FOOD SAFETY AND SYNTHETIC CHEMICALS – AN INTERNATIONAL COMPARISON

AMY S. BERG*

I. INTRODUCTION

Global food trade is integral to the food supply system and necessarily impacts food safety and food security. Over the past thirty years, global food trade expanded and increased in complexity, but the primary exporting countries, including the United States ("U.S."), have remained relatively stable.[1] About one-quarter of all food produced in the world is traded on international markets, with ten nations supplying the bulk of this food.[2] Global food trade facilitates the distribution of essential nutrients and provides nourishment to those most in need.[3] With a growing global population, geopolitical issues, environmental challenges, and changing weather patterns, the global food system will grow in size and complexity, but also become more vulnerable.[4]

Food safety laws and regulations also impact global trade partners. A study of the global trade of maize (a.k.a. corn) and aflatoxin regulations showed that international trade partners had similar food safety regulations.[5] Key trading partners have a large amount of power in determining regulations elsewhere worldwide, and similar food safety regulations can facilitate and influence trade patterns. While protecting human health is the primary consideration, the U.S. and other nations should consider the potential implications and impacts of food safety standards on global trade and their trade partners.

The food system in the U.S. consists of a complex system of production, transport, and processing, imports, and exports that provides consumers with a variety of food and beverage products. The food supply chain includes various points which risk exposure to pathogens, contaminants, and other potential hazards. The Food Safety Modernization Act ("FSMA") and the U.S. Food and Drug Administration's ("FDA") implementing regulations were established to

---

* Partner, Ice Miller LLP; Adjunct Professor, Indiana University Robert H. McKinney School of Law.

1. Jieyong Wang & Chun Dai, *Evolution of Global Food Trade Patterns and Its Implications for Food Security Based on Complex Network Analysis*, 10 FOODS 1, 13 (Nov. 2, 2021), https://www.mdpi.com/2304-8158/10/11/2657 [https://perma.cc/2DN3-3H8G].

2. Joel K. Bourne, Jr., *Eating the Earth: The burgeoning global food trade is a lifeline for billions, but it is fragile and hard on the planet*, 386 SCIENCE 956, 958 (Nov. 29, 2024), https://www.science.org/doi/epdf/10.1126/science.adu8006 [https://perma.cc/W6CA-AGFH].

3. Stephen A. Wood et al., *Trade and the Equitability of Global Food Nutrient Distribution*, 1 NATURE SUSTAINABILITY 34 (2018), https://www.nature.com/articles/s41893-017-0008-6 [https://perma.cc/VGG8-E2SH].

4. Bourne, *supra* note 2.

5. Aflatoxins are mycotoxins, which are secondary metabolites produced by different fungal species. Mycotoxins produced by *Aspergillus* spp. are known as aflatoxins. Aflatoxins are commonly produced by *Aspergillus flavus* and *A. parasiticus*. Saba Shabeer, et al., *Aflatoxin Contamination, Its Impact and Management Strategies: An Updated Review*, 14 TOXINS 307 (Apr. 21, 2022), https://pubmed.ncbi.nlm.nih.gov/35622554/ [https://perma.cc/6UH3-P5FW]; Felicia Wu & Hasan Guclu, *Aflatoxin Regulations in a Network of Global Maize Trade*, 7 PLOS ONE 8 (Sept. 25, 2012), https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0045151 [https://perma.cc/VJ96-ZTQ6].

shift focus from responding to hazards and foodborne illnesses to preventing them.[6] International trade links the diverse global food systems of countries and plays a role in economic development, moving food from surplus to deficit areas or providing a wider variety of food options.[7] While trade may enable global food security, it presents challenges concerning food safety and food standards.[8]

Foods may contain a variety of chemicals, some of which are intentionally added or naturally occurring, and others which are contaminants.[9] The FDA ensures exposure to chemicals in food is safe. This includes chemicals authorized for use in and with foods during production and harvest, food packaging, processing, or other handling, or contaminants that enter the food supply through the growing or processing environment. Under the Federal Food, Drug, and Cosmetic Act ("FFDCA"),[10] a food is deemed adulterated if, among other things, it contains any poisonous or deleterious substance rendering the food injurious to health, an unsafe pesticide residue, or any food additive or new animal drug that is unsafe; its preparation, packaging, or storage under unsanitary conditions rendered the food injurious to health; or its container is composed of any poisonous or deleterious substance rendering the contents injurious to health.[11]

The FDA helps to safeguard the food supply through pre-market and post-market safety evaluations of chemicals as food ingredients and substances that come into contact with food, such as through food packaging, storage or other handling to ensure these uses are safe. The FDA also ensures that industry is

---

6. Food Safety Modernization Act, 21 U.S.C. §§ 2201–2252 (2021).

7. ANDREA ZIMMERMANN & GEORGE RAPSOMANIKIS, SCIENCE AND INNOVATIONS FOR FOOD SYSTEMS TRANSFORMATION 40 (Joachim von Braun, Kaosar Afsana, Louise O. Fresco, Mohamed Hag Ali Hassan eds., 2023).

8. The Food and Agriculture Organization of the United Nations ("FAO") defines food security as a situation that exists when all people, at all times, have physical, social and economic access to sufficient, safe and nutritious food that meets their dietary needs and food preferences for an active and healthy life. Based on this definition, four food security dimensions can be identified: food availability, economic and physical access to food, food utilization, and stability over time. The concept of food security is evolving to also recognize the centrality of agency and sustainability. FAO, IFAD, UNICEF, WFP & WHO, THE STATE OF FOOD SECURITY AND NUTRITION IN THE WORLD 2024 – FINANCING TO END HUNGER, FOOD INSECURITY AND MALNUTRITION IN ALL ITS FORMS 222 (FAO et al. eds., 2024), https://openknowledge.fao.org/handle/20.500.14283/cd1254en [https://perma.cc/PR5P-7WTX].

9. The term "food" means "(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article." 21 U.S.C. § 321(f); "A naturally occurring poisonous or deleterious substance is a poisonous or deleterious substance that is an inherent natural constituent of a food and is not the result of environmental, agricultural, industrial, or other contamination." 21 C.F.R. § 109.3(c); "An added poisonous or deleterious substance is a poisonous or deleterious substance that is not a naturally occurring poisonous or deleterious substance. When a naturally occurring poisonous or deleterious substance is increased to abnormal levels through mishandling or other intervening acts, it is an added poisonous or deleterious substance to the extent of such increase." 21 C.F.R. § 109.3(d).

10. 21 U.S.C. § 321.

11. *Id.* § 342; *see also* 21 U.S.C. § 331 (prohibiting the adulteration of food, including the introduction, delivery for introduction, and receipt in interstate commerce of any food that is adulterated).

preventing when possible, and mitigating when prevention is not possible, unsafe exposure from chemical contaminants that can enter the food supply through the growing and processing environment. The agency monitors the food supply for chemical contaminants and takes action, including through enforcement mechanisms, when the level of a contaminant causes a food to be unsafe. Food manufacturers also have a major role in food chemical safety. The food industry has a responsibility to minimize or prevent hazards from contaminants and ensure the safety of chemicals they use.[12]

To highlight the complexity of the global food system and its myriad food safety laws and regulations, this article describes and compares the evaluation and approval of certain intentionally and unintentionally added synthetic chemicals, specifically food additives, color additives, pesticides, and per- and polyfluoroalkyl substances ("PFAS"), in food or food contact substances under laws established by the U.S. and European Union ("EU"), and under applicable standards established by the Codex Alimentarius Commission.

II. CHEMICALS IN FOOD

The FFDCA defines adulterated as a food that contains any added poisonous or deleterious substance.[13] As such, the FFDCA permits certain intentionally and unintentionally added chemicals in the food supply through the pre-market approval process, with limited exemptions. The word "chemical" can have a negative connotation, especially when associated with food. The Merriam Webster Dictionary website defines a chemical as "a substance obtained by a chemical process or producing a chemical effect."[14] Chemical is a very broad term that includes within the scope of the definition many substances in food that are nutritious, healthy, or otherwise desirable. Consumers tend to be more concerned about a sub-set of chemicals that are synthetic or "man-made."

Generally, synthetic chemicals added to food, whether intentionally or unintentionally, are evaluated using risk analysis. The Renaissance physician Paracelsus (1493-1541) stated "What is there that is not poison? All things are poison, and nothing is without poison. Solely the dose determines that a thing is

12. Food labeling laws and regulations play an important role in food safety but are not discussed in this article.

13. "A food shall be deemed to be adulterated if it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health." 21 U.S.C. § 342(a)(1); "A food shall be deemed to be adulterated if it bears or contains any added poisonous or added deleterious substance (other than a substance that is a pesticide chemical residue in or on a raw agricultural commodity or processed food, a food additive, a color additive, or a new animal drug) that is unsafe within the meaning of section 346 of this title." 21 U.S.C. § 342(a)(2)(A).

14. *Chemical*, MERRIAM-WEBSTER, https://www.merriam-webster.com/dictionary/chemical [https://perma.cc/GV9P-5REU] (last visited Nov. 24, 2024).

not a poison."[15] This statement is often referred to as "the dose makes the poison." Others have also stated that "the timing makes the poison."[16]

A thorough discussion of risk analysis is beyond the scope of this article, but it is nevertheless an important component of the evaluation and establishment of acceptable levels of chemicals in food, and ultimate approval under the FFDCA or other laws. The discussion below highlights certain key provisions in the U.S., EU, and the Codex Alimentarius for approval of use or establishment of maximum limits for synthetic chemicals in food.

A. Additives

Additives are generally defined as substances added to another in relatively small amounts to affect a desired change in properties.[17] In general, food additives are substances not normally consumed as food but are added to food for technical purposes, e.g., to improve safety, storage time, and sensory properties. Food additives may be naturally occurring or man-made. As described in more detail below, food additives, including color additives in the U.S., must be evaluated for their safety before use.

1. Food Additives in the U.S.

The FFDCA broadly defines the term food additive, but explicitly excludes, among other things, pesticide chemicals, color additives, and new animal drugs.[18] Food additives are presumed unsafe, unless an exemption applies.[19] To

---

15. HARTMANN, FRANZ, THE LIFE OF PHILIPPUS THEOPHRASTUS BOMBAST OF HOHENHEIM, KNOWN BY THE NAME OF PARACELSUS: AND THE SUBSTANCE OF HIS TEACHINGS 2 (1887), https://archive.org/details/lifeofphilippust00hartuoft [https://perma.cc/92XF-9JJF].

16. Philippe Grandjean, et al., *The Faroes statement: human health effects of developmental exposure to chemicals in our environment*, 102 BASIC CLINICAL PHARMACOLOGY & TOXICOLOGY 73, 75 (2007), https://onlinelibrary.wiley.com/doi/10.1111/j.1742-7843.2007.00114.x [https://perma.cc/UX4Z-CB95].

17. *Additive*, MERIAM-WEBSTER, https://www.merriam-webster.com/dictionary/additive [https://perma.cc/LD97-UL4T] (last visited Mar. 7, 2025).

18. 21 U.S.C. § 321(s). The breadth of the definition "food additive" is demonstrated here: "The term 'food additive' means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), . . . ; except that such term does not include—

(1) a pesticide chemical residue in or on a raw agricultural commodity or processed food; or
(2) a pesticide chemical; or
(3) a color additive; or
(4) any substance used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to this chapter, the Poultry Products Inspection Act [21 U.S.C. 451 et seq.] or the Meat Inspection Act of March 4, 1907, as amended and extended [21 U.S.C. 601 et seq.];
(5) a new animal drug; or
(6) an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement."

19. 21 U.S.C. § 348(a).

seek approval for use of a food additive, a person may file a petition with FDA proposing the issuance of a regulation establishing conditions for safe usage of the food additive.[20] The petition must be specific to the intended use of the food additive and supporting data, including the physical or technical effect the food additive is intended to produce and the quantity required to produce such effect.[21] Notice of the filing of a petition will be published in the Federal Register.[22]

FDA regulations provide that safe or safety means "there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the conditions of its intended use," and the agency must consider the probable consumption of the additive, the cumulative effect of the additive in the diet, and appropriate safety factors.[23] Therefore, the FDA must determine – based on the best science available – if there is a reasonable certainty of no harm to consumers when a color additive is used as proposed. Following review of a petition and supporting data, the FDA will issue an order prescribing the conditions under which the food additive may be safely used, for each specific use, or deny the petition.[24] Under the Delaney Clause, a food additive cannot be deemed safe if it is shown to induce cancer in humans or animals.[25] Information regarding food additive petitions under review or held in abeyance by FDA's Office of Food Additive Safety ("OFAS") is available on the FDA website.[26]

Under the FFDCA, use of a substance may be characterized as generally recognized as safe or "GRAS."[27] This exemption allows for the use of safe substances in food without review by the FDA. GRAS use of a food additive "may be based only on the view of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food."[28] The expert views may be based on scientific procedures, if equivalent to the quantity and quality of scientific evidence required for a food additive petition.[29] If the food additive was in use prior to January 1, 1958, the expert

---

20. *Id*. at § 348(b).

21. *Id*.

22. 21 C.F.R. § 171.

23. 21 C.F.R. § 170.3(i) (noting "[i]t is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance.").

24. 21 U.S.C. § 348(c).

25. *Id.* § 348(c)(3)(A) ("no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal . . .").

26. *Food Additives and Color Additive Petitions Under Review or Held in Abeyance*, U.S. FOOD & DRUG ADMIN. (Dec. 27, 2024), https://www.hfpappexternal.fda.gov/scripts/fdcc/index.cfm?set=FAP-CAP [https://perma.cc/S8BY-7T42].

27. The GRAS exemption is included in the definition of food additive at 21 U.S.C. § 321(s) ("[I]f such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use.").

28. 21 C.F.R. § 170.30(a).

29. *Id.* § 170.30(a)(1), (b).

views may be based on common use in food, if there is reasonable certainty that the substance is not harmful under the conditions of the intended use.[30] GRAS status may be self-determined, and a person may notify FDA of its determination.[31] However, new information may at any time require reconsideration of the GRAS status of a food ingredient.[32]

2. Color Additives in the U.S.

The FFDCA defines color additives as dyes, pigments, or other substances that impart a color to food, unless the substance is used for purposes other than coloring.[33] Color additives include substances extracted from natural sources as well as synthetic chemicals.[34] Similar to food additives, color additives are presumed unsafe, and a petition must be filed with supporting data showing the color additive is safe for the intended use.[35] There is no GRAS exemption for color additives, so all color additives require premarket approval from FDA. Notice of filing of a petition and a regulation listing the color additive are published in the Federal Register.[36] The FDA will evaluate the safety of the color additive and may list the color additive for use generally with food or for only specific uses.[37] Safe means there is "convincing evidence that establishes

30. *Id.* § 170.30(a)(2).

31. Substances Generally Recognized as Safe, 62 Fed. Reg. 18938 (proposed Apr. 17, 1997) (to be codified at 21 C.F.R. Parts 170, 184, 186, and 570), https://www.govinfo.gov/content/pkg/FR-1997-04-17/pdf/97-9706.pdf [https://perma.cc/H9H4-VVE6].

32. *Id.* § 170.30(l). The FDA published recognized GRAS uses in food in 21 C.F.R. parts 182, 184, and 186.

33. 21 U.S.C. § 321(t). "The term 'color additive' means a material which—
(A) is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source, and
(B) when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction with other substance) of imparting color thereto;
except that such term does not include any material which the Secretary, by regulation, determines is used (or intended to be used) solely for a purpose or purposes other than coloring.
(2) The term "color" includes black, white, and intermediate grays.
(3) Nothing in subparagraph (1) of this paragraph shall be construed to apply to any pesticide chemical, soil or plant nutrient, or other agricultural chemical solely because of its effect in aiding, retarding, or otherwise affecting, directly or indirectly, the growth or other natural physiological processes of produce of the soil and thereby affecting its color, whether before or after harvest."

34. *Id.* § 321(t).

35. 21 C.F.R. § 71.1.

36. *Id.* § 71.2, 71.20.

37. *Id.* § 70.42. In deciding whether a petition is complete and suitable for filing and in reaching a decision on any petition filed, the Commissioner will apply the "safe-for-use" principle. This will require the presentation of all needed scientific data in support of a proposed listing to assure that each listed color additive will be safe for its intended use or uses in or on food, drugs, or cosmetics. The Commissioner may list a color additive for use generally in or on food, in or on drugs, or in or on cosmetics when he finds from the data presented that such additive is suitable and may safely be employed for such general use; he may list an additive only for more limited use or uses for which it is proven suitable and may safely be employed; and he is

with reasonable certainty that no harm will result from the intended use of the color additive."[38] Similar to food additives, if the FDA concludes, based on scientific literature, results from biological testing, or the judgment of qualified scientists, that cancer has been induced by a color additive, including its components or impurities, no regulation may issue which permits its use.[39]

Color additives must comply with individual listing regulations issued by the FDA.[40] The use of an unlisted color additive, the improper use of a listed color additive, or the use of a color additive that does not conform to the purity and identity specifications of the listing regulation may cause a product to be considered adulterated under the FFDCA. The FDA may take enforcement action against such adulterated products.

Certified color additives are synthetically produced and require certification with the FDA.[41] The FDA regulations set forth the process for requesting certification of a batch of color additive.[42] There are currently seven certified color additives approved for use in foods called "FD&C" color additives because they also may be used in drugs and cosmetics.[43] A summary of food additives and the associated regulatory status is available on the FDA website.[44]

3. Food Additives in the European Union

The EU reviews and approves foods additives using a system that is fundamentally similar to the U.S., although the legal frameworks are quite different. The European Food Safety Authority ("EFSA") was established to provide scientific advice and scientific and technical support for legislation and policies impacting food and feed safety.[45] The EU regulates food additives under various regulations governing the conditions of use of food additives, risk analysis, and authorization.[46] Similar to U.S. food statutes and regulations, EU

---

authorized to prescribe broadly the conditions under which the additive may be safely employed for such use or uses. This may allow the use of a particular dye, pigment, or other substance with certain diluents, but not with others, or at a higher concentration with some than with others.

38. *Id.* § 70.3(i).

39. *Id.* § 70.50(a).

40. *See id.* §§ 73, 74, 82 (providing chemical specifications for the color additives, identifying uses and restrictions, labeling requirements for the marketed color additive, and any certification requirements).

41. *Id.* § 80.35.

42. *See id.* § 80.

43. *Id.* § 74, Subpart A (color additives used in food that are subject to certification include FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, Orange B, Citrus Red No. 2, FD&C Red No. 3, FD&C Red No. 40, FD&C Yellow No. 5, and FD&C Yellow No. 6).

44. *Regulatory Status of Color Additives*, U.S. FOOD & DRUG ADMIN. (Oct. 30, 2024), https://www.hfpappexternal.fda.gov/scripts/fdcc/index.cfm?set=ColorAdditives [https://perma.cc/TD5V-SDUC].

45. Council Regulation 178/2002, 2002 O.J. (L 31) (EC), https://eur-lex.europa.eu/eli/reg/2002/178/oj/eng [https://perma.cc/CV35-UT9F] (last visited Feb. 16, 2025).

46. Council Regulation 1331/2008, 2008 O.J. (L 354) (EC), https://eur-lex.europa.eu/eli/reg/2008/1331/oj/eng [https://perma.cc/M65M-V48A] (last visited Feb. 16, 2025); Council

food law is designed to protect the interests of consumers and allow for informed decisions by preventing fraudulent or deceptive practices, adulteration of food, and practices that otherwise mislead consumers.[47] Food shall not be placed on the market if it is unsafe.[48] Food is deemed unsafe if it is injurious to health or unfit for human consumption taking into consideration the normal conditions of the food, information provided to the consumer, short-term and long-term effects and effects on subsequent generations, cumulative toxic effects, and particular health sensitivities.[49] The EU broadly defines the term food, but certain items like animal feed, live animals, and plants prior to harvesting are excluded.[50] The General Food Law Regulation requires the consideration of existing international standards that are relevant and applicable in the development or adoption of food law.[51] Furthermore, the EU and member states are required to contribute and promote international food and feed standards.[52]

Under EU food law, a food additive must be approved before use.[53] As under U.S. law, food additive is broadly defined under European Commission regulations, but, unlike the U.S., the definition includes color additives and does

---

Regulation 1129/2011, 2011 O.J. (L 295) (EC)., https://eur-lex.europa.eu/eli/reg/2011/1129/oj/eng [https://perma.cc/TN67-RH7F] (last visited Feb. 16, 2025).

47. Council Regulation 178/2002, art. 8, 2002 O.J. (L 31) (EC), https://eur-lex.europa.eu/eli/reg/2002/178/oj/eng [https://perma.cc/9GHZ-LF79] (last visited Feb. 16, 2025).

48. *Id.* at art. 14, ¶ 1, 2002 O.J. (L 31) (EC).

49. *Id.* at art. 14, ¶¶ 2–5, 2002 O.J. (L 31) (EC).

50. *See id.* at art. 2, 2002 O.J. (L 31) (EC), which states "For the purposes of this Regulation, 'food' (or 'foodstuff') means any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans.

'Food' includes drink, chewing gum and any substance, including water, intentionally incorporated into the food during its manufacture, preparation or treatment. It includes water after the point of compliance as defined in Article 6 of Directive 98/83/EC and without prejudice to the requirements of Directives 80/778/EEC and 98/83/EC.

'Food' shall not include:

(a) feed;

(b) live animals unless they are prepared for placing on the market for human consumption;

(c) plants prior to harvesting;

(d) medicinal products within the meaning of Council Directives 65/65/EEC and 92/73/EEC;

(e) cosmetics within the meaning of Council Directive 76/768/EEC;

(f) tobacco and tobacco products within the meaning of Council Directive 89/622/EEC;

(g) narcotic or psychotropic substances within the meaning of the United Nations Single Convention on Narcotic Drugs, 1961, and the United Nations Convention on Psychotropic Substances, 1971;

(h) residues and contaminants;

(i) medical devices within the meaning of Regulation (EU) 2017/745 of the European Parliament and of the Council."

51. *Id.* at art. 13, 2002 O.J. (L 31) (EC).

52. *Id.*

53. *See* Council Regulation 1331/2008, 2008 O.J. (L 354) 1 (EC), https://eur-lex.europa.eu/eli/reg/2008/1331/oj/eng [https://perma.cc/M65M-V48A] (last visited Feb. 16, 2025); *see also* Council Regulation 1333/2008, art. 5, 2008 O.J. (L 354) (EC), https://eur-lex.europa.eu/eli/reg/2008/1333/oj/eng [https://perma.cc/FCP2-HA5Y] ("No person shall place on the market a food additive or any food in which such a food additive is present if the use of the food additive does not comply with this Regulation.").

not provide a GRAS exemption.[54] An application for a new food additive is sent to the European Commission, which asks the ESFA to carry out a risk assessment and may include an evaluation by other relevant expert panels under the EFSA.[55] Approved food additives and associated specifications are included on the Union lists under Annexes II and III along with a unique identifier, the food additive name, the foods which the additive may be added, conditions of use, and any other restrictions.[56]

4. Codex Alimentarius

The Codex Alimentarius, or "Food Code" ("Codex") is a collection of standards, guidelines and codes of practice adopted by the Codex Alimentarius Commission ("Commission" or "CAC").[57] The Commission is the central part of the Joint Food and Agriculture Organization of the United Nations ("FAO") and the World Health Organization ("WHO") Food Standards Programme and was established by FAO and WHO to protect consumer health and promote fair practices in food trade.[58] In addition, the Commission is responsible for promoting coordination of food standards work undertaken by international governmental and non-governmental organizations; determining priorities and initiating and guiding the preparation of draft standards; finalizing standards and publishing them in the Codex Alimentarius either as regional or worldwide standards; and amending published standards, as appropriate, in light of developments.[59] Codex can be used to harmonize global food safety standards, guide countries establishing food safety standards, as a standard under international treaties, or as a tool for resolving trade disputes.

---

54. Council Regulation 1333/2008, art. 3, ¶ 2(a), 2008 O.J. (L 354) (EC) ("'[F]ood' additive shall mean any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food, whether or not it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods." (exclusions removed)).

55. *Id.* at art. 3, 2008 O.J. (L 354) (EC).

56. *See* Council Regulation 1129/2011, 2011 O.J. (L 295) (EC), https://eur-lex.europa.eu/eli/reg/2011/1129/oj/eng [https://perma.cc/LG2G-CLBL]; Council Regulation 231/2012, 2012 O.J. (L 83) (EC), https://eur-lex.europa.eu/eli/reg/2012/231/oj/ [https://perma.cc/YK37-UZ4X].

57. FAO & WHO, CODEX ALIMENTARIUS COMMISSION PROCEDURAL MANUAL 7 (28th ed. 2023), https://openknowledge.fao.org/items/dfc93e42-67f3-4de9-9dad-b33fb1600b32 [https://perma.cc/2JV6-SZV8] ("Membership of the Commission is open to all Members and Associate Members of FAO and WHO interested in international food standards. Membership shall comprise such of these nations as have notified the Director-General of FAO or of WHO of their desire to be considered as Members . . . Any Member Nation or Associate Member of FAO or WHO which is not a Member of the Commission but has a special interest in the work of the Commission, may, upon request communicated to the Director-General of FAO or WHO, as appropriate, attend sessions of the Commission and of its subsidiary bodies and ad hoc meetings as Observers.").

58. *Id.*

59. *Id.*

The *General Standard for Food Additives* ("GSFA") was developed to include food additive provisions for standardized and non-standardized foods in the Codex.[60] The GSFA was used as a starting point for the EU regulations, but additional specificity was required.[61] Food additives are only listed in the GSFA if an acceptable daily intake (ADI) is established or if determined, on the basis of other criteria,[62] to be safe by the Joint FAO/WHO Expert Committee on Food Additives ("JECFA").[63] The use of additives in foods standardized by Codex is subject to the conditions of use established by the Codex commodity standards and the GSFA.[64]

5. Soy Leghemoglobin Review and Approval in the U.S. and EU

Soy leghemoglobin is an example of a substance that has undergone multiple food additive or color additive reviews, including under U.S. and EU laws. Impossible Foods, Inc. submitted on October 3, 2017, a notice to FDA that a specific use of soy leghemoglobin preparation is GRAS through scientific procedures.[65] Soy leghemoglobin is an oxygen-binding heme protein produced in nodules that performs a similar function to hemoglobin in animals.[66] The notice related to soy leghemoglobin from a strain of *Komagataella phaffi* (yeast), formerly *Pichia pastoris*, for use at a level up to 0.8% soybean leghemoglobin protein to optimize flavor in ground beef analogue products intended to be cooked. Soy leghemoglobin preparation is a mixture containing soy leghemoglobin protein, *K. phaffi* proteins, sodium chloride, and sodium ascorbate, which is red/brown in color. The FDA issued a letter on July 23, 2018, regarding the GRAS Notice and confirmed it had no questions regarding the

60. *Id.* at 31.

61. Commission Regulation 1129/2011, art. 4, 2011 O.J. (L 295) 1129 (EU).

62. FAO & WHO, PROCEDURAL MANUAL, *supra* note 57, at 2 ("Acceptable Daily Intake (ADI) is an estimate by JECFA of the amount of a food additive, expressed on a body weight basis that can be ingested daily over a lifetime without appreciable health risk . . . For the purposes of this Standard, the phrase 'without appreciable health risk' means that there is a reasonable certainty of no harm to consumers if an additive is used at levels that do not exceed those in this Standard. The provisions of this Standard do not sanction the use of an additive in a manner that would adversely affect consumer health."); *see also* Shabeer, et al., *supra* note 5.

63. FAO & WHO, CODEX ALIMENTARIUS; INTERNATIONAL FOOD STANDARDS 2 (2023) ("'determined, on the basis of other criteria, to be safe" means that the use of a food additive does not pose a safety concern under conditions of use described by JECFA as being of no toxicological concern (e.g. use levels defined circumstances)). *See also* Joel K. Bourne, Jr., *Eating the Earth: The burgeoning global food trade is a lifeline for billions, but it is fragile and hard on the planet*, 386 SCIENCE 956, 958 (Nov. 29, 2024), https://www.science.org/doi/epdf/10.1126/science.adu8006 [https://perma.cc/W6CA-AGFH] (Bourne Jr., *supra* note 2).

64. FAO & WHO, PROCEDURAL MANUAL, *supra* note 57, at 2.

65. U.S. FOOD & DRUG ADMIN., Re: GRAS Notice No. GRN 000737, https://www.centerforfoodsafety.org/files/gras-notice-grn-737-agency-response-letter_31101.pdf [https://perma.cc/RL9E-KMGT] (last visited Feb. 18, 2025).

66. LINCOLN TAIZ & EDUARDO ZEIGER, PLANT PHYSIOLOGY 330-33 (5th ed. 2010) (soil bacteria called rhizobia form a symbiotic relationship with soybeans wherein the bacteria provide fixed nitrogen to the plant in exchange for other nutrients and carbohydrates).

Notice.[67] Impossible Foods was able to use the GRAS exemption because the soy leghemoglobin preparation was used for the purpose of flavor.

Soy leghemoglobin is also useful as a colorant. Therefore, Impossible Foods sought premarket approval and an amendment to the color additive regulations to provide for the safe use of soy leghemoglobin as a color additive. As noted above, the FFDCA does not include a GRAS exemption for color additives. A notice was published in the Federal Register of December 13, 2018, announcing the filing of Impossible Foods' color additive petition, CAP 9C0314.[68] FDA's final rule listing soy leghemoglobin as a color additive exempt from certification was published in the Federal Register of August 1, 2019.[69] FDA's final rule, response to objections, denial of public hearing requests, and removal of administrative stay regarding soy leghemoglobin as a color additive was published in the Federal Register of December 19, 2019.[70]

Impossible Foods also sought approval from the European Commission for the use of soy leghemoglobin as a food additive, and specifically as a color in meat analogue products.[71] Consistent with its regulations, the European Commission requested the EFSA provide a scientific opinion on the safety of the soy leghemoglobin.[72] The EFSA Food Additive and Flavourings ("FAF") Panel concluded that the use of soy leghemoglobin from genetically modified *K. phaffi* as a food additive does not raise a safety concerned at the proposed use and use level.[73] In addition to the FAF Panel, a food additive that is within the scope of the regulation on genetically modified food and feed must be analyzed by the EFSA Panel on Genetically Modified Organisms ("GMO Panel").[74] The GMO Panel concluded that the leghemoglobin from genetically modified *K.*

---

67. *GRAS Notices*, U.S. FOOD & DRUG ADMIN., www.fda.gov/grasnoticeinventory [https://perma.cc/H22H-RFDN] (last updated Feb. 13, 2025).

68. Impossible Foods, Inc.; Filing of Color Additive Petition, 83 Fed. Reg. 64045 (proposed Dec. 13, 2018).

69. Listing of Color Additives Exempt From Certification; Soy Leghemoglobin, 84 Fed. Reg. 37573 (Aug. 1, 2019) (to be codified at 21 C.F.R. Part 73).

70. Listing of Color Additives Exempt From Certification; Soy Leghemoglobin, 84 Fed. Reg. 69620 (Dec. 19, 2019) (to be codified at 21 C.F.R. Part 73).

71. Josep Casacuberta et al., *Assessment of soy leghemoglobin produced from genetically modified Komagataella phaffii, under Regulation (EC) No 1829/2003 (application EFSA-GMO-NL-2019-162)*, 22 EFSA J. e9060 (2024), https://doi.org/10.2903/j.efsa.2024.9060 [https://perma.cc/M2P8-45L6].

72. *See* Regulation 1331/2008, 2008 O.J. (L 354) (EC), https://eur-lex.europa.eu/eli/reg/2008/1331/oj/eng [https://perma.cc/M65M-V48A] (last visited Feb. 16, 2025); Regulation 1333/2008, 2008 O.J. (L 354) (EC), https://eur-lex.europa.eu/eli/reg/2008/1333/oj/eng [https://perma.cc/FV86-PDMY].

73. Maged Younes, et al., *Safety of soy leghemoglobin from genetically modified Komagataella phaffii as a food additive*, 22 EFSA J. e8822 (2024), https://doi.org/10.2903/j.efsa.2024.8822 [https://perma.cc/WD25-2RPM].

74. Regulation, 1333/2008, art. 13 ¶ 1, 2008 O.J. (L 354) (EC) (stating that "[a] food additive falling within the scope of Regulation (EC) No 1829/2003 may be included in the Community lists in Annexes II and III in accordance with this Regulation only when it is covered by an authorization in accordance with Regulation (EC) No 1829/2003"); Regulation 1829/2003, 2003 O.J. (L 268) (EC), https://eur-lex.europa.eu/eli/reg/2003/1829/oj/eng [https://perma.cc/6RMT-4SWY].

phaffii is safe with respect to potential effects on human health and the environment at the proposed use and use level, as far as the scope of its review was concerned as to the impact of the genetic modification.[75]

Soy leghemoglobin is now approved as a food additive and color additive in the U.S. and as a food additive in the EU, and undoubtedly certain scientific data and risk analyses were useful under both legal schemes, but navigating both systems can be nuanced, time consuming, and potentially delay global trade and access to certain foods.

B. Pesticides

Pesticides are used widely in agriculture for pre-harvest and post-harvest operations, which may result in pesticide residues on food. By their nature, pesticides are controversial, and the approval and use of pesticides are highly controlled in the U.S. and EU.

1. U.S. Regulation of Pesticide Residues

Pesticides are defined under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA") as any substance or mixture of substances intended for preventing, destroying, or mitigating any pest, including plant regulators, defoliants, or desiccants.[76] A pesticide must be registered before the pesticide may be distributed or sold.[77] The U.S. Environmental Protection Agency ("EPA") evaluates data submitted by an applicant as part of the registration process.[78] The data includes chemical identity and composition of the pesticide, environmental fate, and residue chemistry, among other things.[79] EPA has authority under the FFDCA to establish, modify, or revoke a tolerance for a pesticide chemical residue in or on food.[80]

EPA evaluates pesticides to ensure that they are safe for human health and the environment when used according to label directions and establishes tolerances,[81] which are the maximum residue level of a specific pesticide

75. Casacuberta et al., *supra* note 71.

76. 7 U.S.C. § 136(u).

77. *Id.* § 136a(a).

78. *Id.* § 136a.

79. 40 C.F.R. § 158.130.

80. 21 U.S.C. § 346a ("The term 'pesticide chemical residue' means a residue in or on raw agricultural commodity or processed food of (A) a pesticide chemical; or (B) any other added substance that is present on or in the commodity or food primarily as a result of the metabolism or other degradation of a pesticide chemical."); 21 U.S.C. 321(q)(2).

81. The EPA Administrator shall register a pesticide if the Administrator determines that, when considered with any restrictions imposed, the pesticide will not cause "unreasonable adverse effects on the environment." 7 USC 136a(c)(5)(C). "The term 'unreasonable adverse effects on the environment' means (1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent

chemical that is permitted in or on a specific human or animal food.[82] Tolerances must be established, and a food with detectable pesticide residues must be below established tolerances for the food to be considered safe for consumption. Specifically, a pesticide is considered unsafe in or on food until a tolerance is established,[83] and a food with an unapproved pesticide residue is automatically deemed adulterated.[84] A raw agricultural commodity is deemed unsafe and adulterated if it contains a level exceeding an established tolerance.[85]

The FFDCA defines "safe" with respect to pesticide chemical residue tolerances to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information."[86] This includes exposure through drinking water and in residential settings but does not include occupational exposure.[87] FFDCA also requires EPA to give special consideration to the exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue[s.]"[88] EPA must consider several factors when making determinations about establishing, modifying, or revoking tolerances, including the validity, completeness, and reliability of available data; the nature of any toxic effect; available information concerning the relationship of the studies to human risk, dietary consumption patterns of consumers, cumulative effects of residues and other substances that have a common mechanism of toxicity, aggregate exposure levels of consumers, and variability of the sensitivities of major identifiable subgroups of consumers; whether the pesticide chemical may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects; and safety factors.[89] Consequently, for a food-use pesticide (*i.e.,* a pesticide use that is likely to result in residues in or on food) to be sold and distributed, the pesticide must not only have appropriate tolerances or exemptions under the FFDCA, but also must be registered under FIFRA.[90] Food-use pesticides not registered in the U.S. must have tolerances or exemptions in order for

---

with the standard under section 346a of title 21. The Administrator shall consider the risks and benefits of public health pesticides separate from the risks and benefits of other pesticides. In weighing any regulatory action concerning a public health pesticide under this subchapter, the Administrator shall weigh any risks of the pesticide against the health risks such as the diseases transmitted by the vector to be controlled by the pesticide." 7 U.S.C. 136(bb).

82. 21 U.S.C. § 346(a)(2)(A).

83. *Id.* § 346a(a)(1).

84. *Id.* § 342(a)(2)(B).

85. *Id.* § 321(r) ("The term 'raw agricultural commodity' means any food in its raw or natural state, including all fruits that are washed, colored, or otherwise treated in their unpeeled natural form prior to marketing.").

86. *Id.* § 346a(b)(2)(A)(ii), (c)(2)(A)(ii).

87. *Id.* § 346a(b)(2)(D).

88. *Id.* § 346a(b)(2)(C).

89. *Id.* § 346a(b)(2)(D).

90. 7 U.S.C. § 136.

commodities treated with those pesticides to be imported into the U.S..[91]

When establishing a tolerance for residues of a pesticide, EPA must determine whether the Codex has established a Maximum Residue Limit ("MRL") for that pesticide.[92] As part of registration review, EPA determines whether international tolerances or MRLs exist for commodities and chemicals for which U.S. tolerances have been established.[93] Where appropriate, EPA's intention is to harmonize U.S. tolerances with those international MRLs to facilitate trade.[94] EPA must explain its reasons for deviating from any Codex MRL.[95] EPA's effort to harmonize with Codex MRLs is summarized in the tolerance reassessment section of the individual human health risk assessments that support each pesticide registration review.[96]

The FDA is responsible for enforcing the EPA tolerances for domestic foods shipped in interstate commerce and foods offered for import into the U.S., except for meat, poultry, catfish (Siluriformes) and certain egg products that are regulated by the U.S. Department of Agriculture's ("USDA") Food Safety and Inspection Service ("FSIS").[97] FDA employs a three-fold strategy to enforce the tolerances for pesticide chemical residues in human and animal foods.[98] FDA selectively tests a broad range of imported and domestic commodities for pesticide residues and may also carry out focused sampling surveys for specific commodities or selected pesticide chemical residues of special interest.[99] In addition, FDA monitors the levels of pesticide chemical residues in foods prepared for consumption in its Total Diet Study ("TDS"), an ongoing program that monitors contaminants and nutrients in the average U.S. diet.[100]

2. EU Regulation of Pesticide Residues

The EU notes that the use of active substances in plant protection products is one of the most common methods of protecting plants and plant products from the effects of harmful organisms,[101] but a possible consequence is the presence

91. 21 U.S.C. § 346a(a)(1).

92. *See id.* § 346a(b)(4).

93. Guidance on Pesticide Import Tolerances and Residue Data for Imported Food, 65 Fed. Reg. 35069 (June 1, 2000).

94. *Id.*

95. 21 U.S.C. § 346a(b)(4).

96. *Id.* § 346a(b)(4).

97. *Id.* § 1401.

98. U.S. FOOD & DRUG ADMIN., PESTICIDE RESIDUE MONITORING PROGRAM FISCAL YEAR 2022 PESTICIDE REPORT 5 (2024), https://www.fda.gov/food/pesticides/pesticide-residue-monitoring-report-and-data-fy-2022 [https://perma.cc/RVJ7-NF6B].

99. *Id.*

100. *Id.*

101. "'[P]esticide residues' means residues, including active substances, metabolites and/or breakdown or reaction products of active substances currently or formerly used in plant protection products . . . which are present in or on the products covered by Annex I to this Regulation, including in particular those which may arise as a result of use in plant protection, in veterinary medicine and as a biocide." Regulation 396/2005, art. 3 ¶ 2(c), 2005 O.J. (L 70) (EC); Active

of residues in the treated products or in animals feeding on those products.[102] Public health should be given priority over the interests of crop protection, and a primary focus is to ensure that active substances or products placed on the market do not adversely affect human or animal health or the environment.[103] Pesticides are evaluated and approved for use in the EU utilizing a distinctly different legal framework than in the U.S., but the foundational principle of each system is the characterization of risk to protect human health and the environment. Plant protection products must meet certain requirements for approval, including effectiveness, immediate and delayed harmful effects (considering vulnerable groups, other sources, and cumulative or synergistic effects), unacceptable effects on plants or plant products, unnecessary suffering and pain to vertebrates to be controlled, and unacceptable effects on the environment.[104] For active substances used on feed or food crops or that indirectly results in residues in food or feed, the dossier submitted for approval of the substance must permit any residue to be defined, predict the residues on food and feed and the effects of processing or mixing, permit a maximum residue level to be defined and methods for detection, permit concentration and dilution factors due to processing or mixing to be defined, and permit, where relevant, a determination of fate and distribution in the environment and non-target species.[105]

Conditions for approval of active substances requires that residues of plant protection products shall not have any harmful effects on human health, including that of vulnerable groups, or animal health, taking into account known cumulative and synergistic effects. . ., or on groundwater, and no unacceptable effect on the environment.[106] MRLs are set after consultation of the EFSA and consideration of the established general principles and requirements of food

---

substances means "substances, including micro-organisms having general or specific action against harmful organisms or on plants, parts of plants or plant products." Commission Regulation 1107/2009, 2009 O.J. (L 309) (EC).; "'[S]ubstances' means chemical elements and their compounds, as they occur naturally or by manufacture, including any impurity inevitably resulting from the manufacturing process." Regulation 396/2005, art. 3, ¶ 2, 2005 O.J. (L 70) (EC); Plant protection products means "products, in the form in which they are supplied to the user, consisting of or containing active substances, safeners or synergists, and intended for one of the following uses: (a) protecting plants or plant products against all harmful organisms or preventing the action of such organisms, unless the main purpose of these products is considered to be for reasons of hygiene rather than for the protection of plants or plant products; (b) influencing the life processes of plants, such as substances influencing their growth, other than as a nutrient; (c) preserving plant products, in so far as such substances or products are not subject to special Community provisions on preservatives; (d) destroying undesired plants or parts of plants, except algae unless the products are applied on soil or water to protect plants; (e) checking or preventing undesired growth of plants, except algae unless the products are applied on soil or water to protect plants." Commission Regulation 1107/2009, art. 2 ¶ 1, 2009 O.J. (L 309) (EC).

102. Regulation 396/2005, 2005 O.J. (L 70) (EC).

103. Commission Regulation 1107/2009, art. 1 ¶ 3-4, 2009 O.J. (L 309) (EC).

104. *Id.* at art. 4 ¶ 3(a)-(e).

105. *Id.* at annex II ¶ 3.1.

106. *Id.* at art. 4 ¶ 2.

law.[107] Considering the EU directive concerning approval of plant protection products, MRLs are to be set at the lowest achievable level consistent with good agricultural practice for each pesticide with a view to protecting vulnerable groups.[108] Additionally, EU trading partners should be consulted about proposed MRLs before adoption, and Codex MRLs should be considered when EU MRLs are set, taking into account the corresponding good agricultural practices. [109]

EU Member States are required to implement a system of controls on pesticide residues to ensure and enforce compliance with regulations.[110] Such controls must include sampling sufficiently to represent the market and appropriate analysis of pesticide residues.[111] Community control programs, National control programs, and annual reporting is also required to assess and report on the risk of exposure to consumers.[112]

3. The Role of Codex in Pesticide Residues

Trade difficulties can arise when maximum legal limits for pesticide residues in foods differ between countries. Codex MRLs can be a useful tool for harmonizing residue limits and facilitating trade. The Codex Committee on Pesticide Residues ("CCPR") is responsible for establishing Codex MRLs for pesticide residues in specific food items or in groups of food or feed that move in international trade.[113]

The process for setting a Codex MRL begins when a Member or Observer nominates a pesticide for evaluation by the Joint FAO/WHO Meeting on Pesticide Residues ("JMPR").[114] Before a Codex MRL can be established, human health risk assessments must be conducted to ensure the food supply is safe. The JMPR is responsible for reviewing the appropriate toxicology and data that reflect approved pesticide use in accordance with good agricultural practice.[115] JMPR's risk assessment includes, among other things, an evaluation

---

107. Regulation 396/2005, recital 6, 2005 O.J. (L 70) (EC); *see* Regulation 178/2002, 2002 O.J. (L 31) (EC).

108. *Id.* at art. 3 ¶ 2(d) ("'[M]aximum residue level' (MRL) means the upper legal level of a concentration for a pesticide residue in or on food or feed set in accordance with this Regulation, based on good agricultural practice and the lowest consumer exposure necessary to protect vulnerable consumers."); *see also* Regulation 396/2005, recital 5, 2005 O.J. (L 70) (EC).

109. *Id.* at recital 25.

110. *Id.* at art. 26 ¶ 1.

111. *Id.* at art. 27 ¶ 1-2.

112. *See id.* art. 29-33.

113. FAO & WHO, PROCEDURAL MANUAL, *supra* note 57, at 127 ¶ 166.

114. *Id.* at 131 ¶ 195, 127 ¶ 167 ("The JMPR consists of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. It is an independent scientific expert body convened by both Directors-General of FAO and WHO according to the rules of both organizations, charged with the task of providing scientific advice on pesticide residues.").

115. *Id.* at 128 ¶ 170 ("Good agricultural practice (GAP) in the use of pesticides includes the nationally authorized safe uses of pesticides under actual conditions necessary for effective and reliable pest control. It encompasses a range of levels of pesticide applications up to the highest

of short-term and long-term dietary exposures.[116] The science-based risk assessments are based on "Working Principles for Risk Analysis for Application in the Framework of the Codex Alimentarius,"[117] and include hazard identification,[118] hazard characterization,[119] exposure assessment,[120] and risk characterization.[121] JMPR recommends specific MRLs to the CCPR, which recommendations, if accepted, are submitted to the Commission for adoption as Codex MRLs ("CXLs").[122] As previously mentioned, Codes MRLs or CXLs are considered by the U.S. and EU is establishing appropriate residue levels for food.

4. Chlorpyrifos – A Complicated Analysis

Chlorpyrifos is an organophosphate insecticide that was registered for use in the U.S. in 1965, and the registration was modified several times since the initial registration. In 2017, chlorpyrifos was the most widely used insecticide in the U.S.[123] Recent developments concerning the registrations and established tolerances (or MRLs) in the U.S. and EU show how differences in the interpretation of the risk analysis and the legal system applied can affect the registration, use, and tolerances (MRLs) of a pesticide.[124]

On September 12, 2007, pursuant to 21 U.S.C. § 346a(d), the Natural Resources Defense Council ("NRDC") and Pesticide Action Network North America ("PANNA") filed a petition with EPA seeking to revoke all tolerances and cancel all registrations for chlorpyrifos.[125] After delays by EPA, plaintiffs sought relief from the court to compel agency action.[126] In 2015, EPA stated it

---

authorized use, applied in a manner which leaves a residue which is the smallest amount practicable. Authorized safe uses are determined at the national level and include nationally registered or recommended uses, which take into account public and occupational health and environmental safety considerations. Actual conditions include any stage in the production, storage, transport, distribution and processing of food commodities and animal feed.").

116. *Id*.

117. *See id*. at 99-103.

118. *Id.* at 104 ("The identification of biological, chemical, and physical agents capable of causing adverse health effects and which may be present in a particular food or group of foods.").

119. *Id.* ("The qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical, and physical agents which may be present in food.").

120. *Id.* ("The qualitative and/or quantitative evaluation of the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant.").

121. *Id.* at 151 ("The qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterization and exposure assessment.").

122. *Id.* at 128 ¶ 171.

123. *See* Chlorpyrifos; Order Denying PANNA and NRDC's Petition to Revoke Tolerances, 82 Fed. Reg. 16581, 16584 (Apr. 5, 2017).

124. Codex MRLs have not been established for chlorpyrifos or chlorpyrifos-methyl.

125. *See* Chlorpyrifos; Final Order Denying Objections to March 2017 Petition Denial Order, 84 Fed. Reg. 35555 (Jul. 24, 2019); *see also* 21 U.S.C. § 346a(d)(1)(A) (allowing "[a]ny person" to file a petition that proposes "revoking a tolerance").

126. Pesticide Action Network North America v. EPA, 798 F.3d 809 (9th Cir. 2015).

was unable to conclude that the risk from aggregate exposure from the use of chlorpyrifos meets the safety standard of the FFDCA.[127] Therefore, EPA proposed to revoke all tolerances for chlorpyrifos and sought comments on retaining any individual tolerances, or group of tolerances, and whether information exists to demonstrate that such tolerance satisfies the FFDCA safety standard.[128] EPA then sought additional comments on its revised human health risk assessment and drinking water exposure assessment.[129] Then in 2017, EPA denied PANNA's petition and concluded that the data provided with the 2007 petition were not sufficiently valid, complete, and reliable to support the request for revocation ("2017 Order").[130] In 2019, EPA also denied all objections to its March 29, 2017, order ("2019 Order").[131]

Several organizations and states filed petitions for review in the Ninth Circuit challenging EPA's orders.[132] The Court granted the petitions for review, vacated EPA's 2017 Order and 2019 Order, and remanded with instructions to EPA to (1) grant the 2007 Petition, (2) issue a final regulation within 60 days of issuance of the mandate either revoking or modifying the chlorpyrifos tolerances, and (3) modify or cancel related FIFRA registrations for food use.[133] The Ninth Circuit determined that's EPA's denial of the 2007 Petition was arbitrary and capricious, and that EPA can only leave tolerances in place if it finds the tolerance to be safe for the general population and for infants and children.[134]

On October 29, 2021, EPA revoked all tolerances for chlorpyrifos.[135] Several organizations challenged the EPA's final rules, and the Eighth Circuit concluded that the EPA's decision to ignore modification as a possibility was "arbitrary [and] capricious."[136] The Court remanded the matter to EPA and emphasized that EPA remains free to exercise its discretion as long as it considers all "important aspect[s] of the problem" and gives a reasoned explanation for whichever option it chooses.[137] Consistent with the Eighth Circuit's opinion, EPA revised the tolerance regulations to reflect the

---

127. *See* Chlorpyrifos; Tolerance Revocations, 80 Fed. Reg. 69080 (proposed Nov. 6, 2015) (to be codified at 40 C.F.R. Part 180).

128. *See id.*

129. *See id.*

130. *See* Chlorpyrifos; Order Denying PANNA and NRDC's Petition to Revoke Tolerances, 82 Fed. Reg. 16581 (April 5, 2017).

131. Chlorpyrifos; Final Order Denying Objections to March 2017 Petition Denial Order, 84 Fed. Reg. 35555 (July 24, 2019).

132. *See* League of United Latin Am. Citizens v. Regan, 996 F.3d 673 (9th Cir. 2021).

133. *Id*.

134. *Id*.

135. *See* Chlorpyrifos; Tolerance Revocations, 86 Fed. Reg. 48315 (Aug. 30, 2021) (to be codified at 40 C.F.R. Part 180). Effective February 28, 2022, EPA denied all objections to its August 30, 2021, final rule, requests for hearing on those objections, as well as requests for stay of the final rule. *See also* Chlorpyrifos; Final Rule, 87 Fed. Reg. 11222 (Feb. 28, 2022) (to be codified at 40 C.F.R. Part 180).

136. Red River Valley Sugarbeet Growers Ass'n v. Regan, 85 F.4th 881, 14 (8th Cir. 2023).

137. *See generally Chemical, supra* note 14.

reinstatement of tolerances for chlorpyrifos.[138] Certain registrations have been voluntarily cancelled or amended, and EPA is evaluating modification of certain tolerances.

In contrast, on December 6, 2019, at the meeting of the Standing Committee on Plants, Animals, Food and Feed ("PAFF Committee"), the EU Member States voted to not renew the approvals of chlorpyrifos and chlorpyrifos-methyl.[139] The European Commission formally adopted the regulations on January 10, 2020.[140] In April 2019, as part of the standard regulatory renewal of approval processes for these substances, experts from EFSA and Member States including relevant experts from the EFSA Panel on Plant Protection Products and their Residues ("PPR Panel") convened to discuss the human health assessment of chlorpyrifos and chlorpyrifos-methyl.[141] Experts concluded that concerns related to human health exist in relation to possible genotoxicity and developmental neurotoxicity.[142] The European Commission mandated EFSA to provide statements on the main findings on human health for chlorpyrifos and chlorpyrifos-methyl.[143]

On August 2, 2019, EFSA published statements for both substances, confirming that concerns for human health have been identified and that safe levels of exposure cannot be determined based on the available data.[144] EFSA concluded that the approval criteria for human health laid down in the EU legislation are not met.[145] A second expert discussion on chlorpyrifos-methyl took place in early September 2019, and on November 26, 2019, EFSA published its updated statement on chlorpyrifos-methyl, confirming its prior findings.[146] The Member States endorsed a proposal by the European Commission to lower the Maximum Residue Levels (MRLs) of chlorpyrifos and chlorpyrifos-methyl in food and feed to the lowest level that can be measured by analytical laboratories.[147] The new lowered MRLs apply both to food produced in the EU and also to imports.

C. PFAS – "Forever Chemicals"

PFAS – per-and polyfluoroalkyl substances – include thousands of human-

138. *See* 40 C.F.R. § 180.342; Chlorpyrifos; Reinstatement of Tolerances, 88 Fed. Reg. 7625 (Feb. 5, 2024) (to be codified at 40 C.F.R. Part 180).

139. EUR. COMM'N, *Chlorpyrifos & Chlorpyrifos-methyl*, https://food.ec.europa.eu/plants/pesticides/approval-active-substances-safeners-and-synergists/renewal-approval/chlorpyrifos-chlorpyrifos-methyl_en [https://perma.cc/R4SK-9UKS] (last visited Feb. 21, 2025).

140. *Id.*

141. EUR. FOOD SAFETY AUTH. (EFSA), *Statement on the available outcomes of the human health assessment in the context of the pesticides peer review of the active substance chlorpyrifos*, 17 EFSA J. 1, 5 (2019), https://doi.org/10.2903/j.efsa.2019.5809 [https://perma.cc/K988-SDXS].

142. FAO, IFAD, UNICEF, WFP & WHO, *supra* note 8.

143. Shabeer et al., *supra* note 5.

144. FAO, IFAD, UNICEF, WFP & WHO, *supra* note 8, at 23.

145. *See* Regulation 1107/2009, art. 4, 2009 O.J. (L 309) (EC).

146. EFSA, *supra* note 141, at 11, 21.

147. *See* Regulation 396/2005, rec. 22, 2005 O.J. (L 70) (EC).

made chemicals that have been used since the 1940s for their beneficial properties including oil repellence, stain resistance, and waterproofing.[148] The definition of PFAS varies among industries, state and federal regulatory schemes, and academia.[149] PFAS may be intentionally added to products or result from unintentional inclusion as a byproduct, contaminant, or impurity during the manufacturing process.[150] There are multiple potential exposure routes including through the use of PFAS-containing products and environmental exposure via soil, biosolids, groundwater, or surface water.[151] Many PFAS are persistent and bioaccumulative, which is the basis for the moniker "forever chemicals."[152] Ingestion of contaminated drinking water and food are the primary exposure pathways.[153] With respect to food and beverages, certain consumer products that contain PFAS include nonstick cookware, disposable food packaging and food service ware.[154]

PFAS exposure has been associated with adverse health effects in the liver, immune system, early-life development, and cardiometabolic system, as well as endocrine disruption and reproductive effects.[155] However, the diversity of PFAS chemicals makes characterization of the health effects difficult.[156] Many different regulatory strategies are being deployed to address PFAS exposure. For example, the EPA developed a Strategic Roadmap concerning PFAS regulations and reporting.[157] EPA has implemented many components of its strategy including the PFAS National Primary Drinking Water Rule.[158]

The Codex Committee on Contaminants in Foods recommended addition of PFAS to the priority list for full evaluation, including toxicological assessment and exposure assessment.[159]

---

148. RTI INT'L & CONSUMER PRODUCT SAFETY COMM'N, CHARACTERIZING PFAS CHEMISTRIES, SOURCES, USES, AND REGULATORY TRENDS IN U.S. AND INTERNATIONAL MARKETS, ES-2 (2023), https://www.cpsc.gov/s3fs-public/CPSC-PFAS-WhitePaper.pdf [https://perma.cc/6WDQ-4QBW].

149. *Id.*

150. *Id.*

151. *Id.*

152. *Id.* at ES-3.

153. *Id.*

154. *Id.*

155. *Id.*

156. *Id.*

157. U.S. ENV'T PROTECTION AGENCY, *PFAS Strategic Roadmap: EPA's Commitments to Action 2021-2024*, Docket No. EPA-100-K-21-002, (Oct. 18, 2021), https://www.epa.gov/pfas/pfas-strategic-roadmap-epas-commitments-action-2021-2024[https://perma.cc/A5HR-3PK5].

158. *See* PFAS National Primary Drinking Water Regulation, 89 Fed. Reg. 32532 (Apr. 26, 2004) (codified at 40 C.F.R. Parts 141 and 142) (establishing maximum contaminant levels (MCLs) in drinking water for perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), perfluorohexane sulfonic acid (PFHxS), perfluorononanoic acid (PFNA), hexafluoropropylene oxide dimer acid (HFPO-DA, commonly known as GenX Chemicals), and perfluorobutane sulfonic acid (PFBS)).

159. CODEX ALIMENTARIUS COMM'N, *Priority List of Contaminants and Naturally Occurring Toxicants Proposed for Evaluation by JECFA*, *in* REPORT OF THE 13RD SESSION OF THE CODE

1. FDA Regulation of PFAS in Foods

PFAS were often used in food contact substances to impart grease and water resistance to the substances.[160] Under the FFDCA, a manufacturer or supplier of a food contact substance may, at least 120 days prior to use in interstate commerce, notify the FDA of the identity, intended use, and safety of such food contact substance.[161] The notification becomes effective 120 days after receipt by FDA of the notification, unless FDA makes a determination that the food contact substance has not been shown to be safe.[162] Food contact substances are deemed unsafe unless the food additive petition and approval process has been followed and a regulation issued, or an effective notification has been submitted.[163]

FDA worked with manufacturers and suppliers regarding the voluntary phase out of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as food contact substances around 2012.[164] On March 16, 2015, FDA announced that it filed a food additive petition submitted by several organization seeking to amend food additive regulations to no longer permit the use of three long-chain PFAS (8 or more carbon atoms in length) as oil and water repellants for paper and paperboard for use in contact with aqueous and fatty foods.[165] FDA agreed with the petition concluding that there was no longer a reasonable certainty of no harm from the food-contact use of the substances.[166] FDA also amended the food additive regulation to no longer provide for the use of two additional PFAS as food contact substances because the uses were abandoned.[167] According to FDA, long-chain PFAS were no longer used as food contact substances in the U.S. as of November 2016, and FDA secured a voluntary phase out of food contact applications in the U.S. of certain short-chain PFAS (7 or fewer carbon atoms in length) that contain 6:2 fluorotelomer

---

COMMITTEE ON CONTAMINANTS IN FOODS 65, 65-66 (2019), https://www.fao.org/fao-who-codexalimentarius/sh-proxy/jp/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-735-13%252FREPORT%252FFinal%252520Report%252FREP19_CFe.pdf [https://perma.cc/PBF3-TJD6].

160. 21 U.S.C. § 348(h)(6) ("[T]he term 'food contact substance' means any substance intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use is not intended to have any technical effect in such food."); *see also* RTI INT'L AND CONSUMER PRODUCT SAFETY COMM'N, *supra* note 148, at 4-14.

161. 21 U.S.C. § 348(h)(1).

162. *Id.* § 348(h)(2)(A).

163. *Id.* § 348(a)(3).

164. *See Market Phase-Out of Grease-Proofing Substance Containing PFAS*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/food/process-contaminants-food/market-phase-out-grease-proofing-substances-containing-pfas [https://perma.cc/MR85-AHYL] (last visited Dec. 17, 2024).

165. *See* Marketing Order Regulating the Handling of Spearmint Oil Produced in the Far West, 80 Fed. Reg. 13508 (proposed Mar. 16, 2015) (to be codified at 7 C.F.R. Part 985).

166. *See* Indirect Food additives: Paper and Paperboard Components, 81 Fed. Reg. 5 (Jan. 4, 2016) (to be codified at 21 C.F.R. Part 176).

167. *See id.*

alcohol beginning in January 2021.[168] The FDA announced in February 2024 that grease-proofing substances containing PFAS are no longer sold for use as food contact substances in the U.S.[169]

Since 2019, the FDA has also been analyzing foods collected as part of its TDS as sources for PFAS.[170] Additionally, the FDA targeted sampling of seafood, which had a greater percentage of samples with detectable PFAS, and food grown in certain geographical areas contaminated with PFAS. Two voluntary recalls were issued due to health concerns associated with exposure to PFOA in canned clams.[171] The FDA has not established tolerances for PFAS in foods.

2. EU Regulation of PFAS in Foods

The EFSA requested that the Scientific Panel on Contaminants in the Food Chain ("CONTAM") prepare an opinion "on the importance of food and the relative contribution of the different foodstuffs and food contact materials to human exposure to PFOS and its salts" and advise on further steps.[172] CONTAM also considered PFOA, and derived Tolerable Daily Intake ("TDI") levels for PFOS and PFOA.[173] Following the 2008 CONTAM opinion, the European Commission recommended EU-wide monitoring of PFAS in food.[174]

After a request from the European Commission, the EFSA published a scientific evaluation of the risks to human health related to the presence of perfluoroalkyl substances in food, focusing on the sum of perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorononanoic acid (PFNA),

---

168. *See Market Phase-Out of PFAS, supra* note 164.

169. *See FDA Announces PFAS Used in Grease-Proofing Agents for Food Packaging No Longer Being Sold in the U.S.*, U.S. FOOD & DRUG ADMIN. (Feb. 28, 2024), https://www.fda.gov/food/hfp-constituent-updates/fda-announces-pfas-used-grease-proofing-agents-food-packaging-no-longer-being-sold-us [https://perma.cc/J9NT-7269].

170. *See* U.S. FOOD & DRUG ADMIN., TOTAL DIET STUDY REPORT FISCAL YEARS 2018-2020 ELEMENTS DATA 1 (2022), https://www.fda.gov/food/fda-total-diet-study-tds/fda-total-diet-study-tds-results [https://perma.cc/BB27-X3JS]. Note that results are limited by the approved analytical methods available to detect various PFAS.

171. *See Company Announcement: Bumble Bee Foods, LLC Issues Voluntary Recall on 3.75 Oz Smoked Clams Due to the Presence of Detectable Levels of PFAS Chemicals*, U.S. FOOD & DRUG ADMIN. (Jul. 6, 2022), https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/bumble-bee-foods-llc-issues-voluntary-recall-375-oz-smoked-clams-due-presence-detectable-levels-pfas [https://perma.cc/49MG-D8F4]; *see also Company Announcement: Crown Prince, Inc. Issues Voluntary Recall of Smoked Baby Clams in Olive Oil Due to the Presence of Detectable Levels of PFAS Chemicals*, U.S. FOOD & DRUG ADMIN. (Jul. 15, 2022), https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/crown-prince-inc-issues-voluntary-recall-smoked-baby-clams-olive-oil-due-presence-detectable-levels [https://perma.cc/NPA6-7MZ8].

172. Diane Benford et al., *Opinion of the Scientific Panel on Contaminants in the Food chain on perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts*, 653 EFSA J. 10 (2008), https://pmc.ncbi.nlm.nih.gov/articles/PMC10193653/ [https://perma.cc/4DK9-GZBX].

173. Wood et al., *supra* note 3.

174. *See* Recommendation 2010/161, 2010 O.J. (L 68) (EU).

and perfluorohexane sulfonic acid (PFHxS), and establishing a group tolerable weekly intake ("TWI") of 4.4 ng/kg bodyweight per week.[175] The EFSA experts also concluded that the main contributors to human dietary exposure include fish meat, fruit, fruit products, eggs and egg products.[176] The EFSA noted that two main processes are thought to lead to contamination of food with PFAS – bioaccumulation in aquatic and terrestrial food chains, and transfer from contact materials used in food processing and packaging.[177] Based on the assessment by EFSA, the EU implemented a regulation setting maximum levels for PFOS, PFOA, PFNA, PFHxS, and their sum in specific food products.[178]

Similar to the requirements under the FFDCA for food contact substances, the EU issued a regulation stating that materials and articles in contact with food[179] must be "manufactured in compliance with good manufacturing practice so that, under normal or foreseeable conditions of use, they do not transfer their constituents to food in quantities which could endanger human health, bring about an unacceptable change in the composition of the food, or bring about a deterioration in the organoleptic characteristics thereof."[180] An application for a new substance for use with a material or article must be submitted and evaluated by the EFSA and approved by the European Commission.[181] There is no process for notification and automatic approval, unless objected to by FDA, as under the FFDCA.

III. CONCLUSION

Substances that are intentionally and unintentionally added to foods are highly regulated in the U.S. and EU. While personal preferences vary regarding the use of synthetic chemicals in or on food, these man-made or synthetic substances undergo rigorous evaluation before approval. The food regulatory systems in the U.S. and EU are also designed to prevent or control, if prevention is not possible, contaminants and other unintentionally added substances. The U.S. food laws were developed over many years, are complex, and can be cumbersome to navigate. The U.S. and EU food laws were developed using similar foundational principles but with different general approaches. As a

175. EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), Dieter Schrenk et al., *Risk to human health related to the presence of perfluoroalkyl substances in food*, 18 EFSA J.157 (2020), https://doi.org/10.2903/j.efsa.2020.6223 [https://perma.cc/C5SC-QNQU].

176. *Id.* at 153.

177. *Id.* at 21.

178. Commission Regulation 2023/915, 2023 O.J. (L 119) (EU).

179. Regulation1935/2004, 2004 O.J. (L 338) (EC) (The regulation applies to "materials and articles, including active and intelligent food contact materials and articles, (hereinafter referred to as materials and articles) which in their finished state: (a) are intended to be brought into contact with food; or (b) are already in contact with food and were intended for that purpose; or (c) can reasonably be expected to be brought into contact with food or to transfer their constituents to food under normal or foreseeable conditions of use.").

180. *See* Organoleptic characteristics refer to any sensory properties of food, including taste, color, smell, and touch; *see also* Regulation 1935/2004, art. 3 ¶ 1, 2004 O.J. (L 338) (EC).

181. Regulation 1935/2004, art. 9-13.

result, these systems can have different end results, which can complicate the global food supply system and global trade. The U.S. and EU are two important systems, but there are also many other countries and laws that are implicated in global trade. While Codex can facilitate trade and harmonizing different systems, trade will continue to be influenced by the key trade partners and the associated food safety requirements, including the use and evaluation of synthetic chemicals, and will likely become even more complicated with new technological advancements, geopolitical issues, and changing environmental conditions.