AMERICA’S SECRET ANIMAL DRUG PROBLEM

HOW LACK OF TRANSPARENCY IS ENDANGERING HUMAN HEALTH AND ANIMAL WELFARE

EXECUTIVE SUMMARY
SEPTEMBER 2015
ABOUT CENTER FOR FOOD SAFETY

CENTER FOR FOOD SAFETY (CFS) is a non-profit public interest and environmental advocacy membership organization established in 1997 for the purpose of challenging harmful food production technologies and promoting sustainable alternatives. CFS combines multiple tools and strategies in pursuing its goals, including litigation and legal petitions for rulemaking, legal support for various sustainable agriculture and food safety constituencies, as well as public education, grassroots organizing and media outreach.

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EXECUTIVE SUMMARY

By now many Americans have realized that most animals raised for food in the United States today are not roaming freely on iconic pasture. Instead, food animal production has shifted dramatically in the past several decades toward large factory-style facilities that hold thousands of animals. By some estimates, 99.9 percent of chicken and 78 percent of beef consumed in the United States comes from animal factories.\(^1\) Extreme growth rates and unsanitary, overcrowded conditions are now commonplace in large industrial animal factories, or Concentrated Animal Feeding Operations (CAFOs).

What many Americans may not realize is that to keep pace with the increasing growth and concentration of livestock raised in animal factories,\(^2\) the animal agriculture industry uses over 450\(^3\) animal drugs, drug combinations, and other feed additives to promote animal growth and to suppress the negative effects that heavily-concentrated confinement has on farm animals. Food animal producers regularly use these drugs for reasons that have nothing to do with medical necessity or animal health—but solely to increase profit.

The U.S. Food and Drug Administration (FDA or the Agency) is the primary agency responsible for approving and regulating these drugs. FDA is required by federal law to ensure animal drugs are safe for both humans and the animals for which they are intended before approving their sale, and to take drugs off the market that

| CENTER FOR FOOD SAFETY AMERICA’S SECRET DRUG PROBLEM | 1 |
FDA is required by federal law to ensure animal drugs are safe for both humans and the animals for which they are intended before approving their sale, and to take drugs off the market that are later found to be unsafe. Yet, Center for Food Safety (CFS) has found that some drugs on the market today may pose significant threats to human, animal, and environmental health and are therefore unsafe. There is alarmingly little information about other drugs, and certainly too little to justify FDA’s safety determination. In either case, FDA and industry are not at all transparent about the information they have on the safety of these drugs.

In the regulatory gap left by FDA, consumers and businesses have begun to take action. Concern for the connection between routine reliance on antibiotics in industrial animal production and the rise of antibiotic-resistant infections in humans, for example, has prompted the public to demand change. However, regulatory action by FDA is critical to institutionalizing these changes. In addition, without action from FDA, market pressures focused solely on antibiotics that successfully reduce or eliminate their ubiquitous use for growth promotion may only cause other growth-promoting drugs to fill the gap. Drugs with significant adverse impacts on human health or animal welfare, such as ractopamine or zilpaterol, may become even more prevalent in industrial animal production.

FDA’s involvement in the oversight of approved animal drugs is generally minimal unless or until questions arise about a drug’s safety. The Agency does not routinely monitor emerging data on approved drugs, but relies on others to bring the data to its attention.

Rather than use its authority to reevaluate the safety of approved animal drugs or require drug manufacturers to do so, FDA has placed the burden on the public to conduct investigations and present the Agency with new data about the uses and
effects of animal drugs. For issues of safety, the Agency relies heavily on private citizens and organizations, like CFS, to submit formal rulemaking petitions requesting that it withdraw approval for a drug. Regardless of who requests review of a drug’s safety, FDA has a mandatory duty to withdraw approval of an animal drug when it finds the drug to be unsafe.4

Assuming this burden, CFS has petitioned FDA several times to evaluate or withdraw approvals for antibiotic, arsenical, and beta agonist animal drugs. In 2014, CFS’s legal and public actions demanding that FDA withdraw approval of arsenicals led drug companies and the Agency to withdraw all but three arsenic-based drugs used in animal agriculture. In 2015, the Agency announced it would move forward with withdrawing the final three. Even with this significant victory, there are many drugs still on the market that FDA should reevaluate and withdraw.

CFS’s review of available literature and data has found few comprehensive, scientific studies investigating the potential impacts of approved drugs on the environment, non-target organisms, and human health. Until FDA thoroughly assesses the safety of animal drugs, and withdraws those found to be unsafe, the well-being of food animals, consumers, and the environment are put at risk by an industry that thrives on keeping the government and the public in the dark.

This report summarizes the current safety information on animal drugs that urgently demand reexamination by FDA. The approved animal drugs reviewed in this report are organized into the broader categories of:

- Beta-agonists
- Steroid hormones
- Antioxidants
- Antibiotics
- Arsenicals
- Coccidiostats

For each drug type, this report provides an overview of the most up-to-date information available, including their use in agriculture; their impacts on animal health, human health, and the environment; efforts to have such drugs withdrawn from the market; and comparisons between United States and international regulations.

**BETA-AGONISTS**

Two beta-agonist drugs, ractopamine and zilpaterol, are widely used in U.S. meat production.5 They are fed to animals during the final period of weight gain before slaughter to encourage a last-minute increase in muscle mass and overall carcass weight. The full risks that these drugs pose to consumers and the environment remain at least partly unknown because no one has conducted an adequate, rigorous assessment. FDA’s own records show, though, that ractopamine has resulted in more reports of sickened or dead pigs than any other livestock drug.6,7 Ractopamine is linked to significant health problems and behavioral changes in animals, such as cardiovascular stress, muscular skeletal tremors, increased aggression, hyperactivity, acute toxicity, and genotoxicity.8 Ractopamine also increases the number of “downer” or lame animals, and is associated with broken limbs, a complete inability to walk,
and death. Some reports indicate animals on ractopamine become so aggressive and hyperactive that they must be medicated to calm them down for shipping to slaughter. The scarce available data on animal health effects of zilpaterol are similarly alarming. There are no rigorous scientific studies available on the risks beta-agonists pose to humans, despite numerous cases in which residues have been detected on retail meat products. The limited existing research suggests that the drugs can negatively affect the heart, posing a particular risk to people with heart conditions.

**STEROID HORMONES**

Six different hormones are approved in U.S. cattle production, administered either by implants or added to feed. In 1988, concerns about the potential health risks of drug residues led the European Union (EU) to ban importation of the meat of hormone-treated animals. While the United States and Canada have vigorously fought the ban through both punitive tariffs and appeals to the World Trade Organization, the EU has expressed hope that new research will provide additional scientific ground to rebut these challenges to its ban. Data are limited on the direct effects of added hormones in meat and dairy production, but there is sufficient evidence in the studies and data CFS has compiled to suggest that significant adverse human health effects may arise as a result of administering steroid hormones to food animals. FDA and industry claim that residues in animal products pose no harm to consumers because they do not exceed natural hormone levels in the human body, but these claims are completely unfounded. Medical and public health organizations have expressed concerns that external exposure to hormones can have adverse impacts on the human reproductive system, in particular fetuses and adolescent females. Recent evidence of the ability hormones have to not only enter the environment from agricultural uses, but to persist for longer than previously thought, also means that food products may not be the only way residues of these animal drugs are reaching humans.

**ANTIOXIDANTS**

Ethoxyquin is a synthetic antioxidant approved as a feed additive. While technically not an animal “drug,” it raises similar concerns as the other drugs outlined in this report. Ethoxyquin helps prevent the fats in livestock feed from becoming rancid, essentially allowing products to have longer shelf lives by inhibiting natural decay processes. Some poultry farms also add ethoxyquin to animals’ drinking water to enhance the yellow color of egg yolk. FDA has long acknowledged the “deleterious and poisonous” effects of ethoxyquin; Agency correspondence in response to Monsanto’s petition for the chemical’s approval demonstrates that ethoxyquin was well recognized as harmful and poisonous. In 1990, FDA nominated ethoxyquin for carcinogenicity testing, reasoning that its toxicological effects were unknown and it appeared “to have a modifying effect on other carcinogenic chemicals.” Despite its expressed concern about the safety of ethoxyquin, to date the Agency has failed to take meaningful action to reevaluate or restrict the use of the addi-
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**ANTIBIOTICS**

Antibiotics are used in food animal production for three different purposes: treating disease (therapy), preventing infections (prophylaxis), or promoting growth and feed efficiency. Disease prevention and growth promotion both involve giving drugs to healthy animals and are considered nontherapeutic uses. Agricultural use of antibiotics has contributed significantly to the development of resistance among the microorganisms that the drugs are designed to target, because exposing organisms to sub-lethal concentrations of antibiotics drives the selection of resistant genes. In the United States, an estimated 60-80 percent of national antibiotic usage—amounting to approximately 20–26 million pounds—is fed to food animals for nontherapeutic uses. Animals absorb roughly only 25 percent of the antibiotics they consume, and excrete the vast majority in their waste. Livestock workers and veterinarians are at particular risk of contracting resistant infections, but antibiotic resistant bacteria can reach consumers through retail meat and poultry. Data from the National Antimicrobial Resistance Monitoring Service (NARMS) shows that the percentage of antibiotic resistant *Campylobacter coli* isolates in retail chicken meat increased from 2010 to 2012 for many classes, including quinolones and macrolides. The data also shows that 40 percent of *Salmonella* isolates on ground turkey were resistant to 3 or more antibiotic classes, and 24 percent of isolates on chicken were resistant to 5 or more classes. The percentage of multi-drug resistant *Escherichia coli* (*E. coli*) also increased in ground turkey and ground beef from 2011 to 2012.
Coccidiostats are a class of anti-parasitic drugs designed to prevent an intestinal infection caused by a single-celled parasite (coccidia) that affects pigs, poultry, and cattle. Existing scientific literature analyzing the environmental and human health impacts of coccidiostats is extremely limited. There was increased interest in coccidiostat residues in food after a number of contamination incidents were reported in the 1990s, with particular attention paid to their high presence in egg yolks. A significant amount of lasalocid, for example, is transferred to the egg when fed to laying hens, and the European Food Safety Authority (EFSA) determined that lasalocid in eggs could reach concentrations 63.6 times of that contained in the feed. EFSA also determined that nicarbazin in feed led to the concentration of low levels of two of its metabolites, dinitrocarbanilide and 2-hydroxy-4,6-dimethylpyrimidine, in eggs. In addition, a 2014 study found clopidol residues in egg yolk, egg white and whole egg in 10 percent of commercial samples, ranging between 10 and 443 parts per billion. Despite the detection of multiple coccidiostat residues in retail foods, few scientific studies have investigated the potential health affects for consumers. The exception is for zoalene, which FDA considers hazardous enough to prohibit as a feed additive for laying hens. However, it is still approved for broilers.

Arsenic based compounds, or arsenicals, were approved for use in animal feed for growth promotion, improved feed efficiency, and desirable pigmentation. Despite increased evidence of the risks associated with arsenic exposure and the voluntary withdrawal of organic arsenical pesticide products due to concerns of negative health impacts, the average American’s cumulative exposure to arsenic greatly increased since FDA first approved arsenicals in animal feed. While EPA has taken steps to reduce public exposure to arsenic in drinking water and organic arsenical pesticides, there is abundant evidence that Americans are exposed to dramatically higher levels of arsenic today than when arsenical feed additives were first approved in the 1940s. Both human and animal studies have confirmed that inorganic arsenic compounds are readily absorbed from the gastrointestinal tracts of humans. Studies by the Institute for Agriculture and Trade Policy (IATP) and Center for a Livable Future (CLF) documented arsenic residues in chicken products purchased by American consumers. CFS and IATP petitioned FDA in 2009, calling for the removal of all arsenic-based animal feeds. As a result of that petition and subsequent litigation, FDA announced that it was withdrawing approval for 98 out of 101 arsenic-based feed additives. The Agency later announced that it would take the remaining arsenicals off the market by 2016. While this is a significant victory, FDA should have acted sooner to protect public health.

**U.S. Standards are Lower than the International Community**

The report also uses the Codex Alimentarius Commission (Codex) standards and information on national standards of other countries, where available, to compare...
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FDA’s drug approvals and established residue tolerance levels with the rest of the world. At least twelve of the specific drugs discussed in this report are prohibited for use as animal drugs in other countries, and the EU has issued a ban on the use of all antibiotics for growth promotion. For six of the drugs, FDA has established residue tolerance levels significantly higher than the international standards. The public interest community has consistently attempted to persuade the Agency to act and either review, suspend, or withdraw certain drug approvals. Over the past several years, CFS has filed requests under the Freedom of Information Act (FOIA) for all information FDA has on ractopamine, zilpaterol, trenbolone, ethoxyquin, and arsenicals, and has received little from the Agency. Nevertheless, CFS conducted a thorough analysis of available research and literature, outlined in this report, and determined that the information casts substantial doubt on the safety of approved animal drugs.

Based on the available data, CFS recommends the following:

**FDA Should Increase Transparency**

FDA should make scientific data on the health and safety of animal drugs within its possession publicly available. It should publish the data on its website as it currently does for Adverse Drug Events, and as the U.S. Department of Agriculture Food Safety and Inspection Service does for the National Residue Program. In addition, FDA should respond adequately and meaningfully to requests for information under the Freedom of Information Act.

**FDA Should Conduct Systematic Re-Reviews of Drug Safety, with the Burden on Industry To Prove Safety**

FDA should use its existing authority under the Federal Food, Drug, and Cosmetic Act (FFDCA) to conduct regular, systematic reviews of the safety of animal drugs.
At least twelve of the specific drugs discussed in this report are prohibited for use as animal drugs in other countries, and the EU has issued a ban on the use of all antibiotics for growth promotion. For six of the drugs, FDA has established residue tolerance levels significantly higher than the international standards. To ensure that they are still safe to be marketed. To bolster FDA’s duty to do so, the FFDCA should be amended to provide for specific re-review procedures, such as those that provide the U.S. Environmental Protection Agency with a duty to periodically reevaluate the safety of pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act.

Where Safety Data are Compelling, FDA Should Take Prompt Action
FDA has authority to immediately suspend approval for any drug that presents an imminent hazard to the health of humans or animals, and has a duty to withdraw approval for drugs that are shown to be unsafe. With respect to beta-agonists and steroid hormones, the available information raises serious questions about the safety of these drugs on the market, which is enough to trigger FDA’s duty to act. FDA should immediately evaluate these data and initiate the process of withdrawing approval for these drugs.

FDA Should Collaborate with USDA to Develop Collection of Producer-Level Drug Usage Data
FDA has already indicated that it intends, in collaboration with the Centers for Disease Control and USDA, to identify strategies for collecting producer-level data for antimicrobials. The Agency should engage seriously in this collaboration and expand its efforts to include collecting usage data for all animal drugs.

States and Localities Can Regulate in the Absence of Federal Action
The FFDCA leaves room for states to regulate in the absence of effective federal legislation. For example, six states—California, Maryland, Minnesota, New York, Pennsylvania, and Vermont—have proposed legislation that would regulate the nontherapeutic use of antibiotics in livestock. More states can take action, without waiting for FDA to step in.

Consumers Should Continue to Exert Market Pressure
Consumer campaigns that call upon food retailers and drug manufacturers to reduce the use and production, respectively, of harmful animal drugs can be an effective tool to curb the harmful proliferation of animal drugs until FDA takes appropriate regulatory action. Consumers can use their power to force these companies to change their practices.
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