prevention.”).

A. The FDCA's Language Incorporates the Precautionary Principle

The language in the FDCA indicates that Congress intended the FDA to adopt the precautionary approach to approving new animal drugs. First, § 360b(d)(1) explains that the FDA must refuse—not approve—applications that fail to demonstrate a drug's safety.¹⁰⁸ Although the drug sponsor bears the burden to prove a new animal drug's safety, the FDA must turn to any relevant information that is available to make an informed decision.¹⁰⁹ The following highlighted portions of the FDCA illustrate how the FDA must exercise caution and deny new animal drug applications where the information or evidence is lacking, including:

- Where the results “do not include adequate tests by *all methods reasonably applicable* to show whether or not *such drug is safe* for use under the conditions prescribed, recommended, or suggested”;¹¹⁰
- Where the results “show that such drug is unsafe for use under such conditions or *do not show that such drug is safe* for use under such conditions;”¹¹¹
- Where the FDA “has *insufficient information* to determine whether *such drug is safe* for use under such conditions;”¹¹² and,
- Where the results lack “*substantial evidence* that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested.”¹¹³

The language in § 360b(d)(1) requires the FDA to affirmatively find that a drug is safe. Accordingly, the FDA must deny any new animal drug application that fails to show the drug's *safety*, provide *sufficient evidence*, or show *substantial evidence* that the drug will do what it

¹⁰⁸ 21 U.S.C. § 360b(d)(1).

¹⁰⁹ *Id.* § 360b(d)(1)(E).

¹¹⁰ *Id.* § 360b(d)(1)(A) (emphasis added).

¹¹¹ *Id.* § 360b(d)(1)(B) (emphasis added).

¹¹² *Id.* § 360b(d)(1)(D) (emphasis added).

¹¹³ *Id.* § 360b(d)(1)(E) (emphasis added).

purports to do. The FDA's affirmative duty aligns with the precautionary principle because it requires the FDA to air on the side of caution and only approve drugs where the sponsor has met its burden of proof.

Similarly, the language in § 360b(d)(2) requires the FDA to adopt a precautionary approach when considering relevant factors for whether a drug is safe and effective.¹¹⁴ Although the FDCA does not define *safe* or *effective*, the factors listed in § 360b(d)(2) help contextualize what drugs the FDA should regard as safe and effective. Overall, these factors further necessitate caution through requiring the FDA to evaluate: (1) how likely the drug will be consumed in or on food; (2) the cumulative effect on animals and humans; (3) expert opinions on the safety factors of animal experimentation data; and (4) whether the prescribed use is likely to be followed in practice.¹¹⁵ This list shows that Congress intended the FDA to approve drugs that are not only safe on paper, but also in practice on the market. Thus, the FDA must contemplate the practical conditions of the drug's use and its cumulative effects before approving a new animal drug application.

The language in § 360b(d)(2) requires the FDA to adopt a precautionary approach when considering whether there is *substantial evidence* proving a drug's effectiveness. When determining whether substantial evidence exists, the FDA must find evidence in "one or more adequate and well controlled investigations," including "a study in a target species; a study in laboratory animals; any field investigation . . . that meets the requirements of subsection (b)(3) . . . a bioequivalence study; or an in vitro study."¹¹⁶ Moreover, the FDA must find that qualified experts with scientific training and experience conducted these studies to ensure that the results are credible and representative of the drug's safety and effectiveness.¹¹⁷ These considerations show Congress intended for the FDA to cautiously rely on evidence when approving new animal drugs by ensuring that the evidence consists of appropriate studies conducted by experts. Additionally, the ADAA's legislative history demonstrates that

¹¹⁴ *Id.* § 360b(d)(2).

¹¹⁵ *Id.*

¹¹⁶ *Id.*

¹¹⁷ *Id.*

Congress expanded the scope of what constitutes substantial evidence to promote *essential drugs* that advance animal welfare or food safety.¹¹⁸ Because beta-agonist drugs generally do not further animal welfare or food safety, the FDA should employ a heightened level of caution and scrutiny when evaluating whether there is substantial evidence proving a drug's safety.

Finally, the language in § 360(e)(1) requires the FDA to employ the precautionary principle when withdrawing new animal drug applications. Overall, this subsection requires the FDA to withdraw applications if the FDA finds there could be an imminent hazard to human or animal health.¹¹⁹ The circumstances Congress listed, requiring the FDA to withdraw new drug applications, demonstrate the intent that the FDA must use all relevant information available to make an informed decision, including:

- “[E]xperience or scientific data [showing] that such drug is *unsafe* for use” under the conditions of use prescribed;¹²⁰
- “[N]ew evidence not contained in such application or not available to the [FDA] until after such application was approved . . . evaluated together with the evidence available to the [FDA] when the application was approved, shows that such drug is *not shown to be safe* . . .”;¹²¹ and,
- “[N]ew information before [the FDA] with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that such drug will have the effect it purports”¹²²

This language expresses the idea that it is better to have a potentially unsafe drug off the market, rather than a drug that could be safe on the market. Because the FDA can consider information beyond what the drug sponsor presents, the FDA should actively look to available scientific data when determining whether a drug poses a health risk to

¹¹⁸ H.R. REP. NO. 104-0823, at 2, 8-9 (1996).

¹¹⁹ 21 U.S.C. § 360b(e)(1).

¹²⁰ *Id.* § 360b(e)(1)(A) (emphasis added).

¹²¹ *Id.* § 360b(e)(1)(B) (emphasis added).

¹²² *Id.* § 360b(e)(1)(C) (emphasis added).

humans or animals.

B. The FDA Has Failed to Meet its Duties Under the FDCA

The FDA failed to employ the precautionary principle—as required by the FDCA—in approving ractopamine-based drugs and Experior. The information found in drug sponsor applications, scientific studies, FDA findings of no significant impact, complaints challenging drug approvals, and amicus briefs filed in support of those challenges, all demonstrate the FDA’s failure to adopt the precautionary approach in approving new animal drugs.

The FDA has ignored scientific data and evidence calling into question ractopamine’s safety when approving new animal drug applications that use ractopamine as an active ingredient.¹²³ For example, multiple environmental organizations challenged the FDA in 2014 for approving 11 new animal drugs without reviewing environmental impacts.¹²⁴ Although the groups focused on the environmental impacts of the drug,¹²⁵ the complaint also presented evidence calling into question the drug’s safety for humans and animals.¹²⁶

The studies provided in the complaint reveal the FDA likely failed to meet its duty under §§ 360b(d)(2)(A)–(B) for two reasons. First, the FDA likely failed to adequately consider the “probable consumption” of ractopamine.¹²⁷ For instance, the complaint referenced a study that found one in five pork products tested positive for ractopamine residues, exposing humans to low amounts of ractopamine.¹²⁸ Although the FDA established residue amounts that

¹²³ Huffstutter, *supra* note 93.

¹²⁴ Complaint for Declaratory and Injunctive Relief ¶¶ 1–6, 22, The Humane Society of the United States et. al. v. Hamburg, No. 04–933 (N.D. Cal. 2014) [hereinafter *Compl.*, *HSUS*].

¹²⁵ *Id.*

¹²⁶ *Id.* ¶¶ 30–49.

¹²⁷ 21 U.S.C. §§ 360b(d)(2)(A)–(B)

¹²⁸ *Compl.*, *HSUS*, *supra* note 124, ¶ 48; *see also Pork Chops and Ground Pork Contaminated with Bacteria*, CONSUMER REPS. (Jan. 2013), <https://www.consumerreports.org/cro/magazine/2013/01/what-s-in-that-pork/index.html> [hereinafter *Pork Chops*, CR].

are “safe” for humans,¹²⁹ dozens of other countries have banned ractopamine due to the lack of evidence demonstrating its safety.¹³⁰ As a result, food safety risks will increase because producers will use more ractopamine given the FDA’s approvals.¹³¹ Second, the FDA failed to consider the cumulative impacts of the drug. The complaint referenced various studies showing that animals are at a higher risk of disease and infection when suffering from the adverse health effects of ractopamine.¹³² The complaint cites to a study that found ractopamine significantly increased *Salmonella*’s growth rate in pigs.¹³³ Based on this information, the FDA likely failed its §§ 360b(d)(2)(A)–(B) duties.¹³⁴

The information in the complaint also shows the FDA likely violated §§ 360b(d)(2)(A)–(B) and § 360(e)(1) based on ractopamine’s known adverse effects to animal health and welfare. Between 1987 and 2011, ractopamine received more adverse event reports for pigs than any other animal drug on the market.¹³⁵ In these reports, producers observed substantial increases in pig mortality,¹³⁶

¹²⁹ Compl., *HSUS*, *supra* note 124, ¶ 31 (“FDA based its original safety approval on just one human health study—a study of six young, healthy men, one of whom dropped out because his heart began racing and pounding abnormally.”); *see also* Gretchen Goetz, *Nonprofits Sue FDA Claiming Agency Hasn’t Proven Safety of Animal Growth Drug*, FOOD SAFETY NEWS (Nov. 7, 2014), https://www.foodsafetynews.com/2014/11/consumer-groups-sue-fda-claiming-agency-hasnt-proven-safety-of-pig-drug/#.VHP5OFfF_fa (comparing U.S. residue limits to other countries).

¹³⁰ *See Pork Chops*, CR, *supra* note 128 (“The European Food Safety Authority, which advises the European Union on food policy, concluded that it couldn’t establish a safe level for ractopamine in food after reviewing the only study of its effect on humans (involving just six men). But it noted that drugs like ractopamine can cause restlessness, anxiety, a fast heart rate, and other conditions.”).

¹³¹ Compl., *HSUS*, *supra* note 124, ¶¶ 5–42 (explaining that at the time of the complaint, producers were giving ractopamine to approximately 60%–80% of cattle, pigs, and turkey in the U.S.).

¹³² *Id.* ¶¶ 42–46.

¹³³ *Id.* ¶ 44.

¹³⁴ 21 U.S.C. §§ 360b(d)(2)(A)–(B).

¹³⁵ Compl., *HSUS*, *supra* note 124, ¶ 41 (reporting 218,116 adverse events in pigs and 160,917 of those pigs were sickened or killed).

¹³⁶ *Id.* ¶ 42. (explaining a producer reported having only one to two pigs die per week before using ractopamine, but with ractopamine they lost ten to twelve per week).

pigs squealing from pain when moving,¹³⁷ and pigs that appeared weak with no energy.¹³⁸ The sheer volume of reports shows that the FDA failed to adequately assess how ractopamine impacts animal health. Furthermore, the FDA has failed to withdraw ractopamine—and instead, continues to approve its use—when presented with new information and evidence. The FDA has failed to fully contemplate the extent that producers use ractopamine, and how its cumulative use affects animal welfare.¹³⁹

More recently, the FDA failed to adequately consider the ALDF, Food Animal Concerns Trust, and the Center for Biological Diversity's petition requesting the FDA to suspend ractopamine's approval given the impacts of the coronavirus (COVID-19) pandemic.¹⁴⁰ These groups presented new information and evidence to the FDA, showing that ractopamine's continued use creates heightened risks for animal safety, human health, and the environment because of COVID-19.¹⁴¹

The petition explained that COVID-19 has forced producers to choose between holding animals on their premises until they can be sent to slaughter, or killing and disposing of their bodies.¹⁴² Given this problem, the petition presented three arguments for why the FDA must suspend or withdraw ractopamine's use: (1) the additional time animals will be given ractopamine as they await slaughter will significantly deteriorate their physical and behavioral health; (2) animals will be given "more ractopamine than the usual course of business," resulting in increased ractopamine residues in food products; and (3) the animals that are killed are often disposed of on-site in mass graves, which increases the risk of ractopamine residues

¹³⁷ *Id.* (showing pigs would squeal when taking steps, as if they were in pain. These reactions were most noticeable during loading for shipment).

¹³⁸ *Id.* (noting that loading required a much more excessive amount of prodding than before because the pigs "seemed to have no energy").

¹³⁹ 21 U.S.C. §§ 360(d)(2)(A)–(B), (e)(1).

¹⁴⁰ *Petition for Emergency Rulemaking*, ANIMAL LEGAL DEF. FUND 1–2 (June 4, 2020),

https://www.biologicaldiversity.org/programs/environmental_health/pdfs/2020-06-03-Ractopamine-Suspension-Petition--ALDF-FACT-Center.pdf.

¹⁴¹ *Id.* at 3.

¹⁴² *Id.*

leaching into the environment.¹⁴³ The petition cited to multiple studies, one of which found that ractopamine has the psychological effect of ecstasy and methamphetamine on cows, turkeys, and pigs.¹⁴⁴

The information and evidence offered in the petition falls within the scope of what the FDA must consider when deciding whether to suspend or withdraw an animal drug.¹⁴⁵ The petition adequately calls into question ractopamine's continued use under COVID-19 and thus should trigger the FDA to review relevant information. The FDA must determine whether ractopamine's continued use poses an imminent hazard to human and animal health. The FDA's failure to respond, thus far, to such a threat violates its duty under § 360b(e)(1).

The FDA failed to adopt the precautionary approach in denying the ALDF's petition for a stay of action for Experior. Within 30 days of the FDA's approval, the ALDF petitioned the FDA to stay Experior pending further review of its safety.¹⁴⁶ Under the FDA's regulation, the FDA must grant a stay in any proceeding when:

- (1) The petitioner will otherwise suffer irreparable injury.
- (2) The petitioner's case is not frivolous and is being pursued in good faith.
- (3) The petitioner has demonstrated sound public policy grounds supporting the stay.
- (4) The delay resulting from the stay is not outweighed by public health or other public interests.¹⁴⁷

¹⁴³ *Id.*

¹⁴⁴ *Id.* at 4 (citing Liu et al., *Ractopamine, a Livestock Feed Additive, Is a Full Agonist at Trace Amine-Associated Receptor 1*, 350 J. PHARMACOL. EXP. THER. 124, 127 (2014)).

¹⁴⁵ 21 U.S.C. § 360b(e)(1).

¹⁴⁶ Plaintiffs' Opposition to Defendants' and Intervenor's Motions to Dismiss at 4–5, *Animal Legal Def. Fund v. Azar*, No. 3:20-cv-03703 (N.D. Cal. Nov. 20, 2020) [hereinafter ALDF, *Opposition*]; see also 21 C.F.R. § 10.35(b) (“An interested person may request the Commissioner to stay the effective date of any administrative action.”).

¹⁴⁷ 21 C.F.R. §§ 10.35(e)(1)–(4).

The ALDF's petition adequately called into question Experior's safety, arguing that its known and unknown risks may jeopardize public health, animal health and welfare, and the environment.¹⁴⁸ The ALDF explained that Elanco failed to reliably predict Experior's effectiveness in "a herd, farm."¹⁴⁹ Therefore, Elanco failed the FDCA's requirements and did not prove Experior's safety for the target animals.¹⁵⁰ Conversely, evidence shows Experior's use may be unsafe and adversely affect animal health—like other beta-agonist drugs—and lead to lameness, heat stress, fatal respiratory and cardiac illnesses, as well as behavioral issues.¹⁵¹ Additionally, beta-agonist drug residues have been linked to heart and respiratory health issues in farm workers, consumers, and producers.¹⁵² Overall, the ALDF's petition adequately stated public policy reasons to stay Experior's approval. The drug's benefit—reduced ammonia—further fails to outweigh the drug's known and unknown risks.¹⁵³ The FDA, again, avoided its duty to take the precautionary approach when presented with evidence casting doubt onto Experior's safety.

C. Legal Challenges Are Inadequate to Safeguard Public and Animal Health

Legal challenges are inadequate to protect human health, animal health, and animal welfare from controversial animal drug approvals. First, litigation occurs too late in the animal drug approval process because litigants need a final agency action to challenge—i.e., the FDA's denial of a citizen petition.¹⁵⁴ Second, the new animal drug approval process lacks transparency, making it difficult for organizations to access information to challenge FDA approvals.

¹⁴⁸ ALDF, *Opposition*, *supra* note 146, at 4–5.

¹⁴⁹ *Id.* at 4.

¹⁵⁰ *Id.*

¹⁵¹ *Id.*

¹⁵² Complaint ¶ 8, *Animal Legal Def. Fund v. Azar*, No. 3:20-cv-03703 (N.D. Cal. June 4, 2020).

¹⁵³ ALDF, *Opposition*, *supra* note 146, at 4–5.

¹⁵⁴ *See supra* Part I.D. (explaining the 9th Circuit held that the FDA's determination on a citizen petition is the final agency action rather than FDA's published approval in the Federal Register).

Third, litigation risks the possibility that courts will dismiss legal challenges to new animal drug approvals for procedural reasons, thereby preventing a decision on the merits. Lastly, organizations must strategically adapt to legal precedent, which may benefit a future suit but often fails to save a current case from an unfavorable decision. This process shifts the burden on the public, rather than the FDA, to guarantee that a new animal drug is safe and effective. As a result, the FDA should amend its regulations to prioritize essential animal drugs that further food safety, public health, and animal welfare, and scrutinize non-essential drugs that pose an array of risks.

Litigation is less than ideal for challenging new animal drug approvals because it is time consuming and occurs too late in the process. An animal drug could go to market during litigation because the FDA's approval becomes effective immediately upon publishing to the Federal Register.¹⁵⁵ The FDCA does not require the FDA to engage in notice-and-comment rulemaking before approving a new animal drug. So, prior to the FDA's approval, the public lacks an opportunity to review or question the animal drug's safety or effectiveness. Instead, the FDA publishes its approval in the Federal Register, alerting the public of the new animal drug after its approval.¹⁵⁶ In addition, the FDA's regulatory scheme fails to provide a mechanism for tracking the drug's use in the food supply once approved. This means that while the ALDF is challenging Experior, neither the FDA, Elanco, nor the feedlots are required to track Experior's use in the market.¹⁵⁷ Consequently, Experior may adversely impact public health, animal health and welfare, and the environment before the court decides the case. Until the court renders a decision, litigation fails to safeguard public health, animal health and welfare, and the environment.

Litigation is also inadequate because the regulatory scheme lacks transparency. The information that the FDA shares—only upon approving a new animal drug—is insufficient for the public to

¹⁵⁵ 21 U.S.C. § 360b(i).

¹⁵⁶ *Id.* § 360b(i).

¹⁵⁷ *See* *Ctr. for Food Safety v. Hamburg*, 696 F. App'x 302, 303–04 (9th Cir. 2017) (litigating for over two years and ultimately dismissing on procedural grounds).

understand whether a new animal drug is safe and efficient.¹⁵⁸ In most instances, the FDA does not release information related to the approval process or provide insight into agency-sponsor interactions.¹⁵⁹ The FDA further fails to provide any information on its website leading up to a new animal drug approval. Patents and trademarks further insulate information, like the drug's composition, from the public.¹⁶⁰ Even though the public has demanded transparency, the FDA seems to believe that the public should trust its decisions without further consideration.¹⁶¹ This creates an information gap that places the burden on the public to investigate whether a new animal drug is truly safe. Overall, the FDA and the drug sponsor complete the animal drug approval process in private, with some information released only after the FDA approves the drug.

Litigation is inadequate to assert genuine challenges to an animal drug's approval because courts often dismiss on procedural grounds without rendering a decision on the merits. For example, in *Center for Food Safety v. Hamburg*, the Ninth Circuit found that the plaintiffs failed to exhaust all administrative remedies before seeking review of the FDA's ractopamine combination-drug approval.¹⁶² The various plaintiffs, including the Center for Food Safety, argued that the FDA's drug approval was a final agency action subject to review as contemplated in the APA.¹⁶³ The court believed the plaintiffs needed to file a citizen petition with the FDA first before asking the court to review the FDA's drug approval.¹⁶⁴ Overall, the case was dismissed

¹⁵⁸ 21 C.F.R. § 10.20(j).

¹⁵⁹ See Schneider, *supra* note 11, at 277–78; 21 U.S.C. § 331(j) (preventing the FDA from revealing information acquired under the authority the Animal Drug approval process); Michael P. McEvelly, *Lack of Transparency in the Pre-market Approval Process for AquAdvantage Salmon*, DUKE L. & TECH. REV. 413, 425–28 (2013) (providing an example of poor transparency in the FDA's approval of the AquAdvantage salmon).

¹⁶⁰ Schneider, *supra* note 11, at 276; 21 C.F.R. § 20.61.

¹⁶¹ See McEvelly, *supra* note 159 at 425–28 (recognizing issues with the lack of transparency from the FDA).

¹⁶² See *Hamburg*, 696 F. App'x at 302–04.

¹⁶³ *Id.* at 304; Nicholas Iovino, *Lawsuit Over Oft-Banned Animal Drug Dropped*, COURTHOUSE NEWS SERV. (Feb. 2, 2018), <https://www.courthousenews.com/lawsuit-over-oft-banned-animal-drug-dropped/>.

¹⁶⁴ *Hamburg*, 696 F. App'x at 303.

and never decided on the merits.¹⁶⁵ Similarly, in *Animal Legal Defense Fund v. Azar*, the ALDF argued against a motion to dismiss for failure to exhaust all administrative remedies.¹⁶⁶ Yet, unlike *Hamburg*, the ALDF filed a petition to stay Experior before seeking judicial review.¹⁶⁷ So, the ALDF argued it exhausted all administrative remedies before seeking review by filing the petition to stay.¹⁶⁸ The United States District Court for the Northern District of California denied the motion to dismiss, finding that the ALDF exhausted its administrative remedies.¹⁶⁹ This court's decision could provide a pathway for the public to challenge FDA approvals and, more importantly, have such issues decided on their merits.

Challenging FDA approvals requires organizations to continually learn and adapt to legal precedent. Although this strategy may benefit a future suit, it often fails to save a current case from an unfavorable decision. For example, the court dismissed the ALDF's suit in *Hamburg* because the ALDF failed to exhaust available administrative remedies *before* filing suit.¹⁷⁰ To avoid dismissal, the ALDF filed a petition to stay the FDA's approval of Experior before filing suit in federal court.¹⁷¹ This difference helped the ALDF survive a motion to dismiss based on exhaustion.¹⁷² The district court explained:

Here . . . plaintiff ALDF filed a petition for stay under § 10.35. Decisions on such petitions are final agency actions, ripe for court review. *See* § 10.45(d). To argue plaintiffs must have *additionally* filed a citizen petition

¹⁶⁵ *Id.* at 303–04.

¹⁶⁶ ALDF, *Opposition*, *supra* note 146, at 23.

¹⁶⁷ *Id.* at 4.

¹⁶⁸ *Id.* at 23.

¹⁶⁹ Order Denying Motions to Dismiss at 8, *Animal Legal Def. Fund v. Azar*, No. 03-703 (N.D. Cal. Feb. 23, 2021).

¹⁷⁰ *Id.* at 8. ALDF adapted its strategy from *Hamburg* by first filing the petition to stay with the FDA. Thus, ALDF could argue it exhausted available administrative remedies. Whereas in *Hamburg*, ALDF argued it did not need to exhaust administrative remedies because the FDA's approval was a final agency action subject to review.

¹⁷¹ *Id.*

¹⁷² *Id.*

under § 10.30, Elanco relies on *Center for Food Safety v. Hamburg*, 696 F. App'x 302 (9th Cir. 2017), in which it also intervened, and where ALDF was also party, represented by the same counsel as here. In *Hamburg*, however, no stay petition under § 10.35 had been filed. The court's pronouncement that a citizen petition was required in those circumstances does not support a conclusion that one would be necessary where a § 10.35 petition was filed. Accordingly, Elanco's motion to dismiss or to stay this action pending exhaustion is denied.¹⁷³

Even though the district court's decision is a positive step towards challenging Experior, this decision came at a cost. The ALDF had to learn from *Hamburg* to achieve this victory. This victory only helps the ALDF in its challenge against Experior and fails to address the FDA's approval of ractopamine combination-drugs at issue in *Hamburg*. Therefore, litigation is an inefficient tool because it requires organizations to take a reactive approach to addressing FDA approvals.

Legal challenges alone are inadequate to protect public and animal health from controversial animal drug approvals. The FDA must not only adopt a precautionary approach to animal drug approvals, but also amend its regulations to prioritize essential animal drugs and scrutinize non-essential drugs that pose risks to animal welfare and human health.

III. FDA MUST PROMULGATE RULES TO SAFEGUARD PUBLIC HEALTH, ANIMAL HEALTH, AND ANIMAL WELFARE

The FDA fails to properly account for the animal welfare, human health, and food safety effects of non-essential drugs because its regulatory scheme treats all new animal drug applications the same. The FDA must promulgate rules specific to the category of drug and whether it serves an essential or non-essential use. This type of regulatory scheme would better account for the unique effects of each drug while prioritizing drugs that serve an essential purpose. In

¹⁷³ *Id.*

addition, this new scheme would better align with Congress's goal to advance animal health and welfare, human health, and food safety. Overall, this hierarchical approach should subject non-essential drugs—like beta-agonists—to a higher threshold of safety and efficiency.

The FDA's regulatory scheme should reflect Congress's intent to further "the health and well-being of animals" and "public health and safety."¹⁷⁴ Congress included a list of congressional findings when it initially proposed the ADAA.¹⁷⁵ These findings offer insight into Congress's motive behind ultimately amending the FDCA. First, Congress found that the current approval process was too slow, preventing the approval of necessary and useful drug therapies.¹⁷⁶ Congress further found that the lack of these approvals placed the health and well-being of animals at risk.¹⁷⁷ Congress stated that animal drug approvals were too often delayed because of an overreliance on field investigations to establish effectiveness.¹⁷⁸ Additionally, Congress found that there are insufficient approved animal drugs to treat every specific disease or condition known in each species of animal.¹⁷⁹ Lastly, Congress stated that the CVM should promptly incorporate Congress's mission so that "the Food and Drug Administration is a global leader as a public health organization that enables the marketing of safe and effective products."¹⁸⁰

Beta-agonist drugs are not the type of drugs Congress contemplated when creating a more flexible approval process in its amendment to the FDCA. First, beta-agonists serve no therapeutic purpose to animals and only serve an economic interest to producers.¹⁸¹ Instead, studies show that ractopamine poses a health risk to animals and humans.¹⁸² Thus, beta-agonist drugs fall outside the

¹⁷⁴ Schneider, *supra* note 11, at 256.

¹⁷⁵ *Id.*

¹⁷⁶ S. 773, 104th Cong. § 2 (1995); *see* H.R. REP. NO. 104-823, at 8-9 (1996) (Conf. Rep.).

¹⁷⁷ S. 773, § 2; H.R. REP. NO. 104-823, at 9.

¹⁷⁸ S. 773, § 2.

¹⁷⁹ *Id.*

¹⁸⁰ *Id.*

¹⁸¹ *See supra* Part I.C.

¹⁸² *See supra* Part II.B.

scope of Congress's findings to approve "useful drug therapies" that further the "health and well-being of animals."¹⁸³ Because beta-agonist drugs only serve an economic purpose, delaying their approval in order to prove their safety and effectiveness would not deprive animals of a "necessary drug." Lastly, while over 160 countries have called into question the use of the beta-agonist drug ractopamine, the U.S. still permits its use, thus failing to become a global leader in the approval of safe and effective products.¹⁸⁴

The FDA should promulgate rules that prioritize necessary and useful drug therapies while holding all other non-essential drugs to a higher approval standard. Non-essential drugs often fail to provide enough benefits to outweigh the need to prove their safety and effectiveness. There is a greater risk to approving a non-essential drug that could be harmful as compared to an essential drug that could be harmful. To address the difference between non-essential and essential drugs, the FDA should establish a hierarchy among drug types. By creating regulations for each drug type, the FDA could directly address concerns known for each type: antibiotics, hormones, beta-agonists, and combination drugs. Then, the FDA could require drug sponsors who are proposing a non-essential drug to address these known concerns and prove the drug's safety to a greater degree of certainty. Addressing the peculiarities and risks of each drug—rather than a one-size fits all approach—could better protect public health, animal welfare, and the environment from adverse effects.

The FDA should promulgate regulations requiring the CVM or the drug sponsor to release information concerning the drug's safety prior to its approval. The public deserves an opportunity to question the drug's effectiveness and safety before the FDA has the final say on the matter. Furthermore, this information should be accessible on the FDA's website, similar to the FDA's adverse event information.¹⁸⁵ A drug application dashboard could help the public track a new animal drug from start to finish and provide an opportunity for public

¹⁸³ See *supra* Part III.

¹⁸⁴ Winders, *supra* note 3.

¹⁸⁵ *FDA Adverse Events Reporting System (FAERS) Public Dashboard*, U.S. FOOD & DRUG ADMIN., <https://fis.fda.gov/sense/app/95239e26-e0be-42d9-a960-9a5f7f1c25ee/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis> (last visited Dec. 8, 2021).

participation. Lastly, increased transparency could allow for peer review of the drug's data, potentially alleviating many concerns *before* the FDA approves the drug and declares its safety.

IV. THE FDA MUST RESTORE CONSUMER CONFIDENCE IN ITS AGENCY DECISIONS

The FDA should reorient its focus to advance food safety, public health, and animal health and welfare. To achieve these objectives, the FDA must consider consumer interests and work towards restoring confidence in the food system. The FDA could restore trust in agency actions through a consumer-centric strategy.¹⁸⁶ A consumer-centric strategy would require the FDA to address: (1) consumer interests in animal welfare and (2) consumer demand.

Generally, consumers are concerned with animal welfare in agriculture, which is why the FDA should pay particular attention to the animal welfare implications of animal drugs.¹⁸⁷ Additionally, animal welfare is part of animal health and, therefore, should be a primary consideration in animal drug approvals.¹⁸⁸ Beta-agonist drugs are especially alarming for consumers because the full scope of the drugs' risks—to humans and animals—are largely unknown.¹⁸⁹ Consumer campaigns have called on the FDA to reevaluate animal

¹⁸⁶ Tony D'Emidio & David Malfara, *4 Reasons Agencies Should Care About the Citizen Experience*, NEXTGOV (Apr. 10, 2017), <https://www.nextgov.com/ideas/2017/04/4-reasons-agencies-should-care-about-citizen-experience/136839/>; see Lee Raine et al., *Trust and Distrust in America*, PEW RSCH. CTR. (July 22, 2019), <https://www.pewresearch.org/politics/2019/07/22/trust-and-distrust-in-america/> (discussing survey results on the public's trust and confidence in the U.S. government).

¹⁸⁷ Alicia Kelso, *Consumers are Willing to Pay a Premium for Animal Welfare Certifications*, GROCERY DIVE (July 17, 2018), <https://www.grocerydive.com/news/grocery--consumers-are-willing-to-pay-a-premium-for-animal-welfare-certifications/533852/> (explaining that Technomic and the American Society for the Prevention of Cruelty to Animal's survey found most consumers—77%—are concerned about animal welfare in the agriculture).

¹⁸⁸ *Animal Welfare: What Is It?*, AM. VETERINARY MED. ASS'N, <https://www.avma.org/resources/animal-health-welfare/animal-welfare-what-it> (last visited Dec. 8, 2021).

¹⁸⁹ Stella & Harsh, *supra* note 75, at 3 (explaining that “no one has conducted an adequate, rigorous assessment” of beta-agonist drugs).

drugs and restrict those that are harmful to animals.¹⁹⁰ Although this tactic alerts the FDA of consumer interests, it is time-consuming, costly, and often unsuccessful.¹⁹¹ Moreover, the burden to police whether animal drugs are safe for animals should not fall on consumers. To shift this burden back to the FDA, the FDA must consider consumer interests in animal welfare.

Domestic and international consumer opinions have an impact on demand.¹⁹² To keep its international demand, Tyson Foods announced its plan to prohibit ractopamine.¹⁹³ China, along with many other countries, believe ractopamine's safety data is insufficient and, therefore, prohibits the drug's import.¹⁹⁴ As a result, interests from abroad have impacted U.S. industry decisions to restrict or prohibit harmful animal drugs, like ractopamine.¹⁹⁵ A more recent domestic example involves pressures to avoid Experior. The ALDF explained that consumers who would like to consume beef cannot because of Experior's health risks:

These members would like to consume conventionally-raised beef with confidence in its safety and with trust that the FDA has carried out its duties to keep such foods, and the animals who comprise them, safe. Because it is exceedingly difficult for consumers to obtain post-approval information about animal drug

¹⁹⁰ *Id.*

¹⁹¹ *See id.* (explaining that in 2014 the Center for Food Safety successfully petitioned the FDA to withdraw arsenic-based drugs); *see also* Carey Gillam, *U.S. Food, Animal Health Groups Petition FDA on Ractopamine*, REUTERS (Dec. 20, 2012), <https://www.reuters.com/article/usa-meat-hormones-idUSL1E8NK72M20121220> (providing an example of Center for Food Safety and Animal Legal Defense Fund petitioning the FDA to reduce allowable levels of ractopamine).

¹⁹² *Tyson to Help Meet Growing Demand for U.S. Pork by Prohibiting Ractopamine Use*, TYSON (Oct. 17, 2019), <https://www.tysonfoods.com/news/news-releases/2019/10/tyson-help-meet-growing-demand-us-pork-prohibiting-ractopamine-use#:~:text=DAKOTA%20DUNES%2C%20S.D.%20%E2%80%93%20October%202017,farmers%20beginning%20in%20February%202020>.

¹⁹³ *Id.*

¹⁹⁴ Winders, *supra* note 3.

¹⁹⁵ *Id.*

use, and because they cannot always find or afford premium, drug-free beef, *they rely on the FDA to ensure the safety of animal drugs* that may end up in the animal products they consume.¹⁹⁶

Consumers should be able to “rely on the FDA to ensure the safety of animal drugs.”¹⁹⁷ However, the global disapproval of drugs, like ractopamine, is indicative that the FDA has failed such duty. The FDA should consider not only domestic consumer interests but also international interests when approving new animal drugs.

CONCLUSION

The FDA has failed to meet its duties under the FDCA, jeopardizing food safety, public health, animal health, and animal welfare. To reorient its agency actions on these objectives, the FDA must prioritize animal drugs that serve an essential purpose. The FDA should use its broad authority to raise the standards for *non-essential* animal drugs to adequately safeguard human health animal health and welfare. Finally, the FDA should increase transparency throughout the animal drug approval process to regain public confidence in the approval system. The FDA must restore consumer confidence in the animal drug approval process, which in turn, will boost consumer confidence in the U.S. food system.

¹⁹⁶ ALDF, *Opposition*, *supra* note 146, at 10 (emphasis added).

¹⁹⁷ *Id.*