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UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

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CENTER FOR FOOD SAFETY, INSTITUTE FOR AGRICULTURE AND TRADE POLICY, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR BIOLOGICAL DIVERSITY, FOOD ANIMAL CONCERNS TRUST, FOOD AND WATER WATCH, OREGON PHYSICIANS FOR SOCIAL RESPONSIBILITY, HEALTH CARE WITHOUT HARM, and SAN FRANCISCO BAY AREA PHYSICIANS FOR SOCIAL RESPONSIBILITY,

Plaintiffs,

v.

KATHLEEN SEBELIUS, SECRETARY OF U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, and MARGARET A. HAMBURG, M.D., COMMISSIONER OF U.S. FOOD AND DRUG ADMINISTRATION,

Defendants.

Case No. CV 13 1975

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Administrative Procedure Act Case

INTRODUCTION

1. This is an action for declaratory and injunctive relief regarding the failure by the United States Food and Drug Administration (FDA or the agency) to respond within a reasonable time to a petition filed by Center for Food Safety and the Institute for Agriculture and Trade Policy (collectively, Petitioners) requesting that FDA revoke all regulations associated with the approval of all New Animal Drug Applications (NADAs) for arsenic-containing compounds used as feed additives in chicken, turkeys, and swine. Petitioners are requesting immediate action because the use of arsenic-based feed additives in food-producing animals poses a serious yet completely avoidable health risk to humans. Petitioners are joined by petition endorsers Center for Environmental Health, Center for Biological Diversity, Food Animal Concerns Trust, Food & Water Watch, Oregon Physicians for Social Responsibility, Health Care Without Harm, and San Francisco Bay Area Physicians for Social Responsibility (collectively, Plaintiffs).

2. FDA began approving arsenic-containing compounds for use in animal feed in the 1940s. More than seventy years later, arsenic-containing feed additives—namely Roxarsone, arsanilic acid, nitarsone, and carbarsone—are still used in chicken, turkey, and swine production. In 2004 and 2005, Plaintiff Institute for Agriculture and Trade Policy tested for total arsenic residues in retail packages of raw chicken and in "fast food" chicken sandwiches and nuggets. Test results revealed detectable levels of arsenic in the majority of supermarket chicken and in all "fast food" chicken. Arsenic levels in chicken from birds for which there was a claim of "no arsenic given" contained no arsenic or such a small amount that it was below the detection limit. These results strongly suggest that the use of arsenic-containing compounds in poultry feed leads to arsenic residues in chicken marketed and eaten in the United States.

3. Inorganic arsenic is a known human carcinogen. It can contribute to cancers, heart disease, diabetes, declines in intellectual function, and can decrease a body's ability to respond to viruses. The organic form of arsenic—the form found in arsenic-containing compounds—was once considered safe at low levels. Recent studies show that organic arsenic can easily convert to inorganic arsenic. Further, organic arsenic may also be toxic in its own right, though an earlier history of organic arsenical toxicity has been largely overlooked by FDA.

4. On December 8, 2009, Petitioners submitted a petition to FDA for rulemaking. Docket No. FDA-2009-P-0594-0001/CP (2009 Petition) (filed concurrently as Exhibit A). Pursuant to § 360b of the Federal Food, Drug, and Cosmetic Act (FFDCA), the 2009 Petition requested that FDA immediately suspend all approvals of NADAs for arsenic-containing compounds used as feed additives in food-producing animals; publish a Notice of Opportunity for an Evidentiary Hearing concerning new evidence related to the NADAs; upon completion of the hearing, issue an order withdrawing all approvals of arsenic-containing animal feed additives; and revoke all regulations associated with approval of all NADAs for arsenic-containing animal feed additives.

5. Since the filing of the 2009 Petition, significant events have occurred that demonstrate both an urgent need and incentive for FDA to use its statutory authority to immediately withdraw approval of arsenic-containing feed additives. In February 2011, FDA completed a final report on a study of the safety of edible tissues from chickens treated with arsenicals, particularly Roxarsone. The study concluded that levels of inorganic arsenic in chicken livers were significantly higher for chickens treated with the arsenical Roxarsone than for chickens not treated with Roxarsone.[1] Shortly following the release of FDA's study, in June 2011, Alpharma (a division of Pfizer) announced it would voluntarily suspend—not revoke—sale of Roxarsone within 30 days.[2] At this time, FDA commented that Roxarsone raised concerns of "completely avoidable exposure to a carcinogen."[3]

6. Even though Pfizer claims it is not currently selling Roxarsone, and Roxarsone raises concerns of "completely avoidable" exposure to a known carcinogen, FDA has not formally withdrawn Roxarsone from the market—the drug could be returned to the market at any

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[1] U.S. Food and Drug Admin., Final Report on Study 275.30, Provide data on various arsenic species present in broilers treated with roxarsone: Comparison with untreated birds 36 (Feb. 10, 2011), *available at* http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/UCM257545.pdf.

[2] Press Release, U.S. Food and Drug Admin., FDA: Pfizer will voluntarily suspend sale of animal drug 3-Nitro (June 8, 2011), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm258342.htm.

[3] *Id.* (emphasis added).

time. Nor has FDA studied the other arsenic-containing compounds referenced in the 2009 Petition or evaluated muscle tissue consumed by humans more frequently than chicken livers. No other arsenical drug manufacturers have voluntarily suspended their sales of other arsenicals, even though other arsenicals are just as likely as Roxarsone to convert to inorganic arsenic and to be present in chicken, turkey, or swine. FDA's failure to act has completely failed to close the loop on an avoidable exposure pathway to a known carcinogen.

7. Nearly three and a half years have now passed since FDA docketed the 2009 Petition for rulemaking. Not only has FDA failed to act under the FFDCA, the agency has not meaningfully responded to the 2009 Petition and is in violation of the Administrative Procedure Act (APA). In the interim, evidence of the negative effects of arsenic-based feed additives continues to mount. This Court should order the agency to respond to Plaintiffs' 2009 Petition without further unlawful delay.

JURISDICTION

8. This Court has jurisdiction over this action pursuant to 28 U.S.C. § 1331 (federal question) and 28 U.S.C. § 1346 (United States as defendant).

9. The relief requested is specifically authorized pursuant to 28 U.S.C. § 1651 (writs) and 28 U.S.C. §§ 2201–02 (declaratory relief). An actual controversy exists between the parties within the meaning of 28 U.S.C. § 2201 (declaratory judgments).

10. Plaintiffs have a right to bring this action pursuant to the APA, 5 U.S.C. § 702.

VENUE

11. Venue properly lies in this Court pursuant to 28 U.S.C. § 1391(e) because one or more of the Plaintiffs reside in this District.

PARTIES

12. Plaintiff Center for Food Safety (CFS) is a Washington, D.C.-based nonprofit organization located at 660 Pennsylvania Avenue S.E., Washington, D.C. 20003. CFS has nearly 300,000 members, including members in every state across the country, many of whom purchase and consume chicken, turkey, and pork that were fed arsenic-based feed additives, and eggs from chickens that were fed arsenic-based feed additives. CFS and its members are being,

and will be, adversely affected by FDA's continued failure to address the risks associated with the use of arsenic-based feed additives.

13. Founded in 1997, CFS is dedicated to addressing the environmental, economic, ethical, human health, and social impacts associated with the development and commercialization of agricultural and food processing technologies. 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, public education, grassroots organizing, and media outreach. CFS is actively involved in the campaign against the use of antimicrobials in food animal production and has specifically focused on arsenic-based feed additives since 2008. CFS members support enhanced animal welfare and regularly purchase organic products, including organic meat and dairy, due to concerns about the use of antimicrobials like arsenic in animal production. CFS and its members believe it is imperative that FDA promote a cautious approach to the use of arsenic-based feed additives and other antimicrobials in food in order to protect human health.

14. CFS also sends action alerts to its membership. These action alerts generate public involvement, education, and engagement with governmental officials on issues related to fighting the health and environmental impacts of industrial agriculture and promoting a more sustainable, healthier food system. Collectively, the dissemination of this material has made CFS an information clearinghouse for public involvement and governmental oversight of food safety issues.

15. Plaintiff Institute for Agriculture and Trade Policy (IATP) is a 501(c)(3) nonprofit organization located at 2105 First Avenue South, Minneapolis, Minnesota 55404. Established in 1986, IATP works locally and globally at the intersection of policy and practice to ensure fair and sustainable food, farm, and trade systems. In 2006, IATP issued a groundbreaking report, *Playing Chicken: Avoiding Arsenic in Your Meat*, examining arsenic residues in retail chicken meat purchased in supermarkets as well as chicken products from "fast food" outlets. Prior to this report, FDA had never tested for the presence of arsenic in chicken muscle, only in chicken liver on a limited basis.

16. Plaintiff Center for Environmental Health (CEH) is located at 528 61st Street, Suite A, Oakland, California 94609. Founded in 1996, CEH is a nonprofit organization dedicated to protecting the public from environmental and consumer health hazards. CEH is committed to environmental justice, reducing the use of toxic chemicals and practices, supporting communities in their quest for a safer environment, and corporate accountability. CEH programs have eliminated health threats to children from pesticides on our food, contamination from lead in imported candies, Polychlorinated Biphenyls (PCBs) in farmed salmon, contamination from harmful chemicals in food packaging, and other food safety threats.

17. Plaintiff Center for Biological Diversity (the Center) is a nonprofit public interest corporation with over 41,000 members and offices throughout the United States. The Center has offices in several locations, including Tucson, Arizona; San Francisco, Los Angeles, and Joshua Tree, California; Portland, Oregon; Silver City, New Mexico; and Washington, D.C. The Center and its members are dedicated to protecting the diverse native species and habitats of North America through science, policy, education, and environmental law. Members of the Center reside or own property and use waterways and environments throughout the United States that are impacted by pollution from animal feeding operations.

18. The Center's Toxics and Endangered Species Campaign employs a broad range of tools to reduce the harmful impacts of toxic contamination from man-made pollution, industrial chemicals, and resource-extractive processes. Through strategic litigation, creative media, policy advocacy, scientific reports, coalition building, and outreach to our members, the Center has mounted an effective campaign to target some of the most harmful toxins in our environment.

19. Plaintiff Food Animal Concerns Trust (FACT) is a nonprofit organization located at 3525 W. Peterson Avenue, Suite 213, Chicago, Illinois, 60659-3314. FACT is dedicated to improving the welfare of farm animals; addressing public health problems such as the safety of meat, milk, and eggs; broadening opportunities for family farmers; and reducing environmental pollution. FACT has an active Public Health Program that identifies and advocates for steps farmers should take to keep their cattle, pigs, turkeys, and chickens from being the cause of human disease. FACT supports appropriate food safety regulation of farms where animals are raised to produce meat, milk, and eggs. An important part of FACT's public health work is to

advocate for actions that reduce the risk that animal products are contaminated by unsafe residues of veterinary drugs including arsenic. FACT does this domestically through engagement with FDA and internationally by participating in the Codex Committee on Residues of Veterinary Drugs in Food.

20. Plaintiff Food & Water Watch (FWW) is a national nonprofit public interest consumer advocacy organization located at 1616 P Street NW, Suite 300, Washington, D.C. 20036, with offices throughout the United States, including New York City, New York, and San Francisco, California. FWW advocates for common sense policies that will result in healthy, safe food and access to safe and affordable drinking water. FWW helps people take charge of where their food comes from; keeps clean, affordable, public tap water flowing freely to our homes; protects the environmental quality of oceans; forces government to do its job protecting citizens; and educates about the importance of keeping the global commons—our shared resources—under public control. To that end, FWW has advocated against various government proposals and polices that would limit consumers' right to healthy and safe products, and negatively impact human health and the overall environment. Specifically on the issue of arsenic, FWW worked for several years in Maryland to support passage of a bill that bans the use of Roxarsone. The bill passed in 2012. FWW has also worked for several years to educate the public about the need for changes to public policy on animal drugs including antibiotics and arsenicals.

21. Plaintiff Oregon Physicians for Social Responsibility (OPSR) is located at 812 SW Washington Street, Suite 1050, Portland, Oregon 97205. It was founded in 1980 as a regional chapter of Physicians for Social Responsibility. Guided by the values and expertise of medicine and public health, OPSR works to protect human life from the gravest threats to health and survival by striving to end the nuclear threat, advance environmental health, and promote peace.

22. Plaintiff Health Care Without Harm (HCWH), founded in 1996, has offices in Reston, Virginia, and worldwide. HCWH works to implement ecologically sound and healthy alternatives to health care practices that pollute the environment and contribute to disease.

23. Since 2005 OPSR has partnered with HCWH on its Oregon Healthy Food in

Health Care Project (the Project). The Project employs market-based forces to increase demand for sustainably-produced foods, improve hospital food quality, educate the public, and bolster the local economy. The principal goal of the Project is to leverage the significant purchasing power and influence of hospitals to support regional markets for sustainable food and to model healthy food choices to the public. The Project provides resources, tools, education, and technical assistance to hospital food service departments. Together, OPSR and HCWH have addressed the issue of antimicrobials, and specifically arsenical usage, in poultry production by supporting greater understanding of the environmental health consequences of the practice and then helping institutional food buyers to seek information from their suppliers to make informed purchasing decisions.

24. Plaintiff San Francisco Bay Area Chapter of Physicians for Social Responsibility (SF PSR), founded in 1979, was the first chapter of Physicians for Social Responsibility to be organized in the country and remains one of the largest of the thirty-one U.S. chapters, with over 2000 members. Physicians for Social Responsibility is a nonprofit advocacy organization that combines the power of community activism with the knowledge and credibility of physicians and other health professionals to promote public policies that support human health. SF PSR is the preeminent medical and public health voice in the San Francisco region on a broad range of critical social and environmental health issues, including building a healthier food system. SF PSR coordinates the Healthy Food in Health Care program in California, a nationwide program of Health Care Without Harm that harnesses the purchasing power and expertise of the health care sector to advance the development of a sustainable food system. Through advocacy and education, SF PSR motivates health care facilities to implement programs that explicitly connect all aspects of the food system with health. SF PSR catalyzes sustainable procurement efforts; organizes clinicians to advocate for local, regional, and national food policy; and inspires health care institutions to become leaders in shaping a food system that supports prevention-based health care.

25. Defendant Kathleen Sebelius is the Secretary of the United States Department of Health and Human Services, and is sued in her official capacity.

26. Defendant Dr. Margaret A. Hamburg is sued in her official capacity as FDA Commissioner. As Commissioner, Dr. Hamburg has the ultimate responsibility for FDA's activities and policies.

27. Dr. Hamburg and the Food and Drug Administration are collectively referred to herein as "FDA" or "the agency."

LEGAL BACKGROUND

Federal Food, Drug, and Cosmetic Act

28. The Secretary of the U.S. Department of Health and Human Services, "through the Commissioner" of FDA, 21 U.S.C. § 393(d)(2), regulates antimicrobials in animal feed as "new animal drugs" under the FFDCA, *id.* § 360b.

29. Under FFDCA § 360b, the Secretary shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of a new animal drug if the Secretary finds:

A) "[E]xperience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved or the condition of use authorized under subsection (a)(4)(A)," *id.* § 360b(e)(1)(A);

B) New evidence, tests, or methods developed since approval of the application show that the drug is not safe for use "under the conditions of use upon the basis of which the application was approved," *id.* § 360b(e)(1)(B); or

C) New information, combined with the evidence available at the time the application was approved, shows a "lack of substantial evidence that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof," *id.* §360b(e)(1)(C).

FDA Regulations on Citizen Petitions

30. FDA's regulations provide that citizens may petition FDA to "issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action." 21 C.F.R. § 10.25.

31. "The Commissioner shall . . . rule upon each petition . . . ." *Id.* § 10.30(e)(1).

32. "[T]he Commissioner shall furnish a response to each petitioner within 180 days of receipt of the petition" by approving, denying, or providing a tentative response to the petition, "indicating why the agency has been unable to reach a decision on the petition. . . ." *Id.* § 10.30(e)(2). "The tentative response may also indicate the likely ultimate agency response, and may specify when a final response may be furnished." *Id.*

33. "The Commissioner may grant or deny such a petition, in whole or in part, and may grant such other relief or take other action as the petition warrants. The petitioner is to be notified in writing of the Commissioner's decision." *Id.* § 10.30(e)(3).

Administrative Procedure Act

34. Under the APA, agencies are required to "give an interested person the right to petition for the issuance, amendment, or repeal of a rule." 5 U.S.C. § 553(e).

35. The APA requires an agency to conclude a matter presented to it "within a reasonable time." *Id.* § 555(b). "Prompt notice shall be given of the denial [of a petition] in whole or in part. . . ." *Id.* § 555(e).

36. The APA grants a right of judicial review to "[a] person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action." *Id.* § 702.

37. Courts "shall compel agency action unlawfully withheld or unreasonably delayed," *id.* § 706(1), and "hold unlawful and set aside agency action, findings, and conclusions found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," *id.* § 706(2)(A). Courts may only review a final agency action, *id.* § 704, and "agency action" includes a "failure to act," *id.* § 551(13).

STATEMENT OF FACTS

Arsenic

38. Arsenic is a semi-metal element in the periodic table. It is odorless and tasteless. Arsenic occurs naturally in the environment as an element of the earth's crust; it is found in rocks, soil, water, air, plants and animals. It can be further released into the environment through natural activities such as volcanic action, erosion of rocks, and forest fires, or through human

actions. Elemental arsenic is combined with other elements such as oxygen, chlorine, and sulfur to form inorganic arsenic compounds.

39. Historically, arsenic compounds were used in many industries, including: as a preservative in pressure treated lumber; as a preservative in animal hides; as an additive to lead and copper for hardening; in glass manufacturing; in pesticides; in animal agriculture; and as arsine gas to enhance junctions in semiconductors. The United States has cancelled the approvals of some of these uses, such as arsenic-based pesticides, for health and safety reasons. Some of these cancellations were based on voluntary withdrawals by producers. For example, manufacturers of arsenic-based wood preservatives voluntarily withdrew their products in 2003 due to safety concerns, and the United States Environmental Protection Agency (EPA) signed the cancellation order. In the Notice of Cancellation Order, EPA stated that it considered the voluntary move a positive step, especially for the nation's children. "[EPA] believes that reducing the potential residential exposure to a known human carcinogen is desirable."[4]

40. Arsenic is an element—it does not degrade or disappear. Therefore, despite efforts to reduce the amount of arsenic in the environment, residual arsenic remains.

Arsenic-Based Feed Additives

41. Arsenic is widely used in animal agriculture, contributing to the overall arsenic burden. FDA first approved the use of an arsenic-containing compound, Roxarsone, for use in animal production in 1944. Since then, FDA has approved more than 100 different arsenical compounds for use in broiler chickens alone.

42. Arsenic-containing compounds are most widely used in chicken production. According to data from the United States Department of Agriculture (USDA), 8,428,847,000 chickens were killed for food in the United States in 2012 alone.

43. In 2002, an estimated seventy percent of chickens were fed arsenic-containing

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[4] Response to Requests to Cancel Certain Chromated Copper Arsenate (CCA) Wood Preservative Products and Amendments to Terminate Certain Uses of other CCA Products, 68 Fed. Reg. 17366, 17367 (Apr. 9, 2003).

compounds at some point in their lives.[5]

44. Chicken production has changed significantly in the last sixty years. Almost all chickens are now raised indoors. A modern broiler house is typically a single story facility, approximately forty feet wide by 400–500 feet long that holds 25,000 to 30,000 birds. A modern broiler "farm" generally has two to six such houses, with up to 150,000 birds or more. Inside these facilities, animals compete for space, food, and water; breathe contaminated air; and live in their own waste. Conditions of overcrowding and poor sanitation significantly increase the chance of large outbreaks of zoonotic diseases in large chicken operations. The relentless drive to produce more animals in less time, with less space, and at a lower cost is what lies behind the routine addition of antimicrobial drugs such as arsenicals to animal feeds.

45. Arsenic-containing feed additives are approved for both non-therapeutic and therapeutic uses. The thousands of animal feeding operations in the U.S. can use arsenic-containing feed additives for non-therapeutic reasons, such as to increase weight gain, improve feed efficiency, and improve pigmentation in animals, 21 C.F.R. § 558.530, or to prevent and control disease among animals that are raised in crowded, stress-inducing conditions that promote disease.

46. Arsenic, like other antimicrobials, is added to animal feed without a prescription. Most food-producing animals receive multiple drugs in their feed or drinking water for the majority of their lives. For example, broiler chickens are fed pre-starter, starter, and grower feeds containing up to three drug components: an antibiotic to promote growth, an arsenical, and an anti-parasite drug. Finisher feed also contains an antibiotic and arsenical, although arsenic is prohibited the last five days of a broiler's short life.

47. While FDA approves proposed arsenical uses, it does not collect data on arsenical sales or use. The most recent data available indicates that in 2010, 706,530 kilograms (kg) of arsenicals were sold for use in food-producing animals.

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[5] *See* 21 C.F.R. §§ 558.35-558.680; H.D. Chapman, Z.B. Johnson, *Use of Antibiotics and Roxarsone in Broiler Chickens in the USA: Analysis for the Years 1995 to 2000*, 81 Poultry Sci. 356, 356-64 (2002).

Arsenic Residue Testing

48. The U.S. approach to food safety generally does not aim to keep chemical contaminants completely out of the food supply—even cancer-causing arsenic. Rather, FDA determines the maximum exposure to that chemical deemed to be "safe," and then legally allows contamination of a particular food product up to the level of consumption that FDA believes results in maximum "safe" exposure (food tolerance residue levels).

49. For enforcement of food tolerance residue levels, FDA relies on USDA's Food Safety Inspection Service (FSIS). The cornerstone of FSIS's effort is the National Residue Program, which since 1970 has monitored chemical residues in food. According to USDA's "Red Book" data, FSIS conducts very little testing of more commonly consumed poultry and pork products. For example, in 2001, FSIS analyzed just 1,207 of the more than eight billion young chickens produced for total arsenic, and then only chicken kidneys and livers, not the muscle meat that most humans consume.[6] In 2009, FSIS tested just 324 young chickens—more than twenty-five percent of these chickens tested positive for arsenic residue.[7] In 2010, the most recent year for which the public has data, FSIS did not analyze chickens for total arsenic at all. FSIS residue testing is the only "protection" American consumers have against arsenic exposure from contaminated meat, yet residue testing is weak and funding for the FSIS National Residue Program is, and has been over the years, unstable. The function of FSIS testing is only to monitor the problem; it does not prevent or correct it.

50. Such sparse FSIS testing was the impetus for Plaintiff IATP's 2004 and 2005 independent residue testing and subsequent report. Plaintiff IATP tested for total arsenic in retail packages of raw chicken and "fast food" chicken sandwiches and nuggets. The results suggest that the use of arsenic-containing compounds in poultry feed leads to arsenic residues in chicken marketed and eaten in the United States.

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[6] USDA, FSIS, 2001 FSIS National Residue Program Data, *available at* http://www.fsis.usda.gov/OPHS/red_book_2001/2001_Residue_Program_Data_Sections1-7.pdf.

[7] USDA, FSIS, United States National Residue Program 2009 Residue Sample Results (May 2011), *available at* http://www.fsis.usda.gov/PDF/2009_Red_Book.pdf.

51. In retail packages of raw chicken, IATP tested thighs, breasts, and livers purchased under both "conventional" and "premium" labels. IATP tested chicken from five of the top twenty-five broiler producers nationally, several premium brands, and one kosher/halal brand. Test results revealed detectable levels of arsenic in the majority—fifty-five percent—of supermarket chicken.

52. Plaintiff IATP also tested ninety samples of cooked "fast food" chicken. The tests revealed detectable levels of total arsenic in 100 percent of the samples tested.

The Health Effects of Arsenic

53. Inorganic arsenic is a known cause of human cancer. The association between inorganic arsenic and cancer is well documented. As early as 1879, high rates of lung cancer in Saxony miners were attributed in part to inhaled arsenic. By 1992, the combination of evidence from Taiwan and elsewhere was sufficient to conclude that ingested inorganic arsenic, such as is found in contaminated drinking water and food, was likely to increase the incidence of several internal cancers. The scientific link to skin and lung cancers is particularly strong and longstanding,[8] and evidence supports conclusions that arsenic may cause liver, bladder, kidney, and colon cancers as well. Under the law, FDA is restricted from approving substances (including animal drugs) found to induce cancer. 21 U.S.C. § 360b(d)(1)(I).

54. At one time, organic arsenic was considered less toxic than inorganic arsenic, carrying fewer health concerns. Recent science reveals, however, that organic and inorganic forms of arsenic can convert to one another in the body and in the environment. Organic arsenic can convert to inorganic arsenic once ingested by humans and animals. Environmental bacteria, including those residing in chicken litter, as well as in the bacterial microflora of the human or chicken gut, convert organic arsenic into inorganic forms, such as arsenate, As(V), and arsenite, As(III), which are classified as human carcinogens and are therefore potentially more toxic than

[8] *See, e.g.,* Int'l Agency for Research on Cancer, World Health Organization, *Some Metals and Metalloid Compounds: Summary of Data Reported and Evaluation,* 23 IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 39 (1980), *available at* http://monographs.iarc.fr/ENG/Monographs/vol23/volume23.pdf.

the parent compound.[9] Further, some organic forms of arsenic created by the body's metabolism appear to be more toxic than inorganic arsenic.

55. A variety of studies in cells demonstrate that exposure to infinitesimally small (nanomolar to low micromolar) concentrations of arsenite stimulates a process of new blood vessel formation called angiogenesis, associated with vascular disease as well as the growth of new tumors.[10] In addition to enhancing tumor growth, increased angiogenesis would contribute to overall growth potential and increased tissue pigmentation—exactly the attributes sought in arsenic-containing compounds' use as a poultry feed additive. Despite arsenic's direct links to cancer, and its use over seventy years in animal agriculture, the effects of arsenic-containing compounds on mammalian cells have not been greatly studied. In one exception, human cells from vascular and lung tissue were studied following exposure to the arsenic-containing compound Roxarsone.[11] The study found that like arsenite, As(III), Roxarsone induces an increase in angiogenesis, but it does so more potently. Moreover, Roxarsone acts via a mechanism that is distinct from and independent of the one induced by As(III). In other words, Roxarsone use and exposure could potentially promote angiogenesis—a key element of cancer tumor growth—via two independent processes, one via conversion to As(III), and another via a more direct mechanism.

56. The United States population is regularly exposed to a cumulative burden of

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[9] A.J. Bednar et al., *Photodegradation of Roxarsone in Poultry Litter Leachates*, 302 Sci. Total Env't 237, 237-245 (2002); J.R. Garbarino et al., *Environmental fate of roxarsone in poultry litter. I. Degradation of roxarsone during composting*, 37 Envtl. Sci. & Tech. 1509, 1509-14 (2003); John F. Stolz et al., *Biotransformation of 3-Nitro-4-Hydroxybenzene Arsonic Acid and Release of Inorganic Arsenic by* Clostridium *Species*, 41 Envtl. Sci. & Tech. 818, 818-23 (2007).

[10] Chandrashekhar D. Kamat et al., *Role of HIF Signaling on Tumorigenesis in Response to Chronic Low-dose Arsenic Administration*, 86 Toxicological Sci. 248, 248–57 (2005); Bing Liu et al., *Opposing Effects of Arsenic Trioxide on Hepatocellular Carcinomas in Mice*, 97 Cancer Sci. 675, 675-81 (2006); Nicole V. Soucy et al., *Arsenic Stimulates Angiogenesis and Tumorigenesis in Vivo*, 76 Toxicological Sci. 271, 271–79 (2003); Nicole V. Soucy et al., *Neovascularization and Angiogenic Gene Expression Following Chronic Arsenic Exposure in Mice*, 5 Cardiovascular Toxicology 29, 29-41 (2005).

[11] Partha Basu et al., *Angiogenic Potential of 3-Nitro-4-Hydroxy Benzene Arsonic Acid (Roxarsone)*, 116 Envtl. Health Persp. 520, 520-23 (2008).

arsenic. For example, drinking water is a major source of arsenic exposure.[12] EPA thus sets an enforceable regulation for arsenic, called a maximum contaminant level (MCL). Recognizing the health problems of arsenic in drinking water, EPA in 2001 lowered the MCL from fifty parts per billion (ppb) to ten ppb. The National Academies of Science estimate that Americans who drink water contaminated with arsenic at the ten ppb level—numbering thirteen million in 2001—have a greater than 1-in-300 risk of developing cancer during their lifetime.

57. While EPA has set an MCL for arsenic in water, there is no similar maximum exposure level for apple juice, which is also known to contain high levels of arsenic. In response to studies showing that apple juice regularly contains high levels of arsenic, and in an effort to limit arsenic in apple juice, in 2012 United States Representatives Frank Pallone and Rosa DeLauro introduced H.R. 3984, the "Arsenic Prevention and Protection from Lead Exposure in Juice Act of 2012," otherwise known as the "APPLE Juice Act of 2012." The legislation would require FDA to establish arsenic and lead standards for fruit juices within two years.[13]

58. Arsenic is also pervasive in food. Arsenic is most commonly found in rice, seaweed, seafood, infant formulas containing brown rice syrup, and of course, meat. In 2011, tests performed by Dartmouth College's Children's Environmental Health and Disease Prevention Center indicated that consuming slightly more than half a cup of cooked rice per day resulted in total urinary arsenic concentrations nearly equal to consuming a liter of water containing the maximum amount of arsenic allowable in public drinking water. Notably, American-grown rice contains 1.4 to 5 times more arsenic on average than rice from Europe, India, and Bangladesh.

59. The several million Americans who currently drink water contaminated at the ten ppb EPA standard, and/or eat certain foods with a high level of arsenic, are at an increased cancer risk from their additional arsenic exposure from meat produced with arsenic-based feed

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12 *See* Press Release, U.S. Food and Drug Admin., FDA Warns Again About Arsenic in Mineral Water (Mar. 24, 2007), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108875.htm.

13 *See* H.R. 3984, 112th Cong. (2012).

additives.

60. In 2010, the European Food Safety Authority (EFSA) issued warnings to consumers about the risks of inorganic arsenic in food.[14] Based on new science on the health risks of arsenic exposure in food, the EFSA panel on contaminants in the food chain (CONTAM) recommended that consumers reduce dietary exposure to inorganic arsenic. CONTAM found that consumers of large amounts of rice, such as certain ethnic groups, and consumers of algae-based products are especially at risk of increased arsenic exposure.

61. Arsenic is not poisonous to everyone to the same degree. Children, infants, and the human fetus are among those most vulnerable to arsenic's toxic effects. This is due to differences in arsenic metabolism between an adult and those very early in life. Moreover, arsenic and its organic metabolites easily pass through the placenta.[15] Carcinogens like arsenic are generally more potent in their early life exposures. Following its review of twenty-three peer-reviewed studies of cancer incidence over the past fifty years, EPA concluded that infants up to age two are, on average, ten times more vulnerable to carcinogenic chemicals than adults, and for some cancer-causing agents are up to sixty-five times more vulnerable; children ages two to five are three times more vulnerable to carcinogens than adults.[16]

62. An increased risk of cancer is not the only adverse impact of arsenic. Arsenic affects nearly all organ systems because it targets ubiquitous enzyme reactions in cells.[17] Studies of in utero exposure to arsenic indicate that early life exposures to compounds can alter

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[14] European Food Safety Auth. Panel on Contaminants in the Food Chain, European Food Safety Auth. (EFSA), *Scientific Opinion on Arsenic in Food*, 7 EFSA Journal 1351 (2009), *available at* http://www.efsa.europa.eu/en/efsajournal/doc/1351.pdf.

[15] Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., Nat'l Research Council, *Arsenic in Drinking Water: 2001 Update* (National Academy Press 2001), *available at* http://www.nap.edu/catalog.php?record_id=10194; M. Nathaniel Mead, *Arsenic: In Search of an Antidote to a Global Poison,* 113 Envtl. Health Persp. A378, A378-86 (2005).

[16] Risk Assessment Forum Technical Panel, U.S. Envtl. Prot. Agency, *Supplemental Guidance for Assessing Cancer Susceptibility from Early-Life Exposure to Carcinogens,* EPA/630/R-03/003F (Mar. 2005), *available at* http://www.epa.gov/ttnatw01/childrens_supplement_final.pdf.

[17] Subcomm. on Arsenic in Drinking Water et al., Nat'l Research Council, *Arsenic in Drinking Water* (National Academy Press 1999), *available at* http://www.nap.edu/catalog.php?record_id=6444; Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., *supra* note 15.

susceptibility of endocrine and reproductive organs. Long-term exposure to arsenic can also cause hyperpigmented skin, skin nodules, vessel disease, and appears to heighten the risk of death from high blood pressure and heart disease. Humans repeatedly exposed to arsenic also have an increased risk of diabetes.[18]

63. Scientists continue to discover new and increasingly dangerous health impacts not previously considered from arsenic exposure. Identification of many of these factors post-date FDA's approval of arsenicals as new animal drugs. For example, evidence now indicates that arsenic is a potent disruptor of hormone function, altering the way in which hormones transmit information between cells at extremely low levels of exposure.[19] Recently, a delayed response in developing immunity to the H1N1 virus was attributed to arsenic exposure in drinking water.[20]

64. The United States population's meat consumption is at a record high. With this increased consumption comes an increased exposure to arsenic. Chicken, pork, and turkey represent the first, third, and fourth most heavily-consumed foods in the United States. Chicken represents an increased risk from meat due to the sheer volume of consumption. From 1966 to 2000, annual chicken consumption rose 253 percent, from 32.1 to 81.2 pounds per person.[21] Many people are not average, however. USDA data indicate that African Americans eat about twenty percent more chicken than does the United States population as a whole. Similarly, due to their small size, toddlers eating chicken baby food may ingest chicken at substantially higher-than-average levels, on a weight-adjusted basis. For these subgroups, arsenic ingestion

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[18] Subcomm. on Arsenic in Drinking Water et al., *supra* note 17; Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., *supra* note 15.

[19] M. Nathaniel Mead, *supra* note 15; Ronald C. Kaltreider et al., *Arsenic Alters the Function of the Glucocorticoid Receptor as a Transcription Factor*, 109 Envtl. Health Persp. 245, 245-51 (2001); Jack E. Bodwell et al., *Arsenic at Very Low Concentrations Alters Glucocorticoid Receptor (GR)-Mediated Gene Activation but not GR-Mediated Gene Repression: Complex Dose-Response Effects Are Closely Correlated with Levels of Activated GR and Require a Functional GR DNA Binding Domain*, 17 Chem. Research in Toxicology 1064 (2004).

[20] Courtney D. Kozul et al., *Low-dose Arsenic Compromises the Immune Response to Influenza A Infection in Vivo*, 117 Envtl. Health Persp, 1441, 1441-47 (2009).

[21] David A. Taylor, *Funky Chicken: Consumers Exposed to Arsenic in Poultry*, 112 Envtl. Health Persp. A50, A50-51 (2004) (reviewing Tamar Lasky et al., *Mean Total Arsenic Concentrations in Chicken 1989-2000 and Estimated Exposures for Consumers of Chicken*, 112 Envtl. Health Persp. 18, 18-21 (2004)).

from contaminated chicken may be substantially higher than average. One in 100 Americans now eats more than three-quarters of a pound (>350 grams) of chicken per day. This person could be expected to ingest 32.5 to 47.07 micrograms of total arsenic per day from chicken alone. One in 1000 Americans eats at least one and one-third pounds of chicken per day. For an average-sized person, this could translate into 56.8 to 82.3 micrograms of total arsenic per day, more arsenic than the average American is estimated to receive from *all* dietary sources.[22]

Arsenic and the Environment

65. Agency-approved arsenicals used in poultry production likely have indirect human and environmental impacts beyond the direct effects of ingesting arsenic residues in meat. The 8.5 billion broiler chickens raised in the United States each year generate twenty-five to fifty-five billion pounds of poultry litter or waste.[23] For example, of the approximately 1.5 million pounds of arsenic-containing compounds fed to animals in 2010—mostly chickens—up to an estimated three-quarters passed unchanged into poultry waste.

66. Poultry litter disposal occurs in several different ways. Around ninety percent is applied to nearby fields and cropland as "fertilizer," which, according to various estimates, may disperse 0.5 to 2.6 million pounds of arsenic-based compounds and their degradation products into the environment annually.[24] Poultry litter containing arsenic is also then fed to beef cattle. In January 2004, FDA proposed banning the practice;[25] however, the agency reversed course in October 2005 and decided to continue allowing it. Poultry litter is also converted into fertilizer

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[22] Tamar Lasky et al., *Mean Total Arsenic Concentrations in Chicken 1989-2000 and Estimated Exposures for Consumers of Chicken*, 112 Envtl. Heath Persp. 18, 18-21 (2004).

[23] Keeve E. Nachman et al., *Arsenic: A Roadblock to Potential Animal Waste Management Solutions*, 113 Envtl. Health Persp. 1123, 1123-24 (2005).

[24] Miguel L. Cabrera & J. Thomas Sims, *Beneficial Use of Poultry By-Products: Challenges and Opportunities, in Land Application of Agricultural, Industrial, and Municipal By-Products* (James F. Power & Warren A. Dick eds., Soil Science Society of America 2000) (2000); D.W. Rutherford et al., *Environmental Fate of Roxarsone in Poultry Litter. Part II. Mobility of Arsenic in Soils Amended with Poultry Litter*, 37 Envtl. Sci. & Tech. 1515, 1515-20 (2003); R.L. Wershaw et al., *Roxarsone in Natural Water Systems*, http://water.usgs.gov/owq/AFO/proceedings/afo/pdf/Wershaw.pdf.

[25] *See* Press Release, U.S. Food & Drug Admin., Expanded "Mad Cow" Safeguards Announced to Strengthen Existing Firewalls Against BSE Transmission (Jan. 26, 2004), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108230.htm.

pellets to be sold for commercial use on crops, for home landscaping, gardening, and on golf courses. This practice opens up entirely new avenues of the public's exposure to arsenic. Arsenic levels in these pellets are reportedly similar to those found in unprocessed poultry waste.[26]

67. Poultry waste can also contaminate peoples' homes. For example, in the chicken-producing town of Prairie Grove, Missouri, house dust in each of thirty-one homes examined was found to contain at least two kinds of arsenic also found in chicken litter.

68. The rising volume of poultry waste, as well as its geographic concentration, means that larger broiler chicken and other poultry production facilities now generate far more waste than can easily be disposed of through land application. In late 2002, Minnesota permitted the first incinerator in the United States for the purpose of burning poultry litter for electricity generation.[27] This questionable practice will contribute to air pollution from toxics and heavy metals such as arsenic contained in the waste. Neither pelletization nor incineration can destroy or detoxify arsenic; both would further disperse it into the human environment.[28]

69. Because arsenic is an element, it neither degrades nor disappears. Therefore, the disposal of arsenic compounds only redistributes arsenic in a different form that can lead to soil and water contamination. It is estimated that seventy to ninety percent of arsenic in poultry litter becomes water soluble, meaning it can readily migrate through soils and into underlying groundwater. Airborne drift of poultry litter dust also contaminates groundwater and indirectly exposes neighbors, farmers, and farmworkers to arsenic.[29] Routine arsenic use in animal feed likely adds to the already significant public health burden from arsenic-contaminated drinking water supplies.

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[26] Keeve E. Nachman et al., *supra* note 23.

[27] Minn. Pollution Control Agency, Fibrominn LLC Air Emission Permit 15100038-001 (Oct. 23, 2002), *available at* http://www.pca.state.mn.us/index.php/view-document.html?gid=10864.

[28] Keeve E. Nachman et al., *supra* note 23.

[29] B.P. Jackson et al., *Trace Element Speciation in Poultry Litter*, 32 J. Envtl. Quality 535, 535-40 (2003); J.R. Garbarino et al., *supra* note 9.

FDA and Plaintiffs' 2009 Petition

70. Defendant FDA has a duty to withdraw approvals of new animal drugs that are no longer considered safe. Studies published during the last fifteen years considering the impacts of arsenic-containing feed additives that were approved decades ago indicate that these compounds are no longer safe for use in food animal production. Despite this new evidence, the agency has not addressed the risks to animal health, human health, and the environment, as it is required to pursuant to the FFDCA.

71. On December 8, 2009, Petitioners submitted a Citizen Petition for rulemaking pursuant to 21 C.F.R §§ 10.25(a), 10.30. The 2009 Petition documented the then-existing body of scientific evidence studying arsenic's use as a feed additive, and the risks stemming from this unsafe practice. Additionally, Petitioners have supplemented the docket with the growing body of new evidence further demonstrating the risks.

72. The 2009 Petition requested, pursuant to the U.S. Constitution, the APA, and FDA regulations, that the Commissioner do the following:

(i) Immediately suspend approval of all NADAs for arsenic-containing compounds used as feed additives for food animals.

(ii) Publish a Notice of Opportunity for an Evidentiary Hearing concerning "new evidence" related to the applications.

(iii) Upon completion of the hearing, issue an order withdrawing approval of all NADAs for arsenic-containing compounds used as feed additives for animals.

(iv) Revoke all regulations associated with approval of all NADAs for arsenic-containing compounds used as feed additives for food animals, including regulations 21 C.F.R. §§ 558.62, 558.120, 558.369, 558.530.

73. Since the filing of the 2009 Petition, several additional events have occurred that demonstrate not only increased urgency, but a straightforward path that FDA can take to immediately withdraw FDA approval of arsenic-containing compounds. Despite these events, FDA has not advanced its response to the 2009 Petition.

74. In February 2011, FDA completed a final report on a study that concluded (like much of the existing scientific literature) that organic arsenic could transform into the toxic carcinogen inorganic arsenic, and that levels of inorganic arsenic in chicken livers were substantially higher for chickens treated with the arsenical Roxarsone than for chickens not treated with Roxarsone.[30] As the 2009 Petition described, evidence indicates that human intestinal bacteria can convert organic arsenic to inorganic arsenic, demonstrating an immediate human health risk. FDA's study did not address other arsenic-containing compounds referenced in the 2009 Petition nor did it evaluate muscle tissue consumed by humans more frequently than chicken livers; more than two years later, FDA has yet to take these steps.

75. In June 2011, Alpharma (a division of Pfizer) announced it would voluntarily suspend—not revoke—sale of Roxarsone within thirty days following the release of FDA's study.[31] At that time, FDA commented that Roxarsone raised concerns of "completely avoidable exposure to a carcinogen."[32] A voluntary withdrawal of Roxarsone by one manufacturer is not enough to protect human health and the environment, and does not meet FDA's duties under the APA and FFDCA. Of note, neither Alpharma nor other arsenical compound manufacturers voluntarily suspended their sales of additional arsenicals.

76. In August 2011, Plaintiff CFS wrote to FDA, informing the agency that Plaintiffs had not received a status report on the 2009 Petition despite FDA's study and that FDA had not suspended arsenic-containing compounds pending investigation, nor scheduled an evidentiary hearing, pursuant to 21 U.S.C. § 360b(e)(1). Plaintiff CFS informed FDA that should it not prioritize the inquiry, Petitioners would seek redress in court.[33] FDA did not respond.

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[30] U.S. Food and Drug Admin., Final Report on Study 275.30, *supra* note 1.

[31] Press Release, U.S. Food and Drug Admin., *supra* note 2.

[32] *Id.*

[33] Letter from Petitioners to Margaret A. Hamburg, Comm'r, U.S. Food and Drug Admin., and Bernadette Dunham, Dir., Ctr. for Veterinary Med. (Aug. 9, 2011) (filed concurrently as Exhibit B).

77. In May 2012 Maryland's Governor signed H.B. 167, a bill banning the use, sale, or distribution of Roxarsone or any other feed additive that contains arsenic or histostat.[34] There are other arsenical compounds that H.B. 167 does not address. Even in light of Maryland's proactive legislation, FDA still failed to respond to the 2009 Petition.

FDA's Failure to Respond to Plaintiffs' 2009 Petition

78. On June 3, 2010, FDA provided an Interim Response in accordance with 21 C.F.R. § 10.30(e)(2), fulfilling the requirement to provide a response within 180 days. The Interim Response stated that FDA was unable to reach a decision on the 2009 Petition "because of the complexity and the number of issues raised in [the] petition." In addition, the Interim Response indicated that "FDA will issue a final response to your citizen petition after completing the analyses of all of the legal and policy issues raised in the petition."[35]

79. Since that time the agency has given no further information concerning when, or if, Petitioners may expect a response to the 2009 Petition. Forty months have passed since FDA received the 2009 Petition. To date, FDA has not directly responded to the 2009 Petition.

80. With Roxarsone currently "off the market," FDA need only permanently withdraw the NADAs for Roxarsone to make this voluntary action a permanent ban, protecting human health, environmental health, and food safety.

81. FDA has developed new testing methods to detect inorganic arsenic in chicken meat. Nevertheless, FDA has not used these methods to test for any other arsenical besides Roxarsone.

82. The burdens on human health and the environment are too great for FDA to depend on the voluntary withdrawal of one arsenical.

83. The public has filed approximately 17,500 comments in the FDA docket for Plaintiffs' 2009 Petition, the overwhelming majority calling on the agency to respond and

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[34] H.B. 167, 2012 Reg. Sess. (Md. 2012), *available at* http://mgaleg.maryland.gov/2012rs/bills/hb/hb0167t.pdf .

[35] Letter from Bernadette Dunham, Dir., Ctr. for Veterinary Med., to Petitioners (June 3, 2010) (filed concurrently as Exhibit C).

address this pressing issue.

Harm to Plaintiffs

84. The interests of Plaintiffs are being and will be adversely affected by Defendants' continued failure to respond to or act on the 2009 Petition. In particular, Defendants' unreasonable delay in responding to the 2009 Petition injures Plaintiff organizations by, *inter alia*, abridging their procedural right to petition a federal agency for rulemaking under the APA. Defendants' unreasonable delay also directly harms Plaintiffs' goals and functions by impeding their ability as public interest, nonprofit organizations to further facilitate public involvement in governmental decision-making, and by foreclosing the statutory right that allows for public participation through petitions for rulemaking.

85. The interests of Plaintiffs' members are being and will be adversely affected by Defendants' continued failure to respond to the 2009 Petition. Members of Plaintiff organizations suffer procedural injury based on the agency's undue delay in responding to their 2009 Petition. Plaintiffs' members are also suffering or will suffer an ongoing threat to their health and the health of their environment so long as arsenic-containing compounds remain unaddressed by FDA.

86. The requested relief will redress this harm by forcing FDA to respond to the 2009 Petition and address these issues, resulting in either (1) a response fulfilling FDA's statutory duties, aimed at protecting the public health and the environment from the growing risks from arsenic-containing compounds; and/or (2) by providing a final agency action that Plaintiffs may challenge if Plaintiffs disagree with the agency's response, in whole or in part.

CAUSE OF ACTION

87. Plaintiffs incorporate by reference all allegations contained in paragraphs 1 through 86 *supra*.

88. The APA requires agencies to "give an interested person the right to petition for the issuance, amendment, or repeal of a rule." 5 U.S.C. § 553(e); *see also id.* § 551(4) (defining "rule" as "the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy"). The APA's right to

petition encompasses the right to petition for a new, revised, or final rule concerning FDA regulation of new animal drug approvals under its statutory purview, including but not limited to arsenical compounds for use in food-producing animals. *See id.* §§ 551-559, 701-706.

89. Upon receipt of an APA petition, the Commissioner and FDA have a duty to respond to the petitioners promptly. *See id.* § 555(e) ("Prompt notice shall be given of the denial in whole or in part of a . . . petition. . . ."). Such response must be substantive, *i.e.*, it must either grant or deny the petition. *See id.*

90. The APA grants a right of judicial review to "[a] person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action." *Id.* § 702. Plaintiffs and their members are adversely affected by FDA's past and continued failure to respond to the 2009 Petition.

91. The APA states that a reviewing court "shall" interpret statutes and "compel agency action unlawfully withheld or unreasonably delayed," *id.* § 706(1), and "hold unlawful and set aside agency action, findings, and conclusions found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," *id.* § 706(2)(A). FDA's failure to respond to and take action on the 2009 Petition is arbitrary and capricious and constitutes unlawfully withheld and unreasonably delayed agency action. *See id.*

RELIEF REQUESTED

WHEREFORE, Plaintiffs respectfully request that this Court enter an Order:

(1) Declaring that the Defendants have violated the APA by failing to respond to the 2009 Petition within a reasonable time;

(2) Declaring that the Defendants continue to be in violation of the APA by failing to respond to the 2009 Petition;

(3) Ordering the Defendants to respond to the 2009 Petition forthwith;

(4) Retaining jurisdiction in this action to ensure compliance with its decree;

(5) Awarding Plaintiffs attorney fees and all other reasonable expenses incurred in pursuit of this action; and

(6) Granting other such relief as the Court deems just and proper.

Respectfully submitted this 30th day of April, 2013.

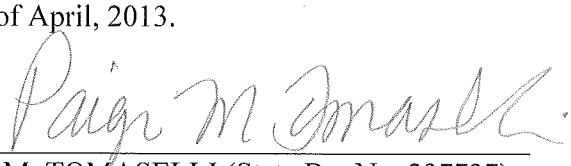

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Exhibit A

CITIZEN PETITION TO THE FOOD AND DRUG ADMINISTRATION

Food and Drug Administration
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CENTER FOR FOOD SAFETY
660 Pennsylvania Ave, SE, Suite 302
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INSTITUTE FOR AGRICULTURE AND TRADE POLICY,
2105 First Avenue South
Minneapolis, MN 55404

et al.,

Petitioners,

v.

Filed With:

MARGARET A. HAMBURG, M.D.
In her official capacity as,
Commissioner of the Food and Drug Administration

DOCKETS MANAGEMENT BRANCH
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Docket Number _____

December 8, 2009

CITIZEN PETITION SEEKING WITHDRAWAL OF APPROVAL OF ROXARSONE AND CERTAIN OTHER ARSENICAL ADDITIVES IN ANIMAL FEED

ACTIONS REQUESTED

Pursuant to the Right to petition the government clause contained in the First Amendment of the United States Constitution,[1] the Administrative Procedure Act,[2] and the Food and Drug Administration's implementing regulations,[3] Petitioners submit this citizen petition for rulemaking and collateral relief under the authority of §360b of the Federal Food, Drug, and Cosmetic Act (FDCA) to request the Commissioner of Food and Drugs to undertake the following actions:

(1) Immediately suspend the approval of all new animal drug applications (NADAs) for arsenic-containing compounds used as feed additives for food animals. The ban should include the arsenic-containing compounds:

- Roxarsone (3-nitro-4-hydroxyphenylarsonic acid)
- Arsanilic acid (p-arsanilic acid)
- Nitarsone (4-nitrophenylarsonic acid)
- Carbarsone (p-ureidophenylarsonic acid)

(2) Publish a Notice of Opportunity for an Evidentiary Hearing concerning "new evidence" related to these applications in accordance with 21 U.S.C. §512(e)(1).

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1 "Congress shall make no law … abridging … the right of the people … to petition Government for a redress of grievances." U.S.Const. amend. I. The right to "petition for redress of grievances is among the most precious of the liberties safeguarded by the Bill of Rights." United Mine Workers of Am. Dist. 12 v. Ill. State Bar Ass'n, 389 U.S. 217, 222 (1967). It shares the "preferred place" accorded in our system of government to the First Amendment freedoms, and "has a sanctity and a sanction not permitting dubious intrusions." Thomas v. Collins, 323 U.S. 516, 530 (1945). "[A]ny attempt to restrict those First Amendment liberties must be justified by the clear public interest, threatened not doubtful or remotely, but by clear and present danger." *Id.* The Supreme Court has recognized that the right to petition is logically implicit in and fundamental to the very idea of a republican form of government. United States v. Cruikshank, 92 U.S. 542, 552 (1875).

2 5 U.S.C. §553(e) (2009).

3 21 C.F.R. §§10.20, 10.30 (2009).

(3) Upon completion of the hearing, issue an order withdrawing the approval of all NADAs for arsenic-containing compounds used as feed additives for animals.

(4) Revoke all regulations associated with the approval of all NADAs for arsenic-containing compounds used as feed additives for animals, including those found at 21 C.F.R. §§558.62, 558.120, 558.369, 558.530.

PETITIONERS

The **Center for Food Safety** (CFS) is a Washington, D.C. based nonprofit located at 660 Pennsylvania Avenue, S.E., Washington D.C. 20003. Established in 1997, CFS works to protect human health and the environment by curbing the proliferation of harmful food production technologies and by promoting organic and other forms of sustainable agriculture.

The **Institute for Agriculture and Trade Policy** (IATP) is a 501(c)(3) organization located at 2105 First Avenue South, Minneapolis, MN 55404. Established in 1986, IATP works locally and globally at the intersection of policy and practice to ensure fair and sustainable food, farm and trade systems.

INTRODUCTION

In November 2009, U.S. Representative Steve Israel of New York announced legislation calling for a ban on the use of the arsenical compound roxarsone.[4] This bill, known as the "Poison-Free Poultry Act of 2009" would prohibit all uses of roxarsone as a food additive in

[4] Poison Free Poultry Act, H.R. 3624, 111th Cong. (2009); Press Release, Congressman Steve Israel, *What Carcinogens are in Your Turkey? Rep. Israel Announces New Legislation to Get Arsenic out of Poultry* (Nov. 23, 2009) (on file with author).

poultry.[5] The introduction of this legislation illustrates the importance and urgency of the issue. Humans are exposed to arsenic from various pathways. Banning arsenic-containing compounds in feed additives would provide an easy solution to lighten the burden on public health. While the Poison-Free Poultry Act is a step in that direction, it would only ban roxarsone, the most widely used arsenic-containing compound. The Food and Drug Administration (FDA) can and should act to address this danger under its existing authority, by withdrawing all new animal drug applications (NADAs) for arsenic-containing compounds in animal feed.

Arsenic-containing compounds have been approved additives to food animal feed since the 1940s and are currently used in chicken, turkey and swine production.[6] Roxarsone is the most common arsenic-containing compound.[7] The Code of Federal Regulations (CFR) explains that when used alone, roxarsone is approved only for increased weight gain, improved feed efficiency, and improved pigmentation.[8] Arsenic-containing feed additives, however, are generally compounds containing an arsenical such as roxarsone plus additional antibiotics and/or other antimicrobials.[9] The European Union has never approved the use of arsenicals in animal feed, acknowledging the lack of science supporting health or safety standards for such use.[10]

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5 Press Release, Congressman Steve Israel, supra n.4.

6 B.K. Anderson and T.N. Chamblee, *The Effect of Dietary 3-Nitro-4-Hydroxyphenylarsonic Acid (Roxarsone) on the Total Arsenic Level in Broiler Excreta and Broiler Litter*, 10 J. Applied Poultry Res. 323, 323–328 (2001).

7 Margaret Mellon et al., Union of Concerned Scientists, *Hogging it: Estimates of Antimicrobial Abuse in Livestock*_app. A, tbl. A-3 (2001), *available at* http://www.ucsusa.org/food_and_agriculture/science_and_impacts/impacts_industrial_agriculture/hogging-it-estimates-of.html (*citing* 21CFR558.62, 558.530).

8 21 C.F.R. § 558.530. Roxarsone and arsanilic acid, when used alone, are only approved for weight gain, improved feed efficiency and improved pigmentation. Id. at § 558.62. However, FDA has approved the labeling of nitarsone and carbarsone alone for prevention and/or control of some diseases. Id. at 558.120; 558.369; 558.530. It is important to note, however, that such uses are much less likely than are uses of roxarsone and arsanilic acid, or uses of combination products that include antibiotics.

9 See generally Margaret Mellon et al., supra n. 7.

10 Comm. for Medicinal Products for Veterinary Use, European Medicines Agency, *Status of MRL Procedures: MRL Assessments in the Context of Council Regulations (EEC),* No. 2377/90, EMEA/CVMP/765/99-Rev.23, *available at* http://www.emea.europa.eu/pdfs/vet/mrls/076599en.pdf.

Arsenic-containing compounds are most widely used in chicken production.[11] The vast majority of chickens will receive feed containing arsenic at some point in their lives. In 2004 and 2005, petitioner Institute for Agriculture and Trade Policy (IATP) tested for total arsenic in retail packages of raw chicken and in "fast food" chicken sandwiches and nuggets. Test results revealed detectable levels of arsenic in the majority of both supermarket and fast food chicken.[12] Relatively higher levels were observed in brands of chicken raised conventionally, with lower or non-detectable levels generally being found in certified organic and other "premium" brands where the use of arsenic-containing feed additives were either legally prohibited or claimed not to have been used. These results strongly suggest the use of arsenic-containing compounds in poultry feed leads to arsenic residues in U.S. marketed and eaten chicken.

The U.S. population is also regularly exposed to a cumulative burden of arsenic, such as that ingested in drinking water; the National Academies of Science estimates that 13 million Americans in 2001 were drinking water contaminated with arsenic at least at a 10 part per billion (ppb) level.[13] FDA has recognized the human health hazard posed by arsenic in drinking water.[14]

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[11] David Wallinga, Inst. for Agric. and Trade Policy, *Playing Chicken: Avoiding Arsenic in Your Meat* 11 (2006), *available at* http://www.iatp.org/iatp/publications.cfm?accountID=421&refID=80529.

[12] Id. at 21.

[13] Subcomm. on Arsenic in Drinking Water et al., Nat'l Research Council, *Arsenic in Drinking Water* (National Academy Press 1999), *available at* http://www.nap.edu/catalog.php?record_id=6444; Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., Nat'l Research Council, *Arsenic in Drinking Water: 2001 Update* (National Academy Press 2001), *available at* http://www.nap.edu/catalog.php?record_id=10194; press release, Nat'l Academies of Sci., *New Evidence Confirms Cancer Risk from Arsenic in Drinking Water* (Sept. 11, 2001), *available at* http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=10194.

[14] U.S. Food and Drug Admin., *Bottled Water: Arsenic Guidance for Industry Bottled Water: Arsenic Small Entity Compliance Guide* (Apr. 2009), *available at* http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ChemicalContaminantsandPesticides/ucm151384.htm; U.S. Beverages: Bottled Water Final Rule, 70 Fed. Reg. 33,694 (June 9, 2005) (to be codified at 21 C.F.R. § 165.110(b)(4)(iii)), *available at* http://www.fda.gov/Food/FoodSafety/Product-SpecificInformation/BottledWaterCarbonatedSoftDrinks/ucm077148.htm; press release, U.S. Food and Drug Admin., *FDA Warns Again About Arsenic in Mineral Water* (Mar. 24, 2007), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108875.htm.

Most of the arsenic ingested in poultry feed is subsequently excreted into poultry waste,[15] where soil microbes (as is also true of microbes residing in gut microflora of humans and poultry) convert the arsenic to inorganic forms classified as human carcinogens.[16] Since much poultry litter is applied as fertilizer to fields, this arsenic from feed is capable of further contaminating cropland or seeping into water tables.[17] Approval of arsenic compounds in animal feed therefore exacerbates an already significant arsenic problem in America's food and drinking water supplies.[18]

Moreover, despite the now-discontinued use of arsenical pesticides, such as in treated wood products,[19] in home products and on cropland,[20] families and schools continue to use decks, playground equipment and other structures made of arsenic-treated wood,[21] and eat arsenic-contaminated foods grown on land previously treated with arsenical pesticides,[22] thereby adding to their cumulative exposure to this potent poison.

Arsenic can cause additional human cancers even at the lower exposure levels currently found in contaminated food, water and the broader environment.[23] Arsenic exposure also contributes to other diseases, including heart disease, diabetes, and declines in intellectual

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[15] Joseph Louis Morrison, *Distribution of Arsenic from Poultry Litter in Broiler Chickens, Soil, and Crops*, J. 17 Agric. & Food Chem. 1288, 1288-90 (1969).

[16] See Infra Statement of Grounds Section IV.B.

[17] J.R. Garbarino et al., *Environmental Fate of Roxarsone in Poultry Litter. I. Degradation of Roxarsone during Composting*, 37 Envtl. Sci. & Tech. 1509, 1509-14 (2003); D.W. Rutherford et al., *Environmental Fate of Roxarsone in Poultry Litter. Part II. Mobility of Arsenic in Soils Amended with Poultry Litter*, 37 Envtl. Sci. & Tech. 1515, 1515-20 (2003).

[18] See Organic Arsenicals; Product Cancellation Order and Amendments to Terminate Uses, 74 Fed.Reg. 50,187 Sept. 30, 2009).

[19] Notice of Receipt of Requests to Cancel Certain Chromated Copper Arsenate (CCA) Wood Preservative Products and Amend to Terminate Certain Uses of CCA Products, 67 Fed. Reg. 8,244 (Feb. 22, 2002), *available at* http://www.epa.gov/EPA-PEST/2002/February/Day-22/p4306.htm.

[20] Supra n. 18.

[21] V.G. Zatarian et al., U.S. Envtl. Prot. Agency, *A Probabilistic Risk Assessment for Children Who Contact CCA-Treated Playsets and Decks* 6 (Feb. 2005) (2003), *available at* http://www.epa.gov/heasd/sheds/CCA_all.pdf; press release, Envtl. Working Group, *90 Percent of Children Face Elevated Cancer Risk* (Nov. 13, 2003), *available at* http://www.ewg.org/node/8700.

[22] *Elevated Arsenic Levels Reported in Rice Grown in South Central States*, Science Daily (Mar. 5, 2007) *available at* http://www.sciencedaily.com/releases/2007/03/070305092336.htm.

[23] See Margaret Mellon et al., supra, at n.7.

function.[24] Additionally, new evidence suggests arsenic exposure inhibits the body's ability to respond to infectious agents, like the H1N1 virus.[25]

Therefore, feeding arsenic to food animals further adds to an already significant human threat from arsenic exposure in our environment. Specifically, the use of arsenic in food animal production, and the likely ingestion of additional arsenic in chicken, is a needless and an unreasonably harmful addition to Americans' already health-impacting cumulative exposure to a carcinogen. Based on these facts, we respectfully request that FDA conduct the necessary evidentiary hearings and withdraw approval of roxarsone and other additional arsenical additives to animal feed.

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[24] Infra n. 51; Subcomm. on Arsenic in Drinking Water et al., supra n. 13; Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., supra n. 13; Gail A. Wasserman et. al., *Water Arsenic Exposure and Children's Intellectual Function in Araihazar, Bangladesh*, 112 Envtl. Health Persp. 1329, 1329-33 (2004); S.Y. Tsai et al., *The Effects of Chronic Arsenic Exposure from Drinking Water on the Neurobehavioral Development in Adolescence*, 24 Neurotoxicology 747, 747-53 (2003).

[25] Courtney D. Kozul et al., *Low-dose Arsenic Compromises the Immune Response to Influenza an Infection in Vivo*, 117 Envtl. Health Persp, 1441, 1441-47 (2009).

STATEMENT OF GROUNDS

I. CURRENT USES: ARSENIC IN POULTRY FEED

Arsenical feed additives are FDA-approved for use in chicken, turkey and swine.[26] Most arsenical feed additives are used in poultry production; for example, according to the U.S. Food and Drug Administration's on-line "Green Book," there are 105 FDA-approved arsenic products for broiler chickens.[27] Of the 8.7 billion or so broiler chickens produced annually in the U.S., an estimated 70 percent are fed arsenic-containing compounds at some point in their lives. Most commonly this is an arsenical called roxarsone, but could also include arsanilic acid or nitarsone.[28]

Unfortunately there are no public data to quantify the amount of arsenic compounds given to poultry.[29] However, the Union of Concerned Scientists (UCS) estimates nearly 2 million pounds of roxarsone alone are given annually to U.S. chickens, based on the 1998 production of 7.8 billion broilers.[30] Applying the UCS estimates to today's broiler production levels would lead to an estimate closer to 2.2 million pounds of roxarsone alone given to chickens annually.

A single company, Alpharma, accounts for the production of over half of all roxarsone-containing products.[31] Alpharma's data provide another basis for estimation of the amount of arsenicals being distributed to poultry. An estimated 70 percent of broiler chickens on starter rations and approximately 74 percent of those on grower rations in the United States are receiving roxarsone,[32] while Alpharma has claimed that a U.S. broiler on roxarsone-containing

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[26] Center for Veterinary Medicine, U.S. Food and Drug Administration, Green Book On-Line, *available at* http://www.fda.gov/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/UCM042847.

[27] Id.

[28] See 21 C.F.R. §558.35-.680 (2009); H.D. Chapman, Z.B. Johnson, *Use of Antibiotics and Roxarsone in Broiler Chickens in the USA: Analysis for the Years 1995 to 2000*, 81 Poultry Sci. 356, 356-64 (2002).

[29] See Margaret Mellon et al., supra, at n.7.

[30] David Wallinga, supra n. 11, at 13 fig. C.

[31] David Wallinga, supra n. 11, at 13 tbl. 5.

[32] H.D. Chapman, supra n. 28.

feed will get 3.5 mg of roxarsone daily for its six-week lifespan (minus a 5-day withdrawal period).[33] Therefore, if 70 percent of all broilers are on arsenical feed additives, then around 1.7 million pounds of roxarsone is fed to broilers annually. Hence, industry and other estimates roughly agree that at least 1.7 to 2.2 million pounds of roxarsone is given to American broiler chickens each year.

II. IATP TEST RESULTS: THE PREVALENCE OF ARSENIC IN RETAIL CHICKEN

From December 2004 to January 2005, a commercial laboratory tested for total arsenic in 151 different packages of retail chicken meat collected by IATP. IATP undertook this testing in large part because, although FDA approves the use of roxarsone and other arsenicals in chicken feed, and sets tolerances or legal levels for total arsenic in food, FDA does not monitor the usage of roxarsone or other arsenicals in animal feed. For enforcement of the tolerances, FDA relies upon USDA's Food Safety Inspection Service (FSIS). While the FSIS subsequently has begun some testing of more commonly consumed poultry and pork products, prior to the IATP testing it had not. In 2001, for example, the FSIS analyzed just 1,207 of the more than 8 billion or so young chickens produced for total arsenic, and then only chicken livers and not the muscle meat that is mostly consumed.[34]

In testing retail raw chicken products, IATP included thighs, breasts and livers purchased under both "conventional" and "premium" labels. IATP tested chicken from five of the top 25 broiler producers nationally, several premium brands, and a single kosher/halal brand. IATP's

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[33] Georges-Marie Momplaisir et al., Nat'l Exposure Research Lab. – Las Vegas, U.S. Envtl. Prot. Agency,,, *Arsenic Speciation Methods for Studying the Environmental Fate of Organoarsenic Animal-Feed Additives* (TIM No. 01-11) (2001), *available at* http://www.epa.gov/esd/chemistry/labmonitor/arsenic.pdf.

[34] U.S. Dept. of Ag., 2001 FSIS National Residue Program Data, at tbl. 3.3 *available at* http://www.fsis.usda.gov/OPHS/red_book_2001/2001_Residue_Program_Data_Sections1-7.pdf; Tamar Lasky et al., *Mean Total Arsenic Concentrations in Chicken 1989-2000 and Estimated Exposures for Consumers of Chicken*, 112 Envtl. Heath Persp. 18, 18-21 (2004).

results indicated that arsenic is common in uncooked chicken products from supermarkets, being detected in 55 percent of tested products.[35]

IATP also tested 90 samples of cooked "fast food" chicken products, purchased from restaurant chains focused on fried chicken, as well as from sandwich and burger outlets that offer chicken sandwiches, strips and nuggets. These tests revealed detectable levels of total arsenic in 100 percent of the tested samples.[36] The IATP testing did not attempt to "speciate" or distinguish organic or inorganic forms of arsenic in the total arsenic detected.[37]

III. AMERICANS INCREASED CONSUMPTION AND THEREBY EXPOSURE TO ARSENIC IN FOOD ANIMALS

Americans are a "nation of meat eaters" whose meat consumption is at a record high.[38] With this increased consumption comes increased exposure to arsenic. Chicken, pork and turkey represent the first, third and fourth most heavily consumed foods from animals in America. While chicken is at the top of the list and by far poses the most significant risk for exposure, Americans' turkey consumption also continues to rise. Statistics from the National Turkey Federation indicate that in 2008, Americans ate an average of 17.6 pounds of turkey, an increase of 108 percent since 1970.[39] Since 1970, the percentage of all turkey consumed for the holidays

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35 David Wallinga, supra n. 11, at 21-22.

36 Id. at 23-24.

37 It is true the levels of arsenic in chicken detected by the IATP methodology are lower than what the FDA would consider a tolerance violation. The purpose of the FDA's more recent testing has been only to determine whether or not there is a tolerance violation. For the purpose of this petition, however, the IATP testing suggests that arsenic is prevalent in chicken meat, and that it contributes to cumulative exposures from this and other sources.

38 USDA, AGRICULTURE FACT BOOK ch. 2, (2002) *available at* www.usda.gov/factbook/chapter2.htm.

39 The National Turkey Federation, The Perfect Protein (2009) *available at* http://www.eatturkey.com/consumer/stats/stats.html.

declined from 50 percent to 29 percent.[40] Moreover, pork consumption remains constant; in 2008, Americans consumed an average of 49.5 pounds of pork.[41]

The routine presence of arsenic in food animals is most significant in light of Americans' increased consumption of chicken. From 1966 to 2000, annual chicken consumption rose 253 percent, from 32.1 to 81.2 pounds per person.[42] Americans on average now eat 250 percent more chicken than they did 40 years ago. Some groups, however, are above average in their chicken consumption, and accordingly in their arsenic exposure. USDA data indicate that African-Americans eat about 20 percent more chicken than does the U.S. population as a whole; similarly, due to their small size, toddlers eating chicken baby food may ingest chicken at substantially higher than average levels, on a weight-adjusted basis.

IV. HUMAN SAFETY: EXPOSURE TO ARSENIC AND THE HEALTH RELATED HARM

A. The Health Effects of Arsenic

Arsenic exists in various forms, both organic and inorganic. Inorganic arsenic is one of the few substances studied well enough in people to be considered a "known" cause of human cancer – as early as 1879, high rates of lung cancer in Saxony miners were attributed in part to inhaled arsenic. By 1992, the combination of evidence from Taiwan and elsewhere was sufficient to conclude that ingested inorganic arsenic, such as is found in contaminated drinking water or food, was likely to increase the incidence of several internal cancers.[43] The link to skin

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40 Id.

41 Id.

42 David A. Taylor, *Funky Chicken: Consumers Exposed to Arsenic in Poultry*, 112:1 Envtl. Health Persp. A50 (2004) (reviewing Tamar Lasky et al., *Mean Total Arsenic Concentrations in Chicken 1989-2000 and Estimated Exposures for Consumers of Chicken*, 112 Envtl. Heath Persp. 18, 18-21 (2004)).

43 Int'l Agency for Research on Cancer, World Health Organization, *Some Metals and Metalloid Compounds: Summary of Data Reported and Evaluation,* 23 IARC Monographs on the Evaluation of Carcinogenic Risks to

and lung cancer is particularly strong and longstanding, although arsenic may cause liver, bladder, kidney and colon cancers as well.[44]

The National Academies of Science estimate that Americans who drink water contaminated with arsenic at a 10 part per billion (ppb) level–numbering 13 million in 2001–have a greater than 1-in-300 risk of developing cancer during their lifetime.[45] For those 13 million Americans, in particular, arsenic-specific cancer risks already are much higher than for the population as a whole, disregarding additional sources of arsenic exposure beyond drinking water.

In 2009, however, the European Food Safety Authority (EFSA) issued new warnings to children and some consumers about the risks of inorganic arsenic *in food.*[46] Based on new science on the health risks of arsenic exposure in food, the EFSA panel on contaminants in the food chain (CONTAM) recommended that dietary exposure to inorganic arsenic should be reduced. CONTAM noted that "since the provisional tolerable weekly intake of 15µg/kg b.w. was established by the Joint FAO/WHO Expert Committee on Food Additive (JECFA), new data has established that inorganic arsenic causes cancer of the lung and urinary tract in addition to skin, and that a range of adverse effects has been reported *at exposures lower than those reviewed by the JECFA.*"[47]

Arsenic also is not poisonous to everyone to the same degree. Children, infants, and the human fetus are among those most vulnerable to arsenic's toxic effects. This is due to differences

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Humans, 39 (1980); Subcomm. on Arsenic in Drinking Water et al., supra n. 13; Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., supra n. 13.

[44] Agency for Toxic Substances and Disease Registry, Ctrs. for Disease Control and Prevention, *Case Studies in Environmental Medicine (CSEM): Arsenic Toxicity Physiologic Effects, available at* http://www.atsdr.cdc.gov/csem/arsenic/physiologic_effects.html#carcino (last accessed Nov. 18, 2009).

[45] Press Release, Nat'l Academies of Science, supra n. 14.

[46] European Food Safety Auth. Panel on Contaminants in the Food Chain, European Food Safety Auth., *Scientific Opinion on Arsenic in Food*, 7 EFSA Journal 1351, Summary at 2 (2009).

[47] Id.

in arsenic metabolism between an adult and those very early in life–arsenic and its organic metabolites easily pass the placenta, for example.[48] Carcinogens like arsenic are generally more potent in their early life exposures. Following its review of 23 peer-reviewed studies of cancer incidence over the past 50 years, for example, the Environmental Protection Agency (EPA) concluded infants up to age two are, on average, ten times more vulnerable to carcinogenic chemicals than adults, and for some cancer-causing agents are up to 65 times more vulnerable; children ages 2-15 are merely three times more vulnerable to carcinogens than adults, EPA found.[49]

An increased risk of cancer is not the only adverse impact of arsenic. Arsenic affects nearly all organ systems because it targets ubiquitous enzyme reactions in cells.[50] Long-term exposure to arsenic can also cause hyperpigmented skin, skin nodules, vessel disease, and appears to heighten the risk of death from high blood pressure and heart disease. Those repeatedly exposed to arsenic also have an increased risk of diabetes.[51]

There has been little effort until recently to study the non-cancer effects of arsenic exposure on early child development. Nevertheless, some animal studies suggest that arsenic causes birth defects and some human studies link arsenic in drinking water to increases in miscarriage, stillbirth, and preterm birth.[52] Among children drinking contaminated water, arsenic has been associated with worse intellectual function and other neurocognitive deficits.[53]

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[48] Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., supra n. 13; M. Nathaniel Mead, *Arsenic: In Search of an Antidote to a Global Poison,* 113:6 Envtl. Health Persp. A378, A378-86 (2005).

[49] Risk Assessment Forum Technical Panel, U.S. Envtl. Prot. Agency, *Supplemental Guidance for Assessing Cancer Susceptibility from Early-Life Exposure to Carcinogens (External Review Draft),* EPA/630/R-03/003, (Feb. 28, 2003) *available at* http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55446.

[50] Supra n. 43.

[51] Subcomm. on Arsenic in Drinking Water et al., supra n. 13; Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., supra n. 13.

[52] Id.

[53] Gail A. Wasserman et. al., supra n. 24; S.Y. Tsai et al., *The Effects of Chronic Arsenic Exposure from Drinking Water on the Neurobehavioral Development in Adolescence*, 24 Neurotoxicology 747, 747-53 (2003).

Scientists continue to discover new health impacts not previously considered from arsenic exposure. For example, evidence now indicates arsenic is a potent disruptor of hormone function, altering the way in which hormones transmit information between cells at extremely low levels of exposure.[54] Recently, a delayed response in developing immunity to the H1N1 virus was attributed to arsenic exposure in drinking water.[55]

B. Organic and Inorganic Arsenic

The National Research Council has found no evidence "that arsenic is an essential element in humans or that it is required for any essential biochemical process."[56] Conventional wisdom used to be that ingesting *organic* arsenics, like those added to animal feed, carried fewer health concerns than ingesting the *inorganic* forms of arsenic, such as those often found in tap water. Very limited study of the toxicity of roxarsone, an organic form of arsenic, had once led to the presumption it was not all that toxic.

More recent science calls that presumption into question. Environmental bacteria, including those residing in chicken litter as well as in the bacterial "microflora" of the human or chicken gut, convert roxarsone into inorganic forms such as arsenate, As(V), and arsenite, As(III), classified as human carcinogens, and therefore potentially more toxic than the parent compound.[57] Further, a variety of studies in cells demonstrate that exposure to infinitesimally small (nanomolar to low micromolar) concentrations of arsenite stimulates a process of new

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[54] M. Nathaniel Mead, supra n. 48; Ronald C. Kaltreider et. al., *Arsenic Alters the Function of the Glucocorticoid Receptor as a Transcription Factor*, 109 Envtl. Health Persp. 245, 245-51 (2001); Jack E. Bodwell et al., *Arsenic at Very Low Concentrations Alters Glucocorticoid Receptor (GR)-Mediated Gene Activation but not GR-Mediated Gene Repression: Complex Dose-Response Effects Are Closely Correlated with Levels of Activated GR and Require a Functional GR DNA Binding Domain*, 17 Chem. Research in Toxicology 1064 (2004).

[55] Supra n. 25.

[56] Subcomm. on Arsenic in Drinking Water et al., supra n. 13.

[57] A.J. Bednar et al., *Photodegradation of Roxarsone in Poultry Litter Leachates*, 302:1-3 Sci. Total Env't. 237, 237-245 (2002); J.R. Garbarino et al., supra n. 17; John F. Stolz et al., *Biotransformation of 3-Nitro-4-Hydroxybenzene Arsonic Acid and Release of Inorganic Arsenic by* Clostridium *Species*, 41 Envtl. Sci. & Tech. 818, 818-23 (2007).

blood vessel formation called angiogenesis, associated with vascular disease as well as the growth of new tumors.[58] In addition to enhancing tumor growth, increased angiogenesis would contribute to overall growth potential and increased tissue pigmentation–exactly the attributes sought in roxarsone's use as a poultry feed additive. In contrast, and despite its use over 60 years, the direct effects of roxarsone on mammalian cells have not been greatly studied so as to ensure its safety. In one exception, human cells from vascular and lung tissue were studied following exposure to roxarsone.[59] The study found that like arsenite, As(III), roxarsone induces an increase in angiogenesis, but it does so more potently. Moreover, roxarsone acts via a mechanism that is distinct and independent of the one induced by As(III). In other words, roxarsone use and exposure could potentially promote angiogenesis–a key element of cancer tumor growth–via two independent processes, one via conversion to As(III), and another via a more direct mechanism.

Further, an earlier history of organic arsenical toxicity has been largely overlooked. Arsenicals were once used to treat human syphilis and parasitic infections, as I.V. trivalent arsenic[60] and as an oral organic arsenical,[61] respectively. In both cases, arsenical encephalopathy, and even death, could result at then recommended dosage levels and even after exposure to a single dose. To our knowledge, potential long-term changes to the brain and nervous system from routine, chronic exposure to organic arsenic residues in meat has never been evaluated.

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[58] Chandrashekhar D. Kamat et al., *Role of HIF Signaling on Tumorigenesis in Response to Chronic Low-dose Arsenic Administration*, 86 Toxicological Sci. 248, 248–57 (2005); Bing Liu B et al., *Opposing Effects of Arsenic Trioxide on Hepatocellular Carcinomas in Mice*, 97 Cancer Sci. 675, 675–81 (2006); Nicole V. Soucy et al., *Arsenic Stimulates Angiogenesis and Tumorigenesis in Vivo*, 76 Toxicological Sci. 271, 271–79 (2003); Nicole V. Soucy et al., *Neovascularization and Angiogenic Gene Expression Following Chronic Arsenic Exposure in Mice*, 5 Cardiovascular Toxicology 29, 29-41 (2005).

[59] Partha Basu et al., *Angiogenic Potential of 3-Nitro-4-Hydroxy Benzene Arsonic Acid (Roxarsone)*, 116 Envtl. Health Persp. 520, 520-23 (2008).

[60] Cole Monroe, et al., *Arsenical Encephalopathy Due to Use of Milibis*, 117 Archive Internal Med. 706, 706-711 (1966);

[61] L. Krainer et al., *Arsenical Encephalopathy In Indian Troops*, 10 J. Neurology Neurosurgery Psychiatry 171, 171-182 (1947).

Moreover, the use of organic arsenicals in animal feed likely contributes to the epidemic spread of antimicrobial resistance currently threatening human as well as animal health. For resistance to form requires the presence of bacteria as well as the genetic elements that when acquired can make those bacteria resistant to one or multiple antibiotics. Animal production facilities, including hog manure and poultry litter, are rich bacterial sources. And the bacteria in poultry litter specifically have been found to contain large numbers of mobile genetic elements, or 'integrons,' that contribute to the spread and persistence of resistance genes.[62] Multiple genes encoding for antibiotic resistance to different antibiotics are often grouped together on integrons that also contain genes coding for resistance to heavy metals, like arsenic. Bacteria with these integrons can survive exposure to any of the antibiotics or heavy metals to which they are resistant. Therefore, feeding heavy metals such as arsenicals routinely to poultry also can contribute to antibiotic resistance.[63]

One final study bears mention. Xie et al. (2004) fed laboratory animals both organic and inorganic arsenic and looked at changes to the liver, an important organ for detoxification.[64] What the scientists found was surprising: arsenic accumulated in the liver regardless of whether it was organic or inorganic arsenic being fed to animals. In addition, *all forms of arsenic altered how liver cells interpret or "express" the genetic information* contained in those cells, even if the specific expression of these genes differed somewhat between organic and inorganic arsenic.

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[62] Jingrang Lu et al.. *Evaluation of Broiler Litter With Reference to the Microbial Composition as Assessed by Using 16S rRNA and Functional Gene Markers,* 69 Applied & Envtl. Microbiology 901, 901-08 (2003); Sobhan Nandi et al., *Gram-positive Bacteria Are a Major Reservoir of Class 1 Antibiotic Resistance Integrons in Poultry Litter*, 101 Proc. Nat'l Acad. Sci. 7118, 7118-22 (2004).

[63] A. Summers, *Genetic Linkage and Horizontal Gene Transfer, the Roots of the Antibiotic Multi-Resistance Problem* 17 Animal Biotechnology 125, 125-35 (2006).

[64] Yaxoing Xie et. al., *Biokinetics and Subchronic Toxic Effects of Oral Arsenite, Arsenate, Monomethylarsonic Acid, and Dimethylarsinic Acid in v-Ha-ras Transgenic (Tg.AC) Mice*, 112 Envtl. Health Persp. 1255 (2004).

In other words, the science demonstrates there are numerous health-based reasons to avoid additional sources of arsenic exposure to our already significant "background" exposure, regardless of whether those additions are to organic or inorganic arsenic.

Earlier this year, EPA reached an agreement in principle with 19 registrants or companies manufacturing organic arsenical pesticides for use as home, garden or agricultural products. The outcome was that in September 2009, these companies withdrew their products from the market, including for example, Ortho Crabgrass Killer, Scotts Spot Grass and Weed Control and Acme Ready-To-Use Weed & Grass Killer, and EPA withdrew its FIFRA approval for these pesticides.[65] The docket for this action indicates the reason for cancellation is EPA's concerns about such uses potentially contributing to additional exposure to inorganic arsenic in drinking water.[66]

C. Americans Total Daily Exposure to Arsenic

While the FDA sets tolerances for arsenic in various individual foods, these limits do not take into consideration the effects of repeated and continued exposure to arsenic from multiple sources. For most Americans, chicken is not the only source of arsenic exposure. One of the most prevalent ways in which Americans have been exposed to arsenic is in drinking water. In 2001, the EPA lowered the 50 year old drinking water standards for arsenic.[67] The amount of arsenic legally allowed in tap water was dropped to 10 parts per billion–five-fold lower than the amount previously permitted.[68] The 13 million Americans (2001 estimates) drinking an average of 2 liters per day of water contaminated with arsenic at the EPA's new standard of 10 ppb

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65 Supra n. 18.

66 Letter from Richard Keigwin, Dir. of Special Review & Reregistration Div., U.S. Envtl. Prot. Agency, to Pesticide Registrants, Re: Amendment to Organic Arsenicals RED (Apr. 22, 2009), *available at* http://www.regulations.gov/search/Regs/home.html#documentDetail?R=090000648096e574.

67 National Primary Drinking Water Regulations; Arsenic and Clarifications to Compliance and New Source Contaminants Monitoring, 66 Fed.Reg. 6975 (Apr. 23, 2001).

68 Id.

would be expected to ingest around 10 micrograms of inorganic arsenic per liter per day, or 20 micrograms in total.[69] Several years later, even with new drinking water standards in place, data suggests that over three million Americans are still exposed to illegal levels of arsenic in drinking water.[70]

Arsenic was also used as a pesticide on "pressure-treated" lumber in the form of chromated copper arsenate (CCA), a pesticide mixture that is 22 percent arsenic by weight. The EPA ended the manufacture and sale of CCA-treated lumber in 2004.[71] Generations of children who played on CCA-treated playground equipment and wood decks were exposed to potentially hazardous levels of arsenic. Disposal hazards from this longstanding use remain today.[72]

Arsenical pesticides were used for decades on crops. Before they were banned, these pesticides contaminated many pesticide manufacturing sites as well as food-producing land. As a result, some Americans could be exposed today to significant dietary arsenic simply from ingesting rice with high arsenic levels.[73] In fact, the EFSA's recent study found particularly high concentrations of arsenic in rice and rice based products.[74]

Location is another factor. Neighbors of the many Superfund sites contaminated with the arsenic residues, including from mine tailings and arsenical pesticides, experience additional potential exposure. The arsenical pesticides sold until late 2009 in many home and garden

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69 Id.

70 Charles Duhigg, *Millions in U.S. Drink Dirty Water, Records Show*, N.Y.TIMES, Dec. 8, 2009, at A-1.

71 U.S. Envtl. Prot. Agency, Pesticides: Regulating Pesticides - Chromated Copper Arsenate (CCA) (Nov. 2008), *available at* http://www.epa.gov/oppad001/reregistration/cca/.

72 Jennar R. Jambeck et al., *Landfill Disposal of CCA-Treated Wood with Construction and Demolition (C&D) Debris: Arsenic, Chromium, and Copper Concentrations in Leachate*, 42 Envtl.. Sci. & Tech. 5740, 5740-5745 (2008).

73 P.N. Williams, et al., *Market Basket Survey Shows Elevated Levels of Arsenic in South Central U.S. Processed Rice Compared to California: Consequences For Human Dietary Exposure*, 41 Envtl. Sci. & Tech. 2178, 2178-83 (2007).

74 Panel on Contaminants in the Food Chain, European Food Safety Authority, *Scientific Opinion on Arsenic in Food*, 7 EFSA J. 1351, summary at 2 (2009).

products, and doubtless remaining on many homeowners' shelves, are an additional source of exposure.

In short, while FDA sets standards or tolerances for allowable levels of arsenic in meat, such levels represent only a portion of the average American's total exposure to arsenic. Avoidable arsenic use in food animal production only adds to the so-far uncounted cumulative risk from our many exposures to arsenic, from both natural and man-made sources. Moreover, the exposure to additional arsenic in poultry and pork meat due to the use of arsenical feed additives is an easily preventable and potentially significant component of Americans' overall total exposure. A piecemeal approach to regulating Americans' exposure to arsenic has thus far been ineffective at measuring and setting standards for cumulative total exposure to a potent carcinogen that contributes to other non-cancer disease as well.

V. ENVIRONMENTAL IMPACT: ARSENIC WRECKING HAVOC ON OUR NATURAL ENVIRONMENT

FDA-approved arsenicals used in poultry production likely have indirect human and environmental impacts beyond the direct effects of ingesting arsenic residues in meat. The more than 8.7 billion U.S. broiler chickens raised each year generate 26 to 55 billion pounds of poultry litter or waste.[75] Of the approximately 2 million pounds of roxarsone fed to chickens each year, up to three-quarters will pass unchanged into poultry waste. As discussed in detail *supra*, roxarsone rapidly breaks down into other organic and inorganic forms of arsenic during waste

[75] Keeve E. Nachman et. al., *Arsenic: A Roadblock to Potential Animal Waste Management Solutions*, 113 Envtl. Health Persp. 1123, 1123-24 (2005).

storage and composting, after land application,[76] and in the water leaching from litter-applied fields.[77]

Poultry litter disposal occurs in several different ways. Around 90 percent is applied to nearby fields and cropland as "fertilizer",[78] which, according to various estimates, may disperse a half million to 2.6 million pounds of roxarsone and its degradation products into the environment annually.[79] Poultry litter containing arsenic is also fed to beef cattle. In January 2004, the FDA proposed banning the practice; however, the agency reversed course in October 2005 and decided to continue allowing it after all.[80] A relatively new practice has developed of converting poultry litter into fertilizer pellets to be sold for commercial use on crops, for home landscaping, gardening and on golf courses. This practice opens up entirely new avenues of arsenic exposure. Arsenic levels in these pellets are reportedly similar to those found in unprocessed poultry waste.[81]

The rising volume of poultry waste, as well as its geographic concentration, means that larger broiler chicken and other poultry production facilities now generate far more waste than can easily be disposed of through land application. In late 2002, Minnesota permitted the first

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[76] J.R. Garbarino et al., supra n. 17; Kris Christen, *Chickens, Manure and Arsenic*, 35 Envtl. Sci. & Tech. 184A, 184A-85A (2001); B.P. Jackson et al., *Trace Element Speciation in Poultry Litter*, 32 J. Envtl. Quality 535, 535-40 (2003).

[77] Yuji Arai et al., *Arsenic Speciation and Reactivity in Poultry Litter*, 37 Envtl. Sci. & Tech. 4083, 4083-90 (2003); L. Elizabeth Williams et. al., *Adsorption and Transport of Arsenic (V) in Experimental Subsurface Systems*, 32 J. Envtl. Quality 841, 841-50 (2003); D.W. Rutherford et al., supra n. 17.

[78] Miguel L. Cabrera & J. Thomas Sims, *Beneficial Use of Poultry By-Products: Challenges and Opportunities, in Land Application of Agricultural, Industrial, and Municipal By-Products* (James F. Power & Warren A. Dick eds., Soil Science Society of America 2000) (2000); D.W. Rutherford et al., supra n. 17; R.L. Wershaw et al., *Roxarsone in Natural Water Systems*, *available at* *http://water.usgs.gov/owq/AFO/proceedings/afo/pdf/Wershaw.pdf.*

[79] Miguel L. Cabrera & J. Thomas Sims, *Beneficial Use of Poultry By-Products: Challenges and Opportunities, in Land Application of Agricultural, Industrial, and Municipal By-Products* (James F. Power & Warren A. Dick eds., Soil Science Society of America 2000) (2000); D.W. Rutherford et al., *Environmental Fate of Roxarsone in Poultry Litter. Part II. Mobility of Arsenic in Soils Amended with Poultry Litter*, 37 Envtl. Sci. & Tech. 1515, 1515-20 (2003); R.L. Wershaw et al., supra n. 78.

[80] Press Release, U.S. Food & Drug Admin., Expanded "Mad Cow" Safeguards Announced to Strengthen Existing Firewalls against BSE Transmission (Jan. 26, 2004), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108230.htm.

[81] Supra n. 75.

U.S. incinerator for the purpose of burning poultry litter for electricity generation.[82] This questionable practice will contribute to air pollution from toxics and heavy metals such as arsenic contained in the waste. Neither pelletization nor incineration can destroy or detoxify arsenic; both would further disperse it into the human environment.[83]

Because arsenic is an element, it neither degrades nor disappears. Therefore, the disposal of arsenic compounds only redistributes arsenic in a different form that can lead to soil and water contamination. It is estimated that 70-90 percent of arsenic in poultry litter becomes water soluble, meaning it can readily migrate through soils and into underlying groundwater.[84] Routine arsenical use in animal feed likely adds to the already significant public health burden from arsenic-contaminated drinking water supplies.[85]

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[82] Minn. Pollution Control Agency, Air Emission Permit 15100038-001, Issued to Fibrominn LLC (Oct. 23, 2002), *available at* http://www.pca.state.mn.us/air/permits/issued/15100038-001-aqpermit.pdf

[83] Supra n. 75.

[84] B.P. Jackson et al., supra n. 76; J.R. Garbarino et al., supra n. 17.

[85] Supra n. 75; Yuji Arai et al., supra n. 77.

STATEMENT OF LEGAL GROUNDS

I. THE NEW ANIMAL DRUGS ROXARSONE, ARSANILIC ACID, NITARSONE AND CARBARSONE ARE NOT SAFE FOR CONSUMPTION AND MUST BE WITHDRAWN FROM THE MARKET.

Arsenic-containing compounds fed to poultry and other farm animals create an unnecessary burden on human health. These compounds form residues in the edible portions of animals grown for food and also collect in the animal manure and litter, which is then recycled into the food system or left to burden the environment as the compounds leach from the manure into surface water and groundwater. These arsenic-containing compounds are classified as New Animal Drugs by the FDA. FDA must withdraw new animal drugs that are no longer considered safe. New science about organic arsenicals indicates that these arsenic-containing compounds approved long ago have not been shown to be safe for use in food animal production. The U.S. population is already burdened with many sources of arsenic. The additional burden presented by arsenic-containing compounds in food animals is a risk not outweighed by the purported benefits of their use. For these and other reasons, FDA must immediately initiate proceedings to re-evaluate the safety of these arsenic-containing compounds and upon conclusion of these proceedings, withdraw the approvals of all arsenic-containing compounds.

A. Although Not New or Novel, Roxarsone and Other Arsenicals Are New Animal Drugs Approved by FDA for Use in Animal Feed.

A "new animal drug" is defined as "*any* drug intended for use for animals other than man, including any drug intended for use in animal feed…"[86] Roxarsone and other arsenic-

[86] 21 C.F.R. § 510.3(g) (2009), emphasis added.

containing compounds are animal drugs administered to food animals in animal feed.[87] FDA approved these arsenic-containing compounds as a "*new animal drug[s]*" for use in growing chickens, turkey and swine for the following purposes:

- Weight gain
- Improved feed efficiency
- Improved pigmentation
- "Control of Infectious Synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline."
- "Control of chronic respiratory disease (CRD) and air sac infection caused by *M. gallisepticum* and *Escherichia coli* susceptible to chlortetracycline."
- "Reduction of mortality *due to E. coli* infect*ions susceptible* to chlortetracycline."
- "As an aid for the prevention of blackhead."[88]

Although the term "*new* animal drug" implies that the drug must be novel to the market, such an assumption is actually misleading. Roxarsone, for instance, was first approved by the FDA in the mid-1940s. Since the 1940s, FDA has approved 105 arsenic-containing compounds for chicken alone. New evidence indicates these new animal drugs are not safe and should be withdrawn from the market.

B. FDA Must Withdraw the Approval of Roxarsone and Other Arsenic-Containing Feed Additive Compounds Because These New Animal Drugs Are Unsafe.

The FDA must withdraw the approval of a previously approved NADA when that drug is found to be unsafe.[89] Under FFDCA §360(b), the Secretary shall, after due notice and

[87] 21 C.F.R. §§ 558.62; 558.120; 558.369; 558.530.
[88] Id.
[89] See 21 U.S.C. § 360b(e)(1).

opportunity for hearing to the applicant, issue an order withdrawing approval of a new animal drug if the Secretary finds:

A) "[E]xperience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved or the condition of use authorized under subsection (a)(4)(A);"[90]

B) New evidence, tests, or methods developed since approval of the application show that the drug is not safe for use "under the conditions of use upon the basis of which the application was approved…; or"[91]

C) New information, combined with the evidence available at the time the application was approved show a "lack of substantial evidence that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof."[92]

The above statutory language as well as Court decisions interpreting and applying it illustrate that this is mandatory duty. In Rhone-Poulenc, Inc. v. FDA, for example, the court held that the Commissioner must withdraw her approval when new evidence shows an animal drug to be unsafe.[93]

When determining whether a new animal drug (or category of new animal drugs, as is the case here) must be withdrawn, two issues are considered: whether there is a reasonable basis from which serious questions about the safety of the new animal drug may be inferred; and, whether the use of the new animal drug under the approved conditions is shown to be safe.[94] Once withdrawal procedures are initiated, the Center for Veterinary Medicine has the "initial burden of producing new evidence that raises serious questions about the ultimate safety" of the

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90 21 U.S.C. § 360b(e)(1)(A) (2009).
91 Id. at (e)(1)(B).
92 Id. at (e)(1)(C).
93 Rhone-Poulenc, Inc. v. FDA, 636 F.2d 750, 752-53 (D.C. Cir. 1980) (upholding FDA's order withdrawing the new animal drug approval for the use of diethylstilbestrol (DES)).
94 Ctr. for Veterinary Med., Proposal to Withdraw Approval of the New Animal Drug Application for Enrofloxacin for Poultry, Docket No. 00N-1571, at 2 (Mar. 16, 2004) (Initial Decision).

new animal drug.[95] When this threshold burden is met, the manufacturer is required to demonstrate the safety and efficacy of the drug.[96]

1. Serious questions exist about the safety of roxarsone and other arsenic-containing compounds.

"'Serious questions' [about the safety of a new animal drug] can be raised where the evidence is not conclusive, but merely suggestive of an adverse effect."[97] The scope of 'new evidence' is not limited to data developed after a NADA is approved but includes the re-evaluation or novel application of pre-existing data.[98]

Since the original approval of roxarsone in the mid-1940s, there is ample new evidence to demonstrate that arsenic-containing compounds are no longer "safe for use." IATP's test results strongly indicate that the arsenic contained in roxarsone and other arsenic-containing compounds is detectable in chicken sold on the market.[99] At the time that roxarsone was first approved the organic form of arsenic contained in these compounds was believed to be less harmful than the inorganic form, which is a known hazard to human health. Evidence now shows that microbes including those residing in the human gut can release inorganic arsenic from roxarsone and other arsenic-containing compounds and therefore the latter must be considered to represent a human health hazard as does the former.[100]

In the decades following roxarsone's initial approval, new evidence has emerged of the extent to which arsenic exposure poses a risk to American health. Today it is widely accepted that exposure to inorganic arsenic leads to cancer, hyperpigmented skin, skin nodules, and vessel

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95 Id. at 5; See also Rhone-Poulenc, Inc., 636 F.2d at 752 (D.C. Cir. 1980).
96 Id.
97 Id.
98 Id.
99 David Wallinga, supra n. 11, at 7-8.
100 John F. Stolz et al., supra n. 57.

disease.[101] In one newly released study, it appears that the ability to develop an immunity to the H1N1 virus is hindered by exposure to arsenic.[102] Arsenic use in animal feeds may spur the development of antibiotic resistant strains of bacteria posing risks to animal and human health.

Further, in September, 2009, EPA announced that 19 companies voluntarily withdrew (and EPA is subsequently canceling) pesticide registrations for organic arsenical pesticides, further evidencing the potential dangers of organic arsenic.[103] Due to "agency concerns about drinking water contamination and ecological risk," EPA determined cancellation was necessary.[104] In support of this decision, EPA asserts that inorganic arsenic converts to organic arsenic in the soil and therefore presents concerns regarding groundwater contamination and drinking water exposure.[105] This and other new evidence discussed *supra* and in the accompanying footnotes and sources included in the administrative record of this petition raise serious questions about the safety of arsenic-containing compounds in animal feed additives.

2. The cumulative effect of human consumption of the arsenic-containing compounds present in food animals along with the various additional sources of arsenic in the environment must be considered.

In evaluating the safety of a new animal drug, the FDA 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, and (B) the cumulative effect on man or animal of such drug, taking into account any chemically or pharmacologically related substance.[106] IATP test results indicate that Americans consume arsenical feed additives when they eat chicken. The

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101 Subcomm. on Arsenic in Drinking Water et al., supra n. 13; Subcomm. to Update the 1999 Arsenic in Drinking Water Report et al., supra n. 13.
102 Supra n. 25.
103 Supra n. 18.
104 Letter from Richard Keigwin, supra n. 66.
105 Id.
106 21 U.S.C. § 360b(d)(2) (2009).

same is likely true for turkey and swine. Arsenic is also present in rice, seaweed, other food products, drinking water, treated wood and elsewhere in the environment.

Arsenic-containing compounds intentionally added to animal feed add to the already significant cumulative effects of arsenic on the U.S. population. Despite increased proof of the risks posed by exposure to arsenic, the average Americans cumulative exposure to arsenic has greatly increased in the years since roxarsone's approval. EPA has taken steps to reduce the public's exposure to arsenic in drinking water, [107] and yet there is now abundant evidence that the average American is still exposed to dramatically higher levels of arsenic from multiple sources, than was true when roxarsone was first approved. This cumulative exposure to arsenic is neither measured nor regulated as a whole. Consequently, ingestion of arsenic that is directly linked to the use of arsenic-containing compounds in animal feed has thus far been permitted to continue, despite new evidence of the extreme health risks associated with exposure to both inorganic *and* organic arsenic. As discussed at length *supra*, this cumulative exposure creates serious health concerns. Due to these serious concerns, FDA must immediately take steps to withdraw all arsenic-containing compounds from use in food animal feed.

3. The purported benefits of roxarsone and other arsenic-containing compounds do not outweigh the risk of harm.

In considering whether an animal drug is safe within the meaning of FFDCA 512(e)(1)(b) the "typical issue for the FDA is not the absolute safety of a drug...the issue for the FDA is whether to allow sale of the drug, usually under specific restrictions. Resolution of this issue inevitably means calculating whether the benefits that the drug produces outweigh the costs of its

[107] 74 Fed. Reg. 50,187; letter from Richard Keigwin, supra n. 66.

restricted use."[108] In other words, a product's "therapeutic benefits must outweigh its risk of harm."[109]

Here, the therapeutic gain does not outweigh the risk of harm. Roxarsone and other arsenic-containing compounds provide questionable benefit and in any case are not necessary for large-scale food animal production. For instance, chicken from the world's largest chicken producer, Tyson, contains little or no arsenic residue.[110] And, while there is abundant large-scale food animal production in the European Union, it never approved arsenic for use in animal feeds, further indicating that U.S. arsenical use is excessive and avoidable.[111]

Juxtaposed against arsenic's well-known cancer-causing properties, new evidence of inorganic arsenic's non-cancer effects on human health, the conversion of organic to inorganic arsenic and the cumulative exposure to arsenic in poultry, other foods, water and the environment, the questionable benefit of arsenic-containing compounds in food animal production presents unsupportable and unnecessary risks to human health.

C. Failure of FDA to Investigate New Evidence Indicating that Roxarsone and Other Arsenic-containing Compounds are Unsafe is Arbitrary and Capricious.

In making a factual inquiry concerning whether an agency decision was "arbitrary and capricious," a reviewing court must consider whether the decision was based on a reasoned

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108 Hess & Clark, Div. of Rhodia, Inc. v. FDA, 495 F.2d 975, 993-94 (D.C.Cir. 1974).

109 FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 140 (2000) citing United States v. Rutherford, 442 U.S. 544, 555 (1979) (noting that "[t]he Commissioner generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use.")

110 David Wallinga, supra n. 11, at 7-8.

111 Council Regulation 2377/90, 1990 O.J. (L 224) (EC) (repealed 2009 by Council Regulation 470/2009, 2009 O.J. (L 152) (EC))(Under Council Regulation 470/2009, Council Regulation 2377/90 remains in effect until new regulation classifying maximum residue limits of pharmacologically active substances come into force); European Medicines Agency, Summary Opinion of the Committee for Veterinary Medicinal Production the Establishment of Maximum Residue Limits: Roxarsone of 14 January 2004, *available at* http://www.emea.europa.eu/pdfs/vet/mrls/mrlopinions/008304en.pdf; David Wallinga, supra n. 11, at 7-8.

evaluation of the relevant factors and whether there has been a clear error of judgment.[112] An agency must cogently explain why it has made a particular decision and enable a court to conclude that it was the product of reasoned decision making.[113]

New evidence about arsenic-containing compounds in poultry feed is now before FDA. IATP's recent tests show that roxarsone and other arsenic-containing compounds in poultry feed lead to arsenic residue in chicken. Because new evidence indicates that the organic arsenic found in these compounds could be as harmful to human health as the inorganic form, roxarsone and other arsenic-containing compounds should be deemed "unsafe for use." Since they are unsafe for the use under which they were originally approved, FDA must initiate procedures to withdraw permission of arsenic-containing compounds in food animal feed. Failing to investigate this new scientific evidence and the cumulative impacts of arsenic in the environment concerning the possible human health risks of arsenic-based feed additives is contrary to the overarching intent of the FFDCA and would be a clear abdication of FDA's legal duty. Failing to initiate an evidentiary hearing on the safety of roxarsone and other arsenic-containing compounds can only be concluded as unreasoned decision making by the agency and an arbitrary and capricious agency action.

CONCLUSION

Americans are already exposed to health significant levels of arsenic from multiple sources. Eliminating the arsenic voluntarily added to animal feeds as an additional source of arsenic exposure is not only feasible, but a necessary preventative step to ensure the health of all Americans already exposed to arsenic in drinking water and other involuntary sources. For the

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[112] Marsh v. Oregon Natural Resources Council, 490 U.S. 360, 378 (1989).
[113] See Motor Vehicle Mfrs. Assn. v. State Farm Mut. Auto Ins. Co., 463 U.S. 29, 49 (1983).

aforementioned reasons, petitioners respectfully request FDA withdraw approval for the routine use of roxarsone, arsanilic acid, nitarsone, and carbarsone in food animal feeds.

In accordance with FDA regulation 21 C.F.R Part 10.30(e)(2), FDA must respond to the above petition within 180 days or risk arbitrarily and capriciously violating the regulation.

ENVIRONMENTAL IMPACT STATEMENT

The specific actions requested by Petitioners will not cause the release of any substance into the environment. They are categorically excluded from the requirement of environmental documentation under 21 C.F.R. § 25.33(g).

ECONOMIC IMPACT STATEMENT

The requested information is only required when requested by the Commissioner following the review of the petition, and therefore an economic impact statement is not provided at this time.

CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the petition.

ENDORSING ORGANIZATIONS

The following organizations have endorsed this petition to FDA requesting that FDA immediately institute procedures to withdraw all new animal drug applications for the arsenical additives to food animal feed roxarsone, arsanilic acid, carbarsone and nitarsone:

Center for Biological Diversity
Center for Environmental Health
Ecology Center of Michigan
Food Animal Concerns Trust
Food and Water Watch
Health Care Without Harm
Institute for a Sustainable Future
National Sustainable Agriculture Coalition
Physicians for Social Responsibility - Oregon Chapter
Physicians for Social Responsibility - San Francisco Chapter

Exhibit B

August 9, 2011

Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Bernadette Dunham, D.V.M, Ph.D
Director
Center for Veterinary Medicine
Food and Drug Administration
7519 Standish Place
HFV-12
Rockville, MD 20855

Re: Citizen Petition Seeking Withdrawal of Approval of Roxarsone and Certain Other Arsenical Additives in Animal Feed FDA-2009-P-0594-0001/CD

Dear Dr. Hamburg,

On December 11, 2009, the Center for Food Safety (CFS) and the Institute for Agriculture and Trade Policy (IATP) (collectively Petitioners) filed the Citizen Petition Seeking Withdrawal of Approval of Roxarsone and Certain Other Arsenical Additives in Animal Feed (Citizen Petition) with the Food and Drug Administration (FDA).

The Citizen Petition requested that FDA:

1) immediately suspend the approval of all new animal drug applications (NADAs) for arsenic-containing compounds used as feed additives for food animals;
2) publish a Notice of Opportunity for an Evidentiary Hearing concerning "new evidence" related to these applications in accordance with 21 U.S.C. § 512(e)(1);
3) upon completion of the hearing, issue an order withdrawing the approval of all NADAs for arsenic-containing compounds used as feed additives for animals, and;
4) revoke all regulations associated with the approval of all NADAs for arsenic-containing compounds used as feed additives for animals, including those found at 21 C.F.R. §§ 558.62, 558.120, 558.369, 558.530.

More than 18 months have elapsed since FDA received this Citizen Petition and opened a docket. Petitioners received a tentative response on June 3, 2010, indicating that FDA

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Email: info@centerforfoodsafety.org • www.centerforfoodsafety.org • www.foodsafetynow.org

was currently considering the issues raised by the Citizen Petition. In the 13 months following this tentative response, Petitioners have not received additional information on the status of this Citizen Petition, FDA has not suspended arsenic-containing compounds pending investigation pursuant to 21 U.S.C. § 360(b), nor has FDA scheduled an Evidentiary Hearing pursuant to 21 U.S.C. § 512(e)(1).

On June 8, 2011, FDA announced that Pfizer will temporarily suspend sales of one arsenic-containing product (3-Nitro) following FDA's release of a study indicating that 3-Nitro increases cancer-causing inorganic arsenic in chicken liver. Press Release, *Food and Drug Administration, FDA: Pfizer will voluntarily suspend sale of animal drug 3-Nitro (June 8, 2011) available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm258342.htm.

Petitioners do not consider this voluntary withdrawal, or any announcements or documents associated with it, a response to the above titled Citizen Petition. As such, Petitioners respectfully urge FDA to take the actions outlined in the Citizen Petition and mandated by the Federal Food Drug and Cosmetics Act and implementing regulations.

As the Citizen Petition details, and FDA's study now confirms, serious questions exist about the safety of arsenic-containing compounds and their presence in animal feed. Tests indicate that these arsenic-containing compounds are present in the human food supply. At one time, organic arsenic—the form of arsenic present in animal feeds—was thought to be less harmful than inorganic arsenic. New evidence indicates that intestinal bacteria in the human gut can convert organic arsenic to the more harmful inorganic arsenic, demonstrating an immediate human health risk. *See* Citizen Petition at 25–26. FDA's new study supports this conclusion. "This analysis indicated that inorganic arsenic was present at higher levels in the livers of chickens treated with the drug 3-Nitro® (Roxarsone) than in untreated chickens. No measurable residues of inorganic arsenic were present in the livers from the untreated control chickens." FDA, *Questions and Answer Regarding 3-Nitro (Roxarsone), available at* http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm258313.htm.

FDA's findings support Petitioners' claim that the use of arsenic-containing compounds in food animal production presents an unnecessary risk to the public and should therefore be banned. This health risk is compounded when the cumulative effects of inorganic arsenic exposure are considered. The human consumption of arsenic-containing compounds in animal feed when added to the numerous other known pathways of arsenic exposure in the environment heightens the human health risks associated with arsenic-containing compounds in animal feed. *See* Citizen Petition at 26–27.

When a petition informs an agency of human health and welfare risks, delays in agency action are less tolerable. *Telecommunications Research and Action Center v. F.C.C.*, 750 F.2d 70, 80 (D.C. Cir 1984). Courts will consider the consequences of delay, including risks to human health and welfare and the environment, when determining whether or not

a delay in agency action is unreasonable. *Cutler v. Hayes*, 818 F.2d 879, 897 (D.C. Cir. 1987). Petitioners remind FDA that there are human health and safety risks from the continued use of any arsenic-containing compounds in animal feed, and therefore brevity is of the utmost importance. Should FDA not prioritize this inquiry and suspend the use of arsenic-containing compounds pending an Evidentiary Hearing and further review, Petitioners will have no choice but to seek redress in court.

Thank you for your prompt attention to this matter.

Sincerely,

Paige M. Tomaselli
Staff Attorney
Center for Food Safety

David Wallinga, MD, MPA
Senior Advisor, Science, Food and Health
Institute for Agriculture and Trade Policy

Cc: Dr. Bernadette M. Dunham, Center for Veterinary Medicine

Exhibit C

DEPARTMENT OF HEALTH & HUMAN SERVICES

3178 10 JUN 14 A11 :39

Food and Drug Administration
Rockville MD 20857

June 3, 2010

Ms. Paige M. Tomaselli
Staff Attorney
Center for Food Safety
660 Pennsylvania Ave, SE
Suite 302
Washington, DC 20003

David Wallinga, M.D.
Director
Food and Health Division
Institute for Agriculture and Trade Policy
2105 First Avenue South
Minneapolis, MN 55404

Re: Docket No. FDA-2009-P-0594

Dear Ms. Tomaselli and Dr. Wallinga:

This is a tentative response to the Citizen Petition (FDA-2009-P-0594) filed with the Food and Drug Administration (FDA) on December 11, 2009, on behalf of the Center for Food Safety and the Institute for Agriculture and Trade Policy. The petition requests that FDA: immediately suspend the approval of all new animal drug applications (NADAs) for arsenic-containing compounds used as feed additives for food animals; publish a Notice of Opportunity for and Evidentiary Hearing related to such applications; issue, upon completion of said hearing, an order withdrawing the approval of all NADAs for arsenic-containing compounds used as feed additives for animals; and revoke all regulations associated with the approval of all NADAs for arsenic-containing compounds used as feed additives for animals..

Pursuant to the administrative regulations at 21 CFR 10.30, FDA is required to respond to your petition within 180 days. FDA is currently considering the issues raised by your citizen petition. However, the agency will require additional time to issue a final response because of the complexity and the number of issues raised in your petition.

FDA will issue a final response to your citizen petition after completing the analyses of all of the legal and policy issues raised in the petition.

Sincerely yours,

for

Bernadette M. Dunham, D.V.M., Ph.D.
Director, Center for Veterinary Medicine

FDA-2009-P-0594

LET

cc: HFA-301 (Docket No. FDA-2009-P-0594)