PIGLET CASTRATION AND PAIN RELIEF DRUGS: REVAMPING "SAFETY" DRUG APPROVAL REQUIREMENTS TO ADDRESS "EFFICACY" REQUIREMENTS FOR NSAIDS

By
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Abstract

This Article investigates the U.S. pork industry's routine practice of piglet castration without pain relief and why no nonsteroidal anti-inflammatory drugs (NSAIDs) have received approval from the United States Food and Drug Administration (FDA) for use in piglets to relieve pain associated with surgical castration. Some countries have approved and even require the use of NSAIDs for surgical castration in piglets. However, the U.S. veterinary pharmaceutical community claims to lack validated scientific methodology to quantify pain in piglets, leading to a lack of substantial evidence to demonstrate NSAID effectiveness and thereby barring FDA-approval of NSAIDs for pain relief in piglets during surgical castration. In order to address the pain quantification methodology challenge that has prevented FDA-approval NSAIDs for piglets during surgical castration despite approvals of NSAIDs in other countries, this Article proposes a path forward that draws on (1) market-based voluntary commitments to end surgical castration without pain relief and (2) new legislation that introduces pain measurements into the safety evaluation of all new food-producing animal drugs and requires data collection and publication on painful procedure methods in food-producing animals.

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I. INTRODUCTION

Every year, the vast majority of the 66 million male piglets born into the United States pork industry[1] undergo painful surgical castration without pharmaceutical pain management, partially due to the fact that no analgesics have approval from the U.S. Food and Drug Administration for use in pigs.[2] However, pain relief drugs are approved and even required in other countries.[3]

In order to address the pain quantification methodology challenges that have prevented the FDA from approving pharmaceutical pain relief for male piglets during surgical castration, the United States should adopt a path forward that draws on (1) market-based voluntary commitments to end surgical castration without pain relief, and (2) new legislation that introduces pain measurements into the safety evaluation of all new food-producing animal drugs, and requires data collection and publication on painful procedure methods in food-producing animals.

Part II of this Article reviews the practice of piglet castration and how animal drugs are regulated in the United States and abroad. Part III of this Article investigates the implications of the crux of the problem: the claim of the veterinary pharmaceutical community that they lack validated scientific methodology to quantify pain in food-producing animals in the United States. Part IV of this Article proposes and defends a two-pronged market- and legislative-driven solution to address the common lack of pain management in piglet castration. Lastly, Part V of this Article concludes with a brief overview of the

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[1] *See* NAT'L AGRIC. STAT. SERV., U.S. DEP'T OF AGRIC., ISSN: 1949-1921, QUARTERLY HOGS AND PIGS 5 (2018) (describing a total U.S. pig crop of 133,176,000 pigs in 2018, of which approximately half are male).

[2] *See* Brooklyn Wagner et al., *Identifying Barriers to Implementing Pain Management for Piglet Castration: A Focus Group of Swine Veterinarians*, 10 ANIMALS, July 15, 2020, at 1202, 1 (describing the lack of FDA approval as one of three key reasons why veterinarians do not prescribe pain relief for piglets during castration).

[3] *See, e.g.*, Council Directive 91/630, art. 4, 1991 O.J. (L 340) (EC) (describing how male pigs over four weeks old may only be castrated under anesthesia in the European Union). *See also, e.g.*, NAT'L FARM ANIMAL CARE COUNCIL, CODE OF PRACTICES: FOR THE CARE AND HANDLING OF PIGS 33 (2014) (describing common industry guidelines in Canada where piglets of any age undergoing castration must be administered analgesics).

novel ideas that add to the conversation on food-producing animal drug regulations.

II. BACKGROUND

A. *Piglet Castration: Why and How*

In many countries, including the United States, male piglets commonly undergo surgical castration within seven days after birth.[4] This practice addresses two issues with entire (non-castrated) male pigs: (1) the development of "boar taint," which is an unsatisfactory smell and taste in the meat of some entire male pigs, and (2) the exhibition of aggression.[5] "Surgical castration involves cutting and manipulating innervated [soft] tissues" and, without pain relief, is painful as demonstrated by "elevated blood cortisol concentrations, high-pitched squealing, and pain-indicative behaviors, such as trembling and lying alone."[6] Pain-related behaviors can last up to five days after castration.[7]

U.S. pork producers most commonly address boar taint and aggression with surgical castration without pain relief,[8] but several alternatives exist. First, surgical castration can be conducted *with* pain relief via an anesthetic, an analgesic (known as non-steroidal anti-inflammatory drugs, or NSAIDs), or a combination of drugs.[9] The use of lidocaine (a local anesthetic) reduces various pain-related responses.[10] The combination of lidocaine with meloxicam (an NSAID) further curtails pain-related responses, as lidocaine reduces pain during castration and meloxicam reduces pain after castration.[11] Second, immunocastration is an alternative that involves a relatively pain-free,[12] two-dose injection of a specific hormone blocker that lessens boar taint and aggression.[13] Third, pork producers can raise entire

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[4] Michael D. Kleinhenz et al., *Invited Review: On-Farm Pain Management of Food Production Animals*, 37 APPLIED ANIMAL SCI. 77, 80 (2021).

[5] *Literature Review on the Welfare Implications of Swine Castration*, AM. VETERINARY MED. ASS'N 1, 1 (2013), https://perma.cc/9KLW-6MA4 (accessed Oct. 9, 2021) [hereinafter *Welfare Implications of Swine Castration*].

[6] *Id.* at 2.

[7] *Id.*

[8] Kleinhenz et al., *supra* note 4, at 81.

[9] *Welfare Implications of Swine Castration, supra* note 5, at 3.

[10] *See, e.g.*, Martin S. Leidig et al., *Pain and Discomfort in Male Piglets During Surgical Castration with and Without Local Anesthesia as Determined by Vocalization and Defence Behaviour,* 116 APPLIED ANIMAL BEHAVIOUR SCI. 174, 174 (2009) (concluding that local anesthesia reduces pain intensity, but that prolonged handling causes additional distress).

[11] Monica Hansson et al., *Effect of Local Anesthesia and/or Analgesia on Pain Responses Induced by Piglet Castration*, 53 ACTA VETERINARIA SCANDINAVICA, 2011, at 1.

[12] Stig Einarsson, *Vaccination Against GnRH: Pros and Cons*, 48 ACTA VETERINARIA SCANDINAVICA, Aug. 7, 2006, at 3 (describing how the administration of Improvac, an immunocastration drug, "caused very little irritation at the injection site of the vaccinated pigs").

[13] *Welfare Implications of Swine Castration*, *supra* note 5, at 1.

male pigs without any form of castration and instead address boar taint by slaughtering the pigs prior to puberty.[14]

Three key reasons U.S. pork producers do not use NSAIDs for surgical castration are: (1) lack of FDA-approved NSAIDs, (2) cost, and (3) lack of veterinary training.[15] The key barrier to FDA-approved NSAIDs, as discussed at length in Part III, is the veterinary pharmaceutical community's claim that they lack validated methodology to measure pain in piglets. Relatedly, the veterinary pharmaceutical community also claims they lack substantial evidence demonstrating drug effectiveness.[16] While Part IV briefly touches on the cost challenges, this Article primarily focuses on how to address the central challenge of the deficiency of FDA-approved NSAIDs, because even *if* pork producers wanted to transition to surgical castration with pharmaceutical pain relief, the current animal drug regulatory framework in the United States makes NSAID administration significantly more difficult.

B. Animal Drug Statutes and Regulations in the United States

The current U.S. statutory and regulatory framework for new animal drugs has made it clear that, in the case of drugs for food-producing animals, production and economic motives trump animal welfare motives.[17] The legislative and regulatory focus is on the safe use of drugs in our food—not the safe use of drugs on animals. In practice, new animal drug approval processes in the United States prioritize drug efficacy over animal safety.

1. Key Statutes and Amendments

The Federal Food, Drug, and Cosmetic Act (FDCA) authorizes the Secretary of the Department of Health and Human Services to regulate new animal drug approvals,[18] an authority delegated to the Commissioner of the FDA.[19] The FDCA prohibits the introduction of any

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[14] *Id.* at 3.

[15] Wagner et al., *supra* note 2, at 6.

[16] *Id.*

[17] *See* Susan A. Schneider, *Beyond the Food We Eat: Animal Drugs in Livestock Production*, 25 DUKE ENV'T. L. & POL'Y F. 227, 256–258 (2015) (explaining how the "purpose of many new animal drugs is not to treat disease but to reduce production costs" which are "economic objectives, not public health objectives, and certainly not animal welfare objectives").

[18] 21 U.S.C. §§ 321(d), 321(g), 355, 371(a).

[19] In 1977, the Secretary of Health and Human Services delegated authority to the FDA to perform FDCA functions. Delegations of Authority to the Commissioner of Food and Drugs, 42 Fed. Reg. 15561 (Mar. 22, 1977) (codified at 21 C.F.R. § 5.10). In 2004, the FDA removed § 5.10 to transfer to an Internet-based system for publishing delegation of authority, specifically referencing FDA Staff Manual Guide § 1410.10 as the new location for former § 5.10. Removal of Delegations of Authority and Conforming Changes to Regulations, 69 Fed. Reg. 17285 (Apr. 2, 2004). *See also* FOOD & DRUG ADMIN., FDA STAFF MANUAL GUIDES, VOLUME II—DELEGATIONS OF AUTHORITY: REGULATORY DELEGATIONS OF AUTHORITY TO THE COMMISSIONER FOOD AND DRUGS 1 (2016).

new drug into interstate commerce without a new drug application approval.[20] New animal drug applications must include, among other requirements, "full reports of investigations which have been made to show whether such drug is *safe* for use and whether such drug is *effective* in use."[21]

Key FDCA amendments have eased animal drug availability and approvals. In 1994, the Animal Medicinal Drug Use Clarification Act (AMDUCA) legalized extra-label drug use in some circumstances.[22] While legalizing extra-label drug use alleviated veterinarians' concerns about the legitimacy of administering existing drugs for unapproved indications,[23] the American Veterinary Medical Association does not view extra-label drug use as a solution to treat widespread animal disease (such as pain during and after piglet castration). Notably, extra-label drug use instead disincentivizes pharmaceutical companies from seeking new animal drug approvals.[24] Ultimately, the AMDUCA highlighted the veterinary community's interest in increasing animal drug availability.[25]

After the AMDUCA, Congress again amended the FDCA to expedite and improve the flexibility of the drug approval process via the Animal Drug Availability Act of 1996[26] (ADAA) and several iterations of the Animal Drug User Fee Acts[27] (ADUFA), respectively. The ADAA grants new animal drug sponsors more flexibility by, in part, clarifying a variety of ways drug sponsors can demonstrate "substantial evidence" of drug efficacy.[28] The ADUFA and the similar iterations of the Animal Generic Drug User Fee Acts[29] have expedited new animal drug approval processes by authorizing the FDA to collect fees from the new animal drug sponsors to support the application reviews.[30] The Ameri-

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[20] 21 U.S.C. § 355(a).

[21] *Id.* § 355(b)(1)(A) (emphasis added).

[22] Animal Medicinal Drug Use Clarification Act of 1994, Pub. L. No. 103–396, § 2(a), 108 Stat. 4153 (codified at 21 U.S.C. § 360b(a)).

[23] *See* ?Eugene I. Lambert, *The Reformation of Animal Drug Law: The Impact of 1996*, 52 FOOD & DRUG L. J. 277, 279–80 (1997) (describing the veterinarian-based motivations for the passage of AMDUCA).

[24] *Extralabel Drug Use and AMDUCA: FAQ*, AM. VETERINARY MED. ASS'N, https://perma.cc/M6XY-MFUC (accessed Sept. 19, 2021).

[25] Lambert, *supra* note 23, at 280.

[26] Animal Drug Availability Act of 1996, Pub. L. No. 104–250, §§ 2(a), 2(d), 110 Stat. 3151, 3153 (1996) (codified at 21 U.S.C. § 360(b)) (improving the flexibility and clarity in the animal drug approval processes for drug sponsors).

[27] *See, e.g.*, Animal Drug User Fee Act of 2003, Pub. L. No. 108–130, 117 Stat. 1361 (2003).

[28] Animal Drug Availability Act § 2(a) (codified at 21 U.S.C. § 360b(d)(3)) (stating that "substantial evidence" of efficacy can come in the form of "stud[ies] in a target species; . . . laboratory animals; . . . field investigation[s] . . .; bioequivalence stud[ies]; or . . . in vitro stud[ies]").

[29] *See, e.g.*, Animal Generic Drug User Fee Act of 2008, Pub. L. No. 110–316, 122 Stat. 3509 (2008).

[30] CONG. RSCH. SERV., R45077, ANIMAL DRUG USER FEE PROGRAMS 1 (2018).

can Veterinary Medical Association has lauded the ADUFA for increasing the number of approved animal drugs.[31]

2. Drug Efficacy

When reviewing new animal drug applications, the FDA has different guidelines and requirements for drug efficacy versus drug safety. The FDA promulgated the rule that "[a]n application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the new animal drug is safe and effective for use as suggested in the proposed labeling."[32] Further, new animal drug applications must demonstrate "substantial evidence" of effectiveness—not safety.[33] An effective new animal drug must "have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."[34] The ADAA clarifies acceptable types of studies that demonstrate "substantial evidence" of effectiveness.[35]

The FDA has issued guidelines regarding effectiveness data for NSAIDs in animals, which "encourage the use of validated methods of pain assessment in the target species."[36] The lack of validated methodologies in the United States to quantitatively measure pain has been a key challenge in obtaining FDA approval for NSAIDs in food-producing animals, [37] as heavily detailed in Part III of this Article. No NSAIDs have received FDA approval for any indication in pigs.[38] The efficacy studies for the only FDA-approved new NSAID for food-producing animals—Banamine Transdermal (flunixin), which helps alleviate pain caused by foot rot in cattle[39]—relies on a person's observation of the ranked lameness of a cow with foot rot, and pressure

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[31] *Animal Drug User Fee Act*, AM. VETERINARY MED. ASS'N (2011), https://perma.cc/G4PT-2MX2 (accessed Sept. 30, 2021). *See also Reauthorization of Animal Drug User Fees: ADUFA and AGDUFA: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Com.*, 115th Cong. 133 (2018) (containing statement from Michael J. Topper, President, American Veterinary Medical Association, stating that the ADUFA and AGDUFA have "helped in bringing new animal drugs to market").

[32] 21 C.F.R. § 514.1(b)(8)(i).

[33] *Id.* § 514.1(b)(8)(ii). *See also, id.* § 360b(d)(3).

[34] *Id.* § 514.4(a).

[35] 21 U.S.C. § 360b(d)(3); *see* discussion *supra* note 28.

[36] CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUM. SERV., NO. 123, GUIDANCE FOR INDUSTRY: ?DEVELOPMENT OF TARGET ANIMAL SAFETY AND EFFECTIVENESS DATA TO SUPPORT APPROVAL OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) FOR USE IN ANIMALS 6 (2006).

[37] Hans Coetzee, Professor & Head, Anatomy & Physiology, Kan. St. Univ., Presentation at the Pain in Animals Workshop: Current State of Acute Pain in Livestock (Oct. 2, 2019), https://perma.cc/3BYP-BZ2H (accessed Oct. 2, 2021).

[38] Wagner et al., *supra* note 2, at 2.

[39] *FDA Approves First Drug to Control Pain in a Food-Producing Animal*, U.S. FOOD & DRUG ADMIN. (Aug. 9, 2018), https://perma.cc/P2T4-8L9Q (accessed Oct. 2, 2021).

mat measurements of force and foot contact areas to assess pain.[40] While this combined method sufficiently quantified pain for cows with foot rot, companion animals have "more validated methods to assess pain" than food-producing animals.[41]

3. Drug Safety

The safety requirements for new animal drugs emphasize how drug residues in animal-based food products will impact humans, a distinction that can yield controversial results.[42] The FDCA defines "safe" as having "reference to the health of man or animal."[43] In the case of animal drugs, the FDCA guides safety determinations with the following:

> In determining whether such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof, the Secretary shall consider, among other relevant factors, (A) *the probable consumption of such drug and of any substance formed in or on food because of the use of such drug*, (B) *the cumulative effect on man* or animal *of such drug, taking into account any chemically or pharmacologically related substance*, (C) *safety factors which in the opinion of experts, qualified by scientific training and experience to evaluate the safety of such drugs, are appropriate for the use of animal experimentation data*, and (D) whether the conditions of use prescribed, recommended, or suggested in the proposed labeling are reasonably certain to be followed in practice.[44]

Notably, the safety requirements heavily focus on humans—as seen by the above-emphasized portions of the statute that apply to humans. Specifically, the statute calls out the human tolerance of consuming the product of an animal that once consumed an animal drug and the safety of humans administering the drug to animals.

Further, FDA regulations require new animal drug sponsors provide methods for assessing the amount of drugs in a food product and set "the proposed tolerance or withdrawal period or other use restrictions to ensure that the proposed use of this drug will be safe" for humans.[45] The FDA regulations explain that a new animal drug "application may be refused unless it contains detailed reports of the investigations . . . in which the purpose, methods, and results obtained

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[40] *Id*. *See also* Intervet, Inc., *Freedom of Information Summary: Original New Animal Drug Application,* NADA 141-150, BANAMINE TRANSDERMAL 1, 13–15 (July 21, 2017), https://perma.cc/7CS8-P5P6 (describing a similar study to determine pain relief in cattle using lameness scores and gait analysis).

[41] *FDA Approves First Drug to Control Pain in a Food-Producing Animal*, *supra* note 40.

[42] *See, e.g.*, Schneider, *supra* note 17, at 249–251 (describing how production-focused food-producing animal drugs, like ractopamine and Zilmax, have negatively impacted animal welfare, but are approved as safe and effective).

[43] 21 U.S.C. § 321(u).

[44] 21 U.S.C. § 360b(d)(2) (emphasis added).

[45] 21 C.F.R. § 514.1(b)(7).

are clearly set forth of acute, subacute, and chronic toxicity . . . ."[46] However, this regulation is poorly applied to animal safety. For example, FDA-approved ractopamine used in pigs to expedite growth has been associated with almost 250,000 adverse events in pigs themselves.[47] Ultimately, approvals of new animal drugs for food-producing animals prioritize efficacy and human safety over animal safety.

C. Animal Drug Regulation and Pain Relief Requirements Abroad

While many countries have similar drug approval processes to the United States, some countries differ from the United States in both approving NSAIDs for piglet castration and commonly administering pharmaceutical pain relief when performing piglet castration.

1. Canada: In Focus

Like the United States, animal drug approvals in Canada require evidence that drugs are safe—to both the target animal and to humans—and effective.[48] The Food and Drugs Act of Canada authorizes the Governor in Council to regulate new drugs.[49]

Similar to the United States, Canada's regulations require that new animal drug applications contain reports demonstrating new drug safety and substantial evidence of effectiveness for the proposed indication.[50] Akin to FDA Guidance, Health Canada Guidance declares that target animal safety reports may require acute, subchronic, and chronic toxicity studies, among other potential studies.[51] Also like FDA Guidance, Health Canada Guidance lists requirements for demonstrating human safety of consuming the products of an animal that received the new drug, including the evaluation of the safety of drug residues.[52] However, Health Canada Guidance deviates from FDA Guidance in that it does not provide specific requirements to demonstrate NSAID efficacy, other than the generic guidance for demonstrating any new animal drug efficacy.[53]

Unlike the FDA, Health Canada has approved several NSAIDs for use in pigs, including approved applications for ketoprofen, meloxicam,

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[46] *Id.* § 514.1(b)(8)(iii).

[47] Kelsey Eberly, *Hog Farming: Past, Present, and Future Panel: Establishing and Enforcing a Right to Truthful Information About Pig Farming in a Fake News Era*, 34 J. LAND USE & ENVTL. L. 291, 297–98 (2019).

[48] *See Guidance for Industry Preparation of Veterinary New Drug Submissions,* VETERINARY DRUGS DIRECTORATE, HEALTH CAN. 74, 83, 88 (2007) (describing requirements for animal safety, efficacy, and human safety for new animal drugs in Canada).

[49] Food and Drugs Act, R.S.C. 1985, c F-27, § 30(1) (Can.).

[50] Foods and Drug Regulations, C.R.C., c 870, §§ C.08.002(2)(g)–(h) (Can.).

[51] *Guidance for Industry Preparation of Veterinary New Drug Submissions*, *supra* note 48, at 74–77.

[52] *Id.* at 88.

[53] *Id.* at 83 (describing requirements for substantial evidence of efficacy but leaving out specificity for pain indications or other NSAID-related requirements).

and flunixin meglumine.[54] Metacam (which contains the active ingredient meloxicam) has specifically been approved for pain relief after procedures like castration.[55]

Moreover, in contrast to the United States, Canadian pork producers commonly use analgesics for piglet castration. Canada's National Farm Animal Care Council (NFACC), is a federally funded, yet private, national organization dedicated to advancing farm animal welfare through upholding a "credible, science-informed approach" to the development of national farm animal care standards called the Codes of Practice.[56] The NFACC includes twenty-eight member organizations, including the Canadian Pork Council,[57] which unites "nine provincial pork industry associations representing 7,000 farms."[58] NFACC members are bound to the Codes of Practice.[59] The *Code of Practice for the Care and Handling of Pigs* requires[60] that piglet castration at any age be performed with analgesic as of July 1, 2016, and piglet castration must be performed with anesthetic *and* analgesic if the piglet is over ten days old.[61] Therefore, the use of analgesic for piglet castration is industry-mandated—but not legally mandated—for Canadian pork producers.

2. *Other Jurisdictions: In Brief*

The European Union (EU) requires that animal drugs be safe and effective.[62] Further, the EU requires use of anesthesia and analgesia

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[54] *See, e.g.*, *Drug Product Database Online Query*, HEALTH PRODUCTS CAN. (Jan. 15, 2021), https://perma.cc/AYQ6-PD5W (accessed Sept. 29, 2021) (containing NSAIDS in product name by searching for, e.g., "Ketoprofen V," "Anafen," "Metacam for Swine," "Banamine," or "Flunazine" in the "Product name" search box).

[55] *Metacam for Swine (Canada)*, DRUGS.COM, https://perma.cc/U2MW-LAMK (accessed Sept. 29, 2021).

[56] *About NFACC*, NAT'L FARM ANIMAL CARE COUNCIL (2021), https://www.nfacc.ca/about-nfacc (accessed Sept. 25, 2021); *see* Emma Gregory, *The History Behind the National Farm Animal Care Council and How It Impacts B.C.*, VICTORIA NEWS (Sept. 6, 2021), https://perma.cc/CGP7-GZFD (accessed Sept. 25, 2021) (explaining that NFACC is funded by the federal Agriculture and Agri-Food department).

[57] *Partners*, NAT'L FARM ANIMAL CARE COUNCIL (2021), https://perma.cc/37UC-YTBA (accessed Sept. 25, 2021).

[58] *About Us*, CANADIAN PORK COUNCIL, https://perma.cc/8AEK-2FNT (accessed Sept. 25, 2021).

[59] *NFACC Membership*, NAT'L FARM ANIMAL CARE COUNCIL (2021), https://perma.cc/FNU4-CV8K (accessed Sept. 25, 2021).

[60] The NFACC defines a "requirement" in its Codes of Practice as an "industry-imposed expectation outlining acceptable and unacceptable practices." It goes on to state that "requirements" are "fundamental obligations relating to the care of animals" and "represent a consensus position that these measures, at minimum, are to be implemented by all persons responsible for farm animal care." *Codes of Practice for the Care and Handling of Farm Animals*, NAT'L FARM ANIMAL CARE COUNCIL, https://perma.cc/72JE-HZS6 (accessed Sept. 25, 2021).

[61] NAT'L FARM ANIMAL CARE COUNCIL, *supra* note 3.

[62] Council Regulation 2019/6, 2018 O.J. (L 4) 45 (EU).

during castration in piglets over seven days old.[63] Other non-EU European countries also require pain relief. For example, Norway requires anesthetic and pain relief for all animal castrations[64] and Switzerland requires anesthetic for all piglet castrations.[65]

Pharmaceutical pain relief for surgical castration is well established throughout most of Europe. In a 2016 study by the Federation of Veterinarians of Europe that surveyed twenty-four European countries regarding castration (or alternative) methods, an estimated 61% of pigs were surgically castrated (of which 46% of surgically castrated pigs were administered anesthetic and/or analgesia), while 36% of pigs were raised as entire males and 3% were immunocastrated.[66] Also in 2016, the European Commission (EC) released a report highlighting the most common castration methods in various countries.[67] Of piglets surgically castrated: castration with analgesia was the primary method of surgical castration in Austria, Belgium, Denmark, Finland, France, and Germany; castration with general anesthesia was the primary method of surgical castration in the Netherlands and Switzerland; castration with local anesthesia was the primary method of surgical castration in Norway and Sweden; castration with neither anesthesia nor analgesic was the primary method of surgical castration in Bulgaria, Croatia, France, Hungary, Italy, Luxembourg, Malta, Poland, Portugal, Slovenia, and Spain.[68] Europe clearly has a patchwork approach to castration methods, but some level of pharmaceutical pain relief is practiced in most countries.[69]

While other jurisdictions maintain stringent standards similar to the United States for new animal drug approvals, many countries have not only approved NSAIDs, but, in some cases, even *require* the use of pharmaceutical pain relief for piglet castration. Even without legal mandates, many countries administer pharmaceutical pain relief as a common industry practice.

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63 "If castration. . .is practiced after seventh day of life, it shall only be performed under anaesthetic and additional prolonged anesthesia by a veterinarian." Commission Directive 2001/93, annex ch. I pt. 8, 2001 O.J. (L 316) 37 (EC).

64 Lov om dyrevelferd 19. oktober 2009 nr. 97 § 9.

65 Loi fédérale du 16. décembre 2005 sur la protection des animaux (LPA), RO 2008, 2965 ff.

66 Nancy De Briyne et al., *Pig Castration: Will the EU Manage to Ban Pig Castration by 2018?*, 2 Porcine Health Mgmt. 1, 3 (2016).

67 CASTRUM Consortium, *Pig Castration: Methods of Anaesthesia and Analgesia for All Pigs and Other Alternatives for Pigs Used in Traditional Products*, EUR. COMM'N 1, 23, 95–105 (2016).

68 *Id.* at 23 (providing a comprehensive overview of castration practices in the twenty-four surveyed European countries can be found at ch. 7.2).

69 *See* Briyne et al., *supra* note 66, at 3 (providing statistics on castration methods and demonstrating that most of the twenty-four European countries in the survey practice at least one form of pharmaceutical pain relief, with the exceptions of Hungary and Ireland (which avoids castration altogether with 100% of male pigs raised as entire males) as well as Latvia and Portugal (85% of male pigs raised as entire males)).

III. THE CRUX OF THE PROBLEM: SCIENTIFIC METHODOLGY TO QUANTIFY PAIN

If analgesics are not only approved but, in some cases, *required* for piglet castration in other countries, why has the United States not yet approved analgesics for use in pigs to provide pain relief during and after castration? Because the U.S. veterinary pharmaceutical community has not yet identified what it believes to be validated methods to quantify pain levels in piglets.

FDA approval of a new NSAID with a pain relief indication requires the drug sponsor to provide substantial evidence of effectiveness by demonstrating that the drug does, in fact, provide pain relief.[70] However, veterinary scientists in the United States claim there is not yet a validated method for quantifying pain levels in many food-producing animals, including for male piglets during and after castration.[71] Ultimately, the FDA determines whether methods are valid, but drug sponsors must first present the methodology to be validated within their responsibilities for new animal drug applications.[72]

The FDA notes that methodology validation relies on acceptable endpoints of animal response,[73] such as possible pain scales, ethograms, and biomarkers for NSAIDs.[74] While the FDA has not yet acknowledged a specific validated methodology for pain assessment in piglets, it has encouraged collaboration with the industry.[75] Without validated methodology, a drug sponsor cannot demonstrate an NSAID's effectiveness, preventing FDA approval. Essentially, the claimed lack of validated pain assessment methodology prevents male piglets from receiving pain relief during and after surgical castration.

The veterinary research community, partly in collaboration with the USDA, has researched pain management in pigs and other food-producing animals for decades.[76] When it comes to quantifying pain in

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[70] *See* Coetzee, *supra* note 37 (recommending that the NSAID must present "control of clinical signs of pain associated with a disease" if a claim for pain relief is present on the label).

[71] Flávia Augusta de Oliveira et al., *Validation of the UNESP-Botucatu Unidimensional Composite Pain Scale for Assessing Postoperative Pain in Cattle*, 10 BMC VETERINARY RSCH. 1, 1–2 (2014).

[72] 21 C.F.R. § 514.117(a).

[73] "An adequate and well-controlled study [for new animal drugs] . . . uses methods to assess animal response that are well defined and reliable . . . describe the *criteria used to assess the response*, and, when appropriate, justify the selection of the methods to assess animal response." 21 C.F.R. § 514.117(b)(8) (emphasis added).

[74] Emily R. Smith, Dr. of Veterinary Med., Div. of Therapeutic Drugs for Food Animals, Food & Drug Admin., Presentation at the Pain in Animals Workshop: FDA/CVM Approval of Drugs to Control Acute Pain in Food Animals – Regulatory Challenges and Opportunities (Oct. 2, 2019), https://perma.cc/5XQW-SD6U (accessed Sept. 16, 2021).

[75] *Id.*

[76] *See, e.g.*, *Welfare Implications of Swine Castration*, *supra* note 5, at 4–5 (citing research conducted into pain mitigation during piglet castration dating back to 1988). *See also, e.g.*, *Research Project: Pain Management in Swine*, AGRIC. RSCH. SERV. (Jan. 2, 2021), https://perma.cc/677Z-LERR (accessed Sept. 23, 2021) (describing a research pro-

animals, the veterinary literature has identified several methods to measure pain in piglets. One promising physiological measure of piglet pain measures hormone levels, such as cortisol and adrenocorticotropin hormone (ACTH).[77] In a review of pig pain assessment studies, it was noted that cortisol and ACTH "[c]an be reliably quantified and [have] been validated in relation to painful conditions."[78] However, these physiological measures can also be impacted by the handling associated with surgical castration[79] and have low specificity when not used in combination with behavioral measures.[80] Demonstrated behavioral measures of pain associated with pig castration include: trembling, shaking their legs, sliding on their hind quarters, wagging their tails, spasms, motionless sitting or standing with their heads down, attempting to escape (as measured by frequency, duration, or intensity), posture changes, "avoiding social contact with littermates," isolation, changes in nursing behavior, and more.[81] While some of these behavioral measures have been validated by various studies, some are prompted solely by being handled (for example, escape behavior) and some need validation specific to the painful condition being observed.[82] Lastly, vocalizations, such as "grunts, squeals, and screams" can be differentiated and measured in decibels to indicate intensity of pain, but piglets "may vocalize regardless of pain" due to being handled.[83]

While the U.S. veterinary community may not have validated pain methodologies, despite decades of research, other countries have. For example, Canada approved Metacam on the basis of the drug's impact on blood cortisol levels and length of time to return to normal behaviors.[84] The evidence for effectiveness came from a 2006 study that compared the post-castration blood cortisol levels of four- to six-day-old

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ject sponsored by the USDA since September 2018 to "evaluate several novel methods of measuring stress when pigs are subjected to different procedures" including castration); *see also, e.g.*, *Protecting the Welfare of Food Producing Animals*, AGRIC. RSCH. SERV. (Jan. 27, 2021), https://perma.cc/Q6US-A2HV (accessed Sept. 23, 2021) (describing a research project sponsored by the USDA since August 2017 to "identify objective measures of distress, pain, and morbidity," including in pigs).

[77] *See* A. Prunier et al., *Effects of Castration, Tooth Resection or Tail Docking on Plasma Metabolites and Stress Hormones in Young Pigs,* 83 J. ANIMAL SCI. 216, 221–22 (2005) (concluding that "[i]f surgical castration cannot be avoided, the welfare of piglets should be improved by local anesthesia combined with prolonged analgesic treatment" and "[m]easurements of plasma lactate, cortisol, and adrenocorticotropin hormone may be useful to assess stress associated with alternative regimens").

[78] Sarah H. Ison et al., *A Review of Pain Assessment in Pigs,* 3 FRONTIERS IN VETERINARY SCI. 1, 10 (2016).

[79] Monique Pairis-Garcia & Anna Johnson, Dep't of Animal Sci., Iowa State U., Presentation at the 2014 World Pork Expo: Pain Management (June 5, 2014), https://perma.cc/AHV7-QUS6 (accessed Sept. 23, 2021).

[80] Ison et al., *supra* note 78, at 10–11.

[81] *Id.* at 3–8 (discussing each behavioral indicator and measurement of pain in piglets associated with castration).

[82] *Id.* at 10.

[83] *Id.* at 7.

[84] Merry Garbutt, *Boehringer Ingelheim (Canada) Ltd. Receives Approval for Metacam® for Swine for Relief of Post-Operative Pain Associated with Soft Tissue Surgery*

piglets that were either castrated without analgesics or castrated with the analgesic meloxicam, which found: "[A]ll piglets castrated without preoperative application of Meloxicam showed significantly increased Cortisol-concentration one and four hours after castration. In contrast, piglets castrated with analgesics resulted in no significant increase during the entire experiment."[85] The study's measure of pain relief sufficiently demonstrated substantial evidence of effectiveness for Canada's drug approval processes.[86]

This begs the question: Why hasn't the U.S. veterinary pharmaceutical community, in partnership with the FDA, validated such methodology in the United States? One might hypothesize that veterinary acknowledgement and quantification of pain in food-producing animals would create a domino effect—demand may rise for pain prevention in *all* food-producing animals that experience painful procedures. This pressure may come at a significant economic cost to virtually all of animal agribusiness.

Further, the lack of pain quantification methodology does not just prevent the approval of pain relief drugs—it also allows for the approval of drugs that cause pain. Production-focused drugs for food-producing animals that have an indication not necessarily related to improving the animal's health or welfare have been FDA-approved despite serious issues with safety and pain.[87] *Ractopamine*, as a prominent example, is classified as "safe"[88] despite pain-related animal welfare concerns[89] and lack of evidence regarding the pain element of safety.[90] The lack of pain quantification methodology has not been a problem for some drugs with non-pain indications (like *ractopamine*) because "safety" evidence does not necessarily consider pain assess-

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Such as Castration, BOEHINGER INGLEHEIM (Sept. 7, 2016), https://perma.cc/C36R-LSNV (accessed Sept. 23, 2021).

[85] Susanne Zöls et al., *Effect of Analgesics on the Castration of Male Piglets*, 119 BERL MUNCH TIERARZTL WOCHENSCHR 193, 193 (2006).

[86] *See* Garbutt, *supra* note 84 (claiming the company received approval due to "a large body of evidence for the efficacy of Metacam generated earlier by the Faculty of Veterinary Medicine at the Ludwig-Maximilians-University in Munich, Germany").

[87] *See What FDA Does and Does Not Regulate*, U.S. FOOD & DRUG ADMIN. (Oct. 19, 2017), https://perma.cc/6WL5-4XLD (accessed Sept. 23, 2021) (detailing how a drug company "must prove that food products made from the treated animals are safe for people to eat" with no mention of requiring the drug not cause pain in the animal); *Ractopamine Fact Sheet: Lean Meat = Mean Meat,* CTR. FOR FOOD SAFETY (Feb. 2013 https://perma.cc/QNG7-Z73L (accessed Sept. 23, 2021).

[88] Drugs must be "safe and effective" to obtain FDA approval. 21 C.F.R. §§ 514.1(b)(8), 514.4(b)(2)(i) (requiring substantial evidence of a drug's safety and effectiveness through adequate testing).

[89] *See* Schneider, *supra* note 17, at 250 (describing adverse events in ractopamine-fed pigs, such as vocalizations suggesting pain).

[90] *See* ELANCO ANIMAL HEALTH, FREEDOM OF INFORMATION SUMMARY: ORIGINAL NEW ANIMAL DRUG APPLICATION, NADA 140–863, RACTOPAMINE HYDROCHLORIDE, 22–26 (Dec. 22, 1999), https://perma.cc/M6C8-CG4S (accessed Sept. 24, 2021) (reporting on studies measuring physical toxicity, reproductive performance, but not reporting on vocalizations or other indications of pain).

ments, but rather reports of abnormal events.[91] There are clear economic motives to fail to acknowledge pain levels, whether avoiding pharmaceutical costs of pain relief drugs or easing the approval of profit-driven, but potentially pain-inducing, drugs.

Despite decades of research and the USDA's involvement to validate methods for quantifying pain in pigs, [92] the USDA's push for research simply does not match the vigor of legislative interest in easing FDA approval of production-focused and profit-driven drugs, such as via the passage of ADAA and ADUFA iterations. The passage of these FDCA animal drug amendments is likely due to the "cooperative approach among industry, FDA, and Congress."[93] The history of animal drug reformation in the United States suggests that any legislative reforms must gain support from the animal agriculture industry, the FDA, and Congress. This conflict of interest sets up key political constraints for any potential legislative solutions that improve access to pain relief drugs for piglets via FDA approval.

Ultimately, as a pharmaceutical company-driven process, which is directly guided by suppliers' needs, the drugs prioritized for FDA approval are the ones that benefit the economic bottom line—not necessarily the ones that will benefit the animals for their own sake. This prioritization ultimately harms animals, who the drugs are theoretically meant to protect. The crux of the main problem of this Article—the lack of FDA approval of NSAIDs for piglets undergoing castration—is the lack of a validated method in the United States for quantifying pain to demonstrate substantial evidence of effective pain relief. This crux is intimately intertwined with a wider problem: current U.S. animal drug regulations do *not* prioritize holistic animal safety to the degree they prioritize efficacy for food-producing animal drugs. These two problems have similar roots. In general, for food-producing animals, U.S. pharmaceutical companies and industrial animal agribusinesses currently lack the economic and regulatory motives to prioritize pain-reduction drug approvals and holistic animal safety in drugs, especially when compared with the economic motivations of profit-maximizing animal drugs. Therefore, a successful solution to either problem must address both the economic and regulatory compliance motivations.

IV. PROPOSED SOLUTION

In order to address the absence of pain relief provided to piglets during routine castrations in the pork industry, a two-pronged solution

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[91] *See* CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH AND HUM. SERVS., NO. 226, GUIDANCE FOR INDUSTRY: ? ?TARGET ANIMAL SAFETY DATA PRESENTATION AND STATISTICAL ANALYSIS 4–7 (2016) (describing the data reporting for target animal studies in new animal drug applications).

[92] *See* 21 C.F.R. § 514.117(b)(8) (citing to statute which lays out what type of methodology should be used for testing pain response for new animal drugs).

[93] Lambert, *supra* note 23, at 289.

that incorporates both a market-based approach and a legislative approach is necessary. These approaches will be strongest together, and are likely to be less effective if implemented individually. The proposed solution will be organized in four sections: (A) describing the market-based approach and its benefits, (B) describing the legislative approach and its benefits, (C) discussing the benefits of the *combined* approach, and (D) acknowledging risks and considerations with the proposed solution.

A. Market-Based Approach: Voluntary Corporate Commitments

In the short term, market-based pressure must move consumer-facing food corporations to voluntarily prioritize pain management during piglet castration. This movement is necessary to address both the proclaimed cost barrier to using pain relief drugs[94] and the political barrier of agency capture in the FDA.[95]

In order to persuade consumer-facing food corporations, such as major retailers, restaurant chains, and food manufacturers with widely known brand names, animal protection advocates can engage in constructive dialogue with the corporate social responsibility departments of major companies regarding the issue of piglet castration. Dialogue between advocates and companies about less painful alternatives to surgical castration, such as immunocastration or administration pain relief drugs pending FDA-approval, may be enough to convince companies to end surgical castration without pain relief in their pork supply chains via a timebound commitment. For companies uninterested in eliminating surgical castration without pain relief in their pork supply chains, animal protection advocates can educate the companies' consumers, investors, employees, and affiliates about how certain companies continue to support surgical castration without pain relief. The term *piglet castration* causes a visceral reaction and is likely to urge audiences to rethink their support of companies engaged in such an action. Companies interested in retaining consumers, investors, and other stakeholders would be wise to address the issue.

In fact, the above-outlined strategy has been used successfully in other animal protection campaigns, even for animals that humans traditionally consider less charismatic than pigs. For example, the animal protection movement in the United States engaged with over 200 companies between 2015 and 2016 to establish voluntary corporate commitments to eliminate cages from their egg supply chains and transition 100% of their egg supply chains to cage-free sources, with

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[94] *See* Wagner et al., *supra* note 2, at 1 (describing cost as one of three key reasons why veterinarians do not prescribe pain relief for piglets during castration).

[95] *See* Allison Parr, *Agribusinesses and Antibiotics: A Market-Based Solution*, 73 FOOD & DRUG L. J. 338, 350–51 (2018) (arguing that the industries the FDA regulates have sufficiently influenced the FDA to benefit the regulated industries instead of the expected beneficiaries of the agency, such as animals in the case of animal drug regulation).

most deadlines by 2025, if not earlier.[96] The adoption of these corporate commitments were made when cage-free shell egg supply was virtually unavailable.[97] Since these corporate commitments were established, cage-free egg production has increased so that, as of October 2021, 32.2% of laying-hen flocks were cage-free.[98] Further, major companies have indicated progress towards cage-free egg commitments,[99] which demonstrates that many major companies follow through on animal welfare commitments despite increased costs of producing higher welfare products.

Corporate commitments to end the purchase of pork from suppliers that castrate pigs without pain relief will reduce the significance of the cost barrier, an estimated $0.11 per piglet, which is one of three key reasons veterinarians do not prescribe pain relief drugs during castration.[100] If pork producers' direct customers (i.e., consumer-facing food companies) require that suppliers use pain relief during castration or eliminate surgical castration altogether, then pork producers that wish to maintain their customers might consider complying—even if that means raising prices by $0.11 per male pig or one-twentieth of one penny per pound of meat carcass weight from a male pig.[101] This virtually negligible cost increase is far less costly than transitioning from cage to cage-free eggs.[102] When pork producers ask private

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[96] *See Cage-Free*, WELFARE COMMITMENTS, https://perma.cc/L8VA-5VLZ (accessed Feb. 22, 2021) (listing over 200 companies, such as Walmart, Costco, Kroger, and McDonald's, that have committed to sourcing cage-free eggs with links to information about their commitments).

[97] In 2015, less than 6% of hens in the U.S. were housed in cage-free environments. *See* SAMARA MENDEZ, U.S. EGG PRODUCTION DATA SET 6 (2021) [hereinafter Mendez report] (compiling data from several monthly USDA reports to determine the percentage of the U.S. egg-laying hen flocks that are cage-free). *See also Shell Eggs: Monthly USDA Cage-Free Shell Egg Report*, U.S. DEP'T OF AGRIC., https://perma.cc/3KKW-HPKD (accessed Sept. 29, 2021) (sharing monthly raw data sets on absolute cage-free laying hen flock size used in the Mendez report); *Chickens and Eggs*, U.S. DEP'T OF AGRIC., https://perma.cc/3SP3-N5MR (accessed Sept. 29, 2021) (sharing monthly raw data sets for absolute total laying hen flock size used in the Mendez report).

[98] U.S. DEP'T OF AGRIC., EGG MARKETS OVERVIEW (Oct. 29, 2021), https://perma.cc/C5W9-AXNQ (accessed Nov. 20, 2021).

[99] Various major food companies, ranging from Walmart to McDonald's, are reporting on the percentage of their egg supply chains that are cage-free. *See, e.g.*, *Egg Track: 2020 Report*, COMPASSION IN WORLD FARMING, 1, 10, 14 (2020), https://perma.cc/L26L-QFRB (accessed Sept. 29, 2021) (reporting on the progress of companies in process of moving to cage-free egg suppliers).

[100] The estimated cost per piglet to administer meloxicam inclusive of the drug, labor, and equipment is $0.11 per piglet. *See* Wagner et al., *supra* note 2, at 6–7 (estimating meloxicam costs at $50 and labor costs at $58.80 for 1000 piglets).

[101] A typical live pig in the United States produces a 207.5-pound carcass. Therefore, if it costs $0.11 to provide pain relief during castration, the cost is $0.0005 per pound of pork and other products. As the $0.0005 figure is only applicable to male pigs, the cost average is approximately $0.00025 per pound of pork and other products inclusive of both male and female pigs. PORK CHECKOFF, PORK STATS 32 (2014), https://perma.cc/XF2Q-HJ7U (accessed Sept. 30, 2021).

[102] In 2018, the average operating and capital cost per dozen eggs was 36% higher in aviaries (cage-free systems) than conventional (cage) systems. Lesley Nernberg, *Cost*

pharmaceutical companies to prioritize development of suitable NSAIDs for pain relief during castration, pharmaceutical companies will have the incentive necessary to validate pain quantification methodology in order to push existing drugs through FDA approval.

A market-based approach should come before any legislative approach, because a market-based intervention can address agency capture within the FDA, as argued by law student Allison Parr with regard to the use of antibiotics in animal agribusiness.[103] Parr argues that the FDA has been "captured" as demonstrated by a failure to address antibiotic resistance through its rulemaking authorities.[104] While a different topic area, Parr's argument of FDA capture applies similarly to regulating pain relief drugs for food-producing animals. Antibiotic drugs that prevent common diseases benefit the animal agribusiness industry's bottom line and have, therefore, influenced FDA interest; whereas potential regulations that might harm the animal agribusiness industry never came to fruition, and were only promulgated as voluntary recommendations.[105] Further, if pain relief drugs for food-producing animals become an interest for the animal agribusiness industry, then such pain relief drugs would likely become an interest for the FDA. Agency capture can also explain why the FDA has not interpreted the FDCA to accept the cortisol-based evidence that meloxicam provides pain relief in piglets, which has been accepted in Canada.[106] Parr's recommendation to address agency capture is a market-based intervention like the one outlined in this Article.[107]

B. Legislative Approach: Amendments in the 2023 ADUFA Reauthorizations

The second part of this Article's proposed solution takes a legislative, rather than regulatory, approach. The drawn-out nature of rulemaking combined with the existing agency capture within the FDA suggest that it is unlikely for the FDA to initiate these proposed changes via regulation, despite its statutory authority to do so.[108]

Differential Between Cage-Free Laying Systems, POULTRY WORLD (Aug. 3, 2018), https://perma.cc/S6NS-CQVU (accessed Sept. 30, 2021).

[103] Parr, *supra* note 95, at 350.

[104] The FDA is captured by the industry as demonstrated by (1) its failure to withdraw approval for tetracyclines and penicillin indications in food-producing animals, despite ample evidence that non-medicinal use contributes to the antibiotic-resistant bacteria problem, and (2) its reliance on non-binding guidance documents in place of rulemaking. *Id.* at 351.

[105] *Id.*

[106] *See* Garbutt, *supra* note 84 (announcing approval of Metacam use in Canada).

[107] "[E]ngaging in a corporate governance regime during this period of deregulation may prove helpful in the future when FDA might again act." Parr, *supra* note 95, at 356.

[108] While a petition for rulemaking is not the recommended path forward, it is worth noting that the FDCA does grant authority to the Secretary of Health and Human Services to "promulgate regulations for the efficient enforcement of [the FDCA], except as otherwise provided in this section[.]" 21 U.S.C. § 371(a). Congress did explicitly state

Thus, a legislative solution is vital because of a unique opportunity that presents approximately every five years: the reauthorization of ADUFA. ADUFA reauthorizations have sunset provisions,[109] essentially requiring that Congress reauthorize the FDA (by way of the Secretary of Health and Human Services) to continue collecting fees from drug sponsors. The sunset provisions have historically caused Congress to demonstrate urgency in passing the reauthorization bills.[110] Accordingly, there is a rare upcoming opportunity in 2023 to prioritize animal drugs issues in the legislative spotlight.

During the 2023 ADUFA reauthorizations, Congress should amend the U.S. Code with two key provisions:

1. Amend 21 U.S.C. § 360b(d)(2) to direct the Secretary of Health and Human Services to, in the case of new drugs for food-producing animals, consider the pain measurements in the context of the drug's impact on the animal's overall health and the alternatives to the drug's use, effective no later than two years after enactment.[111] This amendment would ulti-

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that "[t]he definitions . . . promulgated in accordance with the provisions of this chapter shall be effective for the purposes of the enforcement of this chapter[.]" 21 U.S.C. § 371(d). Congress defines "safe" as with "reference to the health of man or animal[.]" 21 U.S.C. § 321(u). While one interpretation of the first part of the proposed legislative approach in this Article could be redefining the word "safe" for food-producing animal drugs to consider and include pain, this proposal more literally reads as adjusting requirements for demonstrating the safety of a new animal drug. Therefore, readjusting requirements to demonstrate safety would fall under the Secretary of Health and Human Services authority pursuant to the FDCA's new animal drug provisions codified at 21 U.S.C. § 360b. Despite the authority to adjust safety requirements in the suggested manner, it is expected that a petition for rulemaking filed pursuant to the Administrative Procedure Act, 5 U.S.C. § 553, would result in a denial from the FDA based on the above discussion of agency capture. If the denial is appealed through the courts, the FDA would likely receive *Chevron* deference. *See* Chevron U.S.A., Inc. v. Nat'l Res. Def. Council, Inc., 467 U.S. 837 (1984) (asking whether Congress spoke to the precise issue at hand and if the agency's interpretation is reasonable—not necessarily the *most* reasonable). Although, an arbitrary and capricious review may be successful depending on the FDA's reasons for denying a petition. While rulemaking is not out of the question, it will likely face more challenges than a legislative initiative.

109 Animal Drug and Animal Generic Drug User Fee Amendments of 2018, Pub. L. 115-234, § 107(a), 132 Stat. 2427, 2432 (2018) ("Section 740 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 379j–12) shall cease to be effective October 1, 2023.").

110 CONG. RSCH. SERV., *supra* note 30, at 2.

111 What statutory language changes to 21 U.S.C. § 360b(d)(2) could look like with *italic style* denoting additions and strikethrough style denoting deletions: (2) In determining whether such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof, the Secretary shall consider, among other relevant factors, (A) the probable consumption of such drug and of any substance formed in or on food because of the use of such drug, (B) the cumulative effect on man or animal of such drug, taking into account any chemically or pharmacologically related substance, (C) safety factors which in the opinion of experts, qualified by scientific training and experience to evaluate the safety of such drugs, are appropriate for the use of animal experimentation data, and (D) whether the conditions of use prescribed, recommended, or suggested in the proposed labeling are reasonably certain to be followed in practice*, and (E) in the case of a drug for food-producing animals, pain measurements associated with the administration and acute, subacute, and chronic impacts of the drug on the target animal, taking into account the impact of the drug on the target*

> mately trigger a requirement for drug sponsors to report pain measurements in the safety portion of all new animal drug applications for food-producing animals.[112]
>
> 2. Add to 7 U.S.C. Chapter 38 a new subchapter VIII entitled "Painful Procedure Mandatory Reporting" directing the Secretary of Agriculture to collect and publish data on painful procedure methods (defined as routine cutting into or burning of any sensory part of a living animal's body except for the purposes of injection or immediate slaughter) in food-producing animals on a company-level basis for companies directly raising food-producing animals.[113]

The first proposed provision—triggering the incorporation of pain management quantification in the safety portion of new drug applications—utilizes a regulatory strategy similar in nature to 'technology forcing,' which has been successful in some environmental regulation instances.[114] To illustrate, the Clean Air Act[115] requires vehicle emissions and fuel standards that the regulated industries claimed were prohibitively expensive, but upon implementation, novel technologies improved air quality for a much lower cost than the regulated industries originally forecasted.[116] Requiring that drug sponsors report quantified pain measurements to demonstrate the safety of a new animal drug does not force new *technology*, per se; it does, however, challenge the regulated industry to innovate in order to continue submitting new animal drugs applications for food-producing animals—even particularly profitable production-driven drugs. Fortunately, other countries have already validated methods for pain quantification. This 'innovation-forcing' would encourage the method validation such that: (1) drugs can be evaluated *specifically* for pain-related impacts, and (2) validated pain quantification methodology is no longer a barrier to demonstrating substantial evidence of the efficacy of certain

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animal's overall health and whether reasonable alternatives to the use of the drug would result in different levels of pain. Any order issued under this subsection refusing to approve an application shall state the findings upon which it is based.

[112] A person filing application for use of a new animal drug "shall submit to the Secretary as part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe and effective for use . . . ." 21 U.S.C. § 360b(b)(1). Therefore, to fulfill the safety determinations in an application including the proposed consideration of pain measurements, the drug sponsor would be required to report on pain measurements.

[113] Chapter 38 currently has a subchapter entitled "Livestock Mandatory Reporting," 7 U.S.C. §§ 1635–1636i, which requires reporting of price and supply for some food-producing mammals, such as cattle, swine, and lamb. The additional proposed subchapter should take on a similar format to the "Livestock Mandatory Reporting" subchapter, but with a focus on the methods for painful procedure, as defined in this Article's text, instead of price and overall supply, and a scope of company-wide reporting, instead of state or nationwide reporting.

[114] ROBERT V. PERCIVAL ET AL., ENVIRONMENTAL REGULATION: LAW, SCIENCE, AND POLICY 557 (8th ed. 2018) (describing how technology-forcing regulations have been successful for mobile sources of air pollution).

[115] Clean Air Act of 1970, Pub. L. No. 91–604, 84 Stat. 1676 (1970).

[116] PERCIVAL ET AL., *supra* note 114, at 562.

NSAIDs, assuming that certain NSAIDs do provide pain relief as demonstrated in other countries.

Further, the first proposed provision aims to increase research that will not only result in improved methodologies for pain assessment—therefore validating methodology needed to demonstrate NSAID efficacy for pain relief—but also improve the pain-associated welfare outcomes of production-focused drugs. While the provision would only impact *new* animal drug applications for food-producing animals, it would prevent future animal drugs from improving production and profitability at the expense of animal wellbeing. Additionally, the provision would not result in an outright rejection of a drug if it results in pain. As an example, in relation to humans, while vaccinations with needles may cause momentary pain, or even pain at the injection site over the course of a few days, a vaccination should still be approved if it meets all other drug approval criteria. The pain is considered to be minimal relative to the overall health benefits and the alternative of not receiving the vaccination (falling ill and/or risking death). Similarly, in order to prioritize an animal's safety—including protecting the animal from pain—new drug approvals for production-focused drugs should consider pain within the larger context.[117]

The second provision provides transparency to the public about how a company chooses to administer painful procedures—including surgical castration, dehorning, branding, tail docking, ear notching, debeaking, and more—in food-producing animals. This level of transparency will *heavily* encourage meat suppliers to move toward less painful alternative procedures, if not eliminating some procedures altogether. If company-level reporting data is unlikely, the proposed provision could alternatively collect and publish data on procedures at a national level, as is done with laying hen housing, for example.[118]

Ultimately, the proposed legislation will not require pain relief during surgical castration in male piglets, but will expedite the process for FDA approval of pain relief drugs by shifting pharmaceutical companies' focus towards validating methodology for quantifying pain in food-producing animals. While stopping short of a ban on castration without pain relief drugs is strategic for animal welfare nationwide, this legislation will not preempt stronger state statutes regarding on-farm animal welfare, including both existing state statutes[119] and potential future state statutes.

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117 *See also* Schneider, *supra* note 17, at 279 ("?Drug uses that increase animal suffering in any way should . . . be prohibited. ?Relatedly, new drug approvals should be guided by a safety analysis that truly includes consideration of the safety of the animal to which the drug is administered.").

118 *See* USDA ECON., STAT. & MKT. INFO. SYS., *supra* note 97 (compiling USDA Agriculture Marketing Services' reports on cage-free shell egg supply on a national level).

119 *See, e.g.*, 4 R.I. GEN. LAWS § 4-1-6.1 (2012) (mandating that tail docking requires veterinary oversight with anesthesia). *See also* Elizabeth R. Rumley, *States' Farm Animal Confinement Statutes*, NAT'L AGRIC. L. CTR., https://perma.cc/ZX4R-CSKK (ac-

C. *Benefits of the Combined Market-Based and Legislative Approaches*

The outlined market-based and legislative approaches operate synergistically to address pain relief for surgical castration in three significant ways.

First, corporations would be far more likely to implement and fulfill voluntary commitments to phase out surgical castration without pain relief if pain relief drugs are FDA approved.[120] Relatedly, pharmaceutical companies would be far more likely to spend resources validating pain management quantification methodology if there is both regulatory and agribusiness industry pressure. The incorporation of pain management quantification measures in the safety portion of new animal drug applications would remove the existing scientific barrier to the FDA's approval of NSAIDs for food-producing animals. This FDA approval is necessary to help corporations fulfill voluntary commitments to phase out surgical castration without pain relief. Additionally, the voluntary corporate commitments will add another level of stakeholder pressure to encourage pharmaceutical companies to abide by the 'innovation-forcing' regulatory tool.

Second, the proposed legislative provision provides the transparency necessary to hold food corporations accountable to voluntary commitments. For example, if a major supermarket retailer voluntarily commits to procure all pork products from farms that do not engage in surgical castration without pain relief drugs, then the public could ensure that the retailer follows through with its commitment by tracking the painful procedure statistics from the retailer's pork supplier(s). Even if this proposed provision adjusts to only report data on a national level, instead of company level, this would still allow added transparency and better monitoring of an industry-wide transition to the use of pain relief drugs during piglet castration

Third, by encouraging pork purchasers (and, indirectly, pork suppliers) to commit to phase out the practice of piglet castration without pain relief in their supply chains, the committed corporations will be motivated to support the proposed legislation that helps to achieve their animal welfare goals. This combined approach aims to transform expected opponents into legislative allies.

D. *Risks and Considerations*

In order to provide the best path forward for the proposed solutions, two key risks must be addressed. First, as with any legislative

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cessed Sept. 29, 2021) (compiling a comprehensive list of state statutes that place restrictions on how farm animals can be confined).

[120] Corporations could fulfill voluntary commitments in other ways that do not require FDA-approval or extra-label drug use of NSAIDs or other pain relief drugs, such as transitioning to immunocastration or raising entire male pigs. *See* discussion *supra* Part II.A.

initiative, political support from most key stakeholders is essential. Second, as the proposed solution does not legislatively mandate the use of pain relief drugs during piglet castration, consideration of how the voluntary nature of this solution will ultimately impact pain relief for male piglets is imperative.

Why would the proposed legislative amendments be attractive to most, if not all, key stakeholders? Such legislation would result in increased costs to pharmaceutical companies—costs which will be passed on to animal agribusiness and, ultimately, consumers. Given increased cost, what would optimize buy-in for animal agribusiness, the pharmaceutical industry, the FDA, and Congress?

As discussed in Part IV.C, applying the market-based approach prior to the legislative approach turns potential animal agribusiness opponents into allies: pork producers are motivated to support legislation that serves their retailer, restaurant, and other customers as well as achieves the animal welfare goals necessary to retain their business.

While pharmaceutical companies will almost certainly display hesitation at increased requirements for new animal drug approvals, the legislation will ultimately open up a new field of possible drugs to sell—pain relief drugs for food-producing animals. This new field would be an increasingly lucrative category, as transparency increases regarding painful procedures.

Assuming the FDA has truly been captured by the industry, as Parr argues,[121] the FDA would likely support the proposed legislation because (1) it would not be lobbied otherwise by voluntary commitment-bound animal agribusiness nor pharmaceutical companies wishing to sell more product to the voluntary commitment-bound animal agribusinesses, and (2) the proposed legislation leaves the onus on the drug sponsors—not the FDA—to develop the required pain quantification methodology for reports on safety.[122]

Lastly, Congress is highly motivated to pass ADUFA reauthorizations every five years, as a lapse in animal drug user fee authorization has the detrimental consequence of potentially laying off highly specialized animal drug review staff that are difficult to replace.[123] Further, the proposed legislation indirectly addresses an issue that is likely to produce visceral reactions amongst constituents: piglet castration. Various consumer surveys in foreign countries indicate the concept of piglet castration is deeply disturbing to most people.[124]

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[121] Parr, *supra* note 95, at 350–51.

[122] The onus is already on drug sponsors for providing the required information on new animal drug applications. *From an Idea to the Marketplace: The Journey of an Animal Drug through the Approval Process*, U.S. FOOD & DRUG ADMIN. (Aug. 14, 2020), https://perma.cc/56PH-BQC6 (accessed Sept. 30, 2021).

[123] CONG. RSCH. SERV., R45077, ANIMAL DRUG USER FEE PROGRAMS.

[124] Maria J. Hötzel, et al., *On the Road to End Pig Pain: Knowledge and Attitudes of Brazilian Citizens Regarding Castration*, 10 Animals 1826, 2 (2020) ("?Although citizens in general are unaware of the husbandry practices and technologies used in animal

Even the U.S. swine veterinary community is aware of how controversial and risky the continuation of surgical castration without anesthesia is, given changing consumer preferences towards improved animal welfare.[125]

As upsetting as piglet castration is to the general population, the legislation is relatively moderate as it does not mandate any on-farm changes. People would still retain consumer choice. The legislation only ensures that new drug applications for food-producing animals consider pain evaluations and that, in the case of pharmaceutical pain relief during and after piglet castration, research into effectiveness methodology is much closer to providing for an approved drug. Overall, incorporating pain quantification into safety evaluations of new animal drugs is a relatively moderate legislative proposal and is thus more likely to garner bipartisan support than other more radical proposals, such as regulations on on-farm welfare practices.

The second proposed legislative provision requiring company-level reporting may face hurdles in gaining support from all stakeholders—most notably animal agribusiness and, resultantly, the USDA. The pharmaceutical industry would likely support required reporting of methods for painful procedures due to an increase in pain relief drug sales. The USDA (as the implementing agency, rather than the FDA) would likely oppose the proposed legislative provision, as the USDA is notorious for agency capture[126] and will probably follow the interests of animal agribusiness. Congress would presumably be most interested in balancing the interests of their constituents with the powerful animal agribusiness lobby. Animal agribusiness has historically fought transparency by legislatively acting on the offensive at the state level to limit public awareness of their practices through a suite of agricultural gag ("Ag-Gag") state laws.[127] Expectantly, animal agribusiness would lobby congressional members to oppose the proposed provision requiring reporting of painful procedure methods as it would shed light on controversial practices. While publishing company-level

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production, when asked about surgical castration of pigs without anesthesia, most classify these practices as detrimental to animal welfare.") (internal citations omitted).

[125] *See, e.g.*, *Welfare Implications of Swine Castration*, *supra* note 5, at 2 ("?Consumers are not generally aware that pigs are castrated nor are they aware of boar taint. When informed, consumers view surgical castration without anesthesia as a serious animal welfare concern.") (internal citations omitted). *See also* Coetzee, *supra* note 37 ("Analgesic drug approvals in food animals are . . . rapidly becoming a consumer expectation.").

[126] *See, e.g.*, Bruce Friedrich & Stefanie Wilson, *Coming Home to Roost: How the Chicken Industry Hurts Chickens, Humans, and the Environment*, 22 ANIMAL L. 103, 157–59 (2015) (providing examples of former animal agribusiness leaders accepting high-ranking USDA jobs and other political influence from the animal agribusiness industry that has resulted in USDA policymaking heavily supporting animal agribusiness interests).

[127] Ag-Gag state laws use a variety of means to criminalize one or more of the actions necessary for undercover investigators to capture footage of on-farm practices. These laws have been struck down by the courts in several states. *See, e.g.*, Eberly, *supra* note 47, at 304–05.

data about painful procedure methods would be most useful for the public interested in how a company castrates (or dehorns, debeaks, otherwise mutilates) food-producing animals, this provision could be watered down to industry-level data publication to be more politically palatable. Industry-level, nationwide data publication might reduce opposition, as it would not call out specific companies for employing particularly painful procedures.

A second key risk is the actual impact of the proposed legislative provisions. As the proposed legislation does not require the development of pain quantification methodologies for male piglets, how will the proposed solutions actually achieve the outcome of improved pain management during and after castration? This concern is notable given that the FDA approved the immunocastration drug, *Improvest*, in March of 2011.[128] Yet, *Improvest* is not knowingly used in any substantial volumes in the United States due to stakeholder concern about consumer acceptance of immunocastration.[129] While FDA approval of Improvest did not result in the wide use of immunocastration as an alternative to physical castration without pain relief, FDA approval was not accompanied by substantial animal agribusiness interest in implementation. Fortunately, the proposed legislation, in combination with voluntary corporate commitments from the market-based approach, can drive change to impact the precise issue at hand—pain management for piglet castration.

V. CONCLUSION

Piglet castration without pain relief is a common, but unnecessarily, cruel practice. Food corporations can address this issue through voluntary corporate commitments to eliminate the practice of castration without pain relief. Moreover, Congress can address this issue through legislative reform regarding: (1) consideration of pain measurements in the safety assessments for *all* new drugs for food-producing animals, which will likely incentivize the research needed to approve pain relief drugs for food-producing animals, and (2) required data reporting on painful procedure methods.

This Article sheds light on how the U.S. veterinary community and the FDA have fallen behind other countries in improving pain relief during physical castration for approximately 66 million male piglets annually. Further, the proposed legislative provision offers a novel 'innovation-forcing' regulatory tool—an application of the 'technology-forcing' environmental regulatory tool applied to the field of animal drug regulations.

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[128] Implantation or Injectable Dosage Form New Animal Drugs; Gonadotropin Releasing Factor-Diphtheria Toxoid Conjugate, 76 Fed. Reg. 27,888, 27,889 (May 13, 2011) (codified at 21 C.F.R. § 522.1083) (May 4, 2011).

[129] *See* Hötzel et al., *supra* note 124, at 2 (describing different cultural and regulatory issues associated with alternative castration methods).

With the combination of historically successful market-driven approaches to improving animal welfare and novel legislative provisions, the United States stands a greater chance at catching up with other countries' approvals of pain relief medications for use in food-producing animals. This Article's proposed market and legislative approaches, together, have the potential to positively impact and reduce pain for 66 million male piglets born in the United States every year. Even further, the proposed legislation would lay groundwork to reduce pain associated with procedures for the vast majority of the nearly 10 billion food-producing animals in the United States.

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