APPENDIX 5: **FDA AND EPA SAFETY LEVELS IN REGULATIONS AND GUIDANCE**

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the telephone number listed on the title page of this guidance.

This appendix lists FDA and EPA levels relating to safety attributes of fish and fishery products. In many cases, these levels represent the point at which the agency could take legal action to include removing product from market. Consequently, the levels contained in this table may not always be suitable for critical limits.

Regardless of an established level or not, FDA may take legal action against food deemed to be adulterated as defined by the Federal Food, Drug and Cosmetic Act (FD&C Act) [21 U.S.C. 342]. A food is adulterated if the food bears or contains any poisonous or deleterious substance which may render it injurious to health under section 402 (a)(1) of the FD&C Act. Additionally, a food is adulterated if the food has been prepared, packed or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health under section 402 (a)(4) of the FD&C Act.

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ANIMAL DRUGS

Products	Levels	References
All fish [10]	Drugs prohibited for extra-label use in animals: No residue permitted for the following: • Chloramphenicol; • Clenbuterol; • Diethylstilbestrol (DES); • Dimetridazole, Ipronidazole, and other Nitroimidazoles; • Furazolidone, Nitrofurazone, and other nitrofurans; • Fluoroquinilones; • Glycopeptides.	21 CFR 530.41
Finfish and lobster	Sum of tetracycline residues, including oxytetracycline, chlortetracycline, and tetracycline [1]: • ≥ 2.0 ppm (muscle tissue)	21 CFR 556.500
Salmonids	Azamethiphos [9]: • ≥ 0.02 ppm (muscle/adhering skin)	Import Tolerance (https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm)
Atlantic salmon and Rainbow trout	Benzocaine [9]: • ≥ 0.05 ppm (muscle with adhering skin)	Import Tolerance (https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm)
Salmonids and Walleye	Chloramine-T [1] (para-toluenesulfonamide-marker residue): • ≥ 0.90 ppm (muscle/skin)	21 CFR 556.118

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Products	Levels	References
Freshwater-reared finfish (other than catfish) and salmonids, and catfish	Florfenicol (florfenicol amine-the marker residue): • Freshwater-reared finfish (other than catfish) and salmonids: ≥ 1.0 ppm (muscle/skin); • Catfish: ≥ 1.0 ppm (muscle)	21 CFR 556.283
Salmonids	Lufenuron [9]: • ≥ 1.35 ppm (muscle/adhering skin)	Import Tolerance (https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm)
Salmonids and catfish	Sulfadimethoxine/ormetoprim combination [1]: • ≥ 0.1 ppm for each drug (edible tissue)	21 CFR 556.640
Trout	Sulfamerazine [1]: • No residue permitted	21 CFR 556.660
Atlantic salmon	Telflubenzuron [9]: • ≥ 0.5 ppm (muscle/adhering skin)	Import Tolerance (https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm)

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BIOLOGICAL

Products	Levels	References
All fish [10]	*Clostridium botulinum:* • Presence of viable spores or vegetative cells in products that will support their growth; OR • Presence of toxin [12]	International Commission on Microbiology Specifications for Food (ICMSF). 1996. Microorganisms in Food 5. Microbiological specification of food pathogens. London: Blackie Academic and Professional
All fish [10]. that is Ready-to-eat (RTE) as defined in 21 CFR 117.3 (including raw and cooked)	*Listeria monocytogenes:* • Presence of organism [12]	Shank F.R., E. L. Elliot, I. K. Wachsmuth, and M. E. Losikoff. 1996. US position on *Listeria monocytogenes* in foods. Food Control. 7: 229-234
All fish [10]	*Salmonella* spp.: • Presence of organism [12]	Sec. 555.300 Compliance Policy Guide
All fish [10]	*Staphylococcus aureus:* • Positive for staphylococcal enterotoxin; OR • ≥ 10^4/g (MPN); OR • Levels indicative of insanitary conditions [12]	Compliance Program 7303.842
All fish [10] that has been previously cooked	*Vibrio* spp.: • Presence of organism [12]	International Commission on Microbiology Specifications for Food (ICMSF. 1996. Microorganisms in Food 5. Microbiological specification of food pathogens. London: Blackie Academic and Professional

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Products	Levels	References
Raw bivalve shellfish [11]	*Vibrio cholerae:* • Presence of toxigenic organism	National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish
Raw fish [10] other than raw bivalve shellfish that is ready-to-eat (RTE) as defined in 21 CR 117.3	*Vibrio cholerae:* • Presence of organism [12]	International Commission on Microbiology Specifications for Food (ICMSF. 1996. Microorganisms in Food 5. Microbiological specification of food pathogens. London: Blackie Academic and Professional
Post-harvest processed clams, mussels, oysters, and whole and roe-on scallops, fresh or frozen, that make a label claim of "processed to reduce *Vibrio parahaemolyticus* to non-detectable levels."	*Vibrio parahaemolyticus:* • ≥ 30 MPN/g	National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish
Raw bivalve shellfish [11]	*Vibrio parahaemolyticus:* • ≥ 1×10^4/g	National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish
Post-harvest processed clams, mussels, oysters, and whole and roe-on scallops, fresh or frozen, that make a label claim of "processed to reduce *Vibrio vulnificus* to non-detectable levels."	*Vibrio vulnificus:* • ≥ 30 MPN/g	National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish

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CHEMICAL

Products	Levels	References
Fish and shellfish [13]	2,4-Dichlorophenoxyacetic acid (2,4-D) [1]: • Fish: > 0.1 ppm; • Shellfish: > 1.0 ppm	40 CFR 180.142
All fish [10]	Aldrin and dieldrin: • ≥ 0.3 ppm (edible portion).	Sec. 575.100 Compliance Policy Guide
Crayfish	Bensulfuron methyl • >0.05 ppm	40 CFR 180.445
Frog legs	Benzene Hexachloride (BHC): • ≥ 0.3 ppm (edible portion)	Sec. 575.100 Compliance Policy Guide
Fish freshwater [13]	Bispyribac-sodium [1]: • > 0.01 ppm	40 CFR 180.577
Oysters [13]	Carbaryl [1]: • > 0.25 ppm	40 CFR 180.169
Fish and shellfish [13]	Carfentrazone-ethyl [1]: • > 0.3 ppm	40 CFR 180.515
Crayfish	Chlorantraniliprole • >8.0 ppm	40 CFR 180.628
All fish [10]	Chlordane: • ≥ 0.3 ppm (edible portion)	Sec. 575.100 Compliance Policy Guide

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Products	Levels	References
All fish [10]	Chlordecone: • Crabmeat: ≥ 0.4 ppm; • Other fish: ≥ 0.3 ppm (edible portion)	Sec. 575.100 Compliance Policy Guide
All fish [10]	DDT, TDE, and DDE: • ≥ 5.0 ppm (edible portion)	Sec. 575.100 Compliance Policy Guide
Fish – • freshwater finfish • freshwater finfish, farm raised • saltwater finfish, tuna, other	Deltamethrin: • >0.1 ppm	40 CFR 180.435
Fish and shellfish [13]	Diquat [1]: • Fish: > 2.0 ppm; • Shellfish: > 20.0 ppm	40 CFR 180.226
Fish – freshwater finfish, farm raised [13]	Diuron and its metabolites [1]: • > 2.0 ppm	40 CFR 180.106
Fish [13]	Endothall and its monomethyl ester [1]: • > 0.1 ppm	40 CFR 180.293
All fish [10]	Ethoxyquin: • > 0.5 ppm (edible muscle)	21 CFR 172.140
Fish, freshwater [13]	Flumioxazin [1]: • > 1.5 ppm	40 CFR 180.568

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Products	Levels	References
Crayfish, and Fish [13]	Fluridone [1]: • > 0.5 ppm	40 CFR 180.420
Fish – • Freshwater finfish, • Shellfish, crustacean, and • Shellfish, mollusc [13]	Florpyrauxifen-benzyl [1]: • Freshwater Finfish: > 2.0 ppm; • Shellfish, crustacean: > 0.5 ppm; • Shellfish, mollusc: > 20.0 ppm	40 CFR 180.695
Fish, and shellfish [13]	Glyphosate [1]: • Fish: > 0.25 ppm; • Shellfish: > 3.0 ppm	40 CFR 180.364
All fish [10]	Heptachlor and heptachlor epoxide: • ≥ 0.3 ppm (edible portion)	Sec. 575.100 Compliance Policy Guide
Scombrotoxin-forming fish, e.g., Tuna, mahi-mahi, and related fish	Histamine: • ≥ 500 ppm - toxic; • ≥ 50 ppm - decomposed	Sec. 540.525 Compliance Policy Guide
Fish and shellfish [13]	Imazapyr [1]: • Fish: > 1.0 ppm; • Shellfish: > 0.1 ppm	40 CFR 180.500
Crayfish	Imazethapyr: • > 0.15 ppm	40 CFR 180.447

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Products	Levels	References
Fish and Shellfish, molluscs	Imidacloprid: • Fish: > 0.05 ppm • Shellfish, and molluscs: > 0.05 ppm	40 CFR 180.472
All fish [10]	Methylmercury [2]: • ≥ 1.0 ppm	Sec. 540.600 Compliance Policy Guide
All fish [10]	Mirex: • ≥ 0.1 ppm (edible portion)	Sec. 575.100 Compliance Policy Guide
Crayfish	Pendimethalin: • >0.05 ppm	40 CFR 180.361
Fish, • Fish • Shellfish, crustacean, and • Shellfish, mollusc [13]	Penoxsulam [1]: • Fish: > 0.01 ppm; • Shellfish, crustacean: > 0.01 ppm; • Shellfish, mollusc: > 0.02 ppm	40 CFR 180.605
All fish [10]	Polychlorinated Biphenyls [1]. (PCBs): • ≥ 2.0 ppm (edible portion)	21 CFR 109.30
Crayfish	Propanil • >0.05 ppm	40 CFR 180.274
Fish – Shellfish, crustacean	Quizalofop ethyl • > 0.04 ppm	40 CFR 180.441
Fish – freshwater finfish, and Fish – Shellfish, crustacean [13]	Saflufenacil [1]: • > 0.01 ppm	40 CFR 180.649

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Products	Levels	References
Fish, Fish – Shellfish, crustacean, and Fish – shellfish, mollusc [13]	Spinosad [1]: • > 4.0 ppm	40 CFR 180.495
Fish and shellfish [4]	Triclopyr and its metabolites and degradates [1]: • Fish: > 3.0 ppm. • Shellfish: >3.5 ppm	40 CFR 180.417
Fish – • Freshwater finfish, • Saltwater finfish, • Shellfish, crustacean, and • Shellfish mollusc [13]	Topramezone [1]: • > 0.05 ppm	40 CFR 180.612

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NATURAL TOXINS

Products	Levels	References
Bivalve shellfish [11]	Azaspiracid [3, 6] (Azaspiracid Shellfish Poisoning (AZP)): • ≥ 0.16 mg/kg azaspiracid-1 equivalents (i.e., combined azaspiracid-1, -2, and -3)	National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish
Clams, mussels, oysters, and whole and roe-on scallops, fresh, frozen, or canned [11]	Brevetoxin [5, 6] (Neurotoxic Shellfish Poisoning (NSP)): • ≥ 0.8 mg/kg (20 mouse units/100 g) brevetoxin-2 equivalent or 5,000 cells/L	National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish
Finfish (primarily reef fish)	Ciguatoxin [4] (Ciguatera Fish Poisoning (CFP)): • Caribbean ciguatoxins: ≥ 0.1 µg/kg Caribbean ciguatoxin-1 (C-CTX-1) equivalents; • Indian ciguatoxins: Guidance levels have yet to be established; • Pacific ciguatoxins: ≥ 0.01 µg/kg Pacific ciguatoxin-1 (P-CTX-1) equivalents	Dickey, R.W. and S.M. Plakas. 2010. Ciguatera: A public health perspective. Toxicon 56(2): 123-136. Dickey, R. W. 2008. Ciguatera toxins: chemistry, toxicology, and detection, p. 479–500. In L. M. Botana (ed.), Seafood and freshwater toxins: pharmacology, physiology, and detection, 2nd ed. CRC Press/Taylor & Francis
All fish [10]	Domoic acid [6] (Amnesic Shellfish Poisoning (ASP)): • ≥ 20 mg/kg domoic acid (except Dungeness crab viscera); • > 30 mg/kg domoic acid (Dungeness crab viscera ONLY)	Compliance Program 7303.842. National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish: FDA Memorandum, Director, Office of Seafood. Marine Biotoxins in Dungeness Crab. January 14, 1993
Clams, mussels, oysters, and whole and roe-on scallops, fresh, frozen, or canned [11]	Okadaic acid [3] (Diarrhetic Shellfish Poisoning (DSP)): • ≥ 0.16 mg/kg total okadaic acid equivalents (i.e., combined free okadaic acid, dinophysistoxins-1 and -2, and their acyl-esters)	National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish

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Products	Levels	References
All fish [10]	Saxitoxin [3, 6] (Paralytic Shellfish Poisoning (PSP)): • ≥ 0.8 mg/kg saxitoxin equivalent (80 µg/100 g)	Sec. 540.250 Compliance Policy Guide. Compliance Program 7303.842

PHYSICAL

Products	Levels	References
All fish 10	Hard or sharp foreign object: • Generally, 0.3 (7 mm) – 1.0 (25 mm) in length	Sec. 555.425 Compliance Policy Guide

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ACRONYMS: MPN = Most probable number; **CTX** = ciguatoxin.

FOOTNOTES:

1. These values are tolerances. (Reference: 21CFR 109, 21CFR 556 and 40 CFR 180).
2. Refer to Chapter 10 – Methylmercury for additional information.
3. AZP, DSP, and PSP equivalents are based on chemical abundance as determined by instrumental analysis. In some cases (i.e. AZP, DSP, and PSP), toxicity equivalent factors (TEFs) may be available and should be considered in determining total toxin equivalents.
4. CFP equivalents are based on in vitro (cell culture bioassay) toxicity.
5. NSP equivalents are based on in vivo (mouse bioassay toxicity).
6. Refer to the National Shellfish Sanitation Program: Guide for Control of Molluscan Shellfish for details on approved methodologies for Biotoxin analysis of molluscan shellfish. (https://www.fda.gov/Food/GuidanceRegulation/FederalStateFoodPrograms/ucm2006754.htm).
7. Refer to Chapter 6 – Natural Toxins for additional information.
8. Guidance levels used to confirm illnesses (i.e., CFP), inform advisories for at risk harvest areas (i.e., CFP) and/or make a determination for harvest area closures (i.e., ASP, AZP, DSP, NSP, and PSP.) Guidance levels are not intended to be identified in the HACCP plan as a control measure.
9. These values are import tolerances (Reference: https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm).
10. The term "fish" and "fishery products" are defined in the Fish and Fishery Products Regulation (21 CFR 123.3(d) and 123.3(e)) as follows:
    - Fish – Fresh or saltwater finfish, crustaceans, other forms of aquatic animal life (including, but not limited to, alligator, frog, aquatic turtle, jellyfish, sea cucumber, and sea urchin and the roe of such animals) other than birds or mammals, and all mollusks, where such animal life is intended for human consumption
    - Fishery products – any human food product in which fish is a characterizing ingredient.
11. The term "shellfish" is defined in the NSSP as all species of:
    a. Oysters, clams, or mussels, whether:
        i. Shucked or in the shell;
        ii. Raw, including post-harvest processed;
        iii. Frozen or unfrozen;
        iv. Whole or in part; and
    b. Scallops in any form, except when the final product form is the adductor muscle only.
12. Detectable by methods equivalent to FDA's Bacteriological Analytical Manual.
13. Products and "fish" are defined through EPA's References. Refer to the EPA for explanation.

NOTES: