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.
# TABLE A-5

## FDA AND EPA SAFETY LEVELS IN REGULATIONS AND GUIDANCE

### ANIMAL DRUGS

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>All fish ¹⁰</td>
<td>Drugs prohibited for extra-label use in animals:</td>
<td>21 CFR 530.41</td>
</tr>
<tr>
<td></td>
<td>• No residue permitted for the following:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Chloramphenicol;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Clenbuterol;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Diethylstilbestrol (DES);</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Dimetridazole, Ipronidazole, and other Nitroimidazoles;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Furazolidone, Nitrofurazone, and other nitrofurans;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Fluoroquinolones;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Glycopeptides</td>
<td></td>
</tr>
<tr>
<td>Finfish and lobster</td>
<td>Sum of tetracycline residues, including oxytetracycline, chlortetracycline, and tetracycline³:</td>
<td>21 CFR 556.500</td>
</tr>
<tr>
<td></td>
<td>• ≥ 2.0 ppm (muscle tissue)</td>
<td></td>
</tr>
<tr>
<td>Salmonids</td>
<td>Azamethiphos⁹:</td>
<td>Import Tolerance</td>
</tr>
<tr>
<td></td>
<td>• ≥ 0.02 ppm (muscle/adhering skin)</td>
<td><a href="https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm">https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm</a></td>
</tr>
<tr>
<td>Atlantic salmon and Rainbow trout</td>
<td>Benzocaine⁴:</td>
<td>Import Tolerance</td>
</tr>
<tr>
<td></td>
<td>• ≥ 0.05 ppm (muscle with adhering skin)</td>
<td><a href="https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm">https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm</a></td>
</tr>
<tr>
<td>Salmonids and Walleye</td>
<td>Chloramine-T¹ (para-toluenesulfonamide-marker residue):</td>
<td>21 CFR 556.118</td>
</tr>
<tr>
<td></td>
<td>• ≥ 0.90 ppm (muscle/skin)</td>
<td></td>
</tr>
</tbody>
</table>

Appendix 5: FDA and EPA Safety Levels in Regulations and Guidance

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## TABLE A-5
FDA AND EPA SAFETY LEVELS IN REGULATIONS AND GUIDANCE

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
</table>
| 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). |

### BIOLOGICAL

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
</table>
| All fish\(^10\) | Clostridium botulinum:  
• Presence of viable spores or vegetative cells in products that will support their growth;  
OR  
| All fish\(^10\) that is Ready-to-eat (RTE) as defined in 21 CFR 117.3 (including raw and cooked) | Listeria monocytogenes:  

Appendix 5: FDA and EPA Safety Levels in Regulations and Guidance

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<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>All fish\textsuperscript{10}</td>
<td>\textit{Salmonella} spp.:</td>
<td>Sec. 555.300 Compliance Policy Guide</td>
</tr>
<tr>
<td></td>
<td>• Presence of organism\textsuperscript{12}</td>
<td></td>
</tr>
<tr>
<td>All fish\textsuperscript{10}</td>
<td>\textit{Staphylococcus aureus}:</td>
<td>Compliance Program 7303.842</td>
</tr>
<tr>
<td></td>
<td>• Positive for staphylococcal enterotoxin;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ( \geq 10^4 / \text{g (MPN)} );</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Levels indicative of insanitary conditions\textsuperscript{12}</td>
<td></td>
</tr>
<tr>
<td>All fish\textsuperscript{10} that has been previously cooked</td>
<td>\textit{Vibrio} spp.:</td>
<td>International Commission on Microbiology Specifications for Food (ICMSF, 1996. Microorganisms in Food 5. Microbiological specification of food pathogens. London: Blackie Academic and Professional</td>
</tr>
<tr>
<td></td>
<td>• Presence of organism\textsuperscript{12}</td>
<td></td>
</tr>
<tr>
<td>Raw bivalve shellfish\textsuperscript{11}</td>
<td>\textit{Vibrio cholerae}:</td>
<td>National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish</td>
</tr>
<tr>
<td></td>
<td>• Presence of toxigenic organism.</td>
<td></td>
</tr>
<tr>
<td>Raw fish\textsuperscript{10} other than raw bivalve shellfish that is ready-to-eat (RTE) as defined in 21 CR 117.3</td>
<td>\textit{Vibrio cholerae}:</td>
<td>International Commission on Microbiology Specifications for Food (ICMSF, 1996. Microorganisms in Food 5. Microbiological specification of food pathogens. London: Blackie Academic and Professional</td>
</tr>
<tr>
<td></td>
<td>• Presence of organism\textsuperscript{12}</td>
<td></td>
</tr>
<tr>
<td>Post-harvest processed clams, mussels, oysters, and whole and roe-on scallops, fresh or frozen, that make a label claim of “processed to reduce \textit{Vibrio parahaemolyticus} to non-detectable levels”</td>
<td>\textit{Vibrio parahaemolyticus}:</td>
<td>National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish</td>
</tr>
<tr>
<td></td>
<td>• ( \geq 30 \text{ MPN/g} )</td>
<td></td>
</tr>
<tr>
<td>Raw bivalve shellfish\textsuperscript{11}</td>
<td>\textit{Vibrio parahaemolyticus}:</td>
<td>National Shellfish Sanitation Program Guide for the Control of Molluscan Shellfish</td>
</tr>
<tr>
<td></td>
<td>• ( \geq 1 \times 10^4 / \text{g} )</td>
<td></td>
</tr>
</tbody>
</table>

Appendix 5: FDA and EPA Safety Levels in Regulations and Guidance

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### TABLE A-5
FDA AND EPA SAFETY LEVELS IN REGULATIONS AND GUIDANCE

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
</table>
| 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 |

### CHEMICAL

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
</table>
| 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                 |
| 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                                      |
| All fish\(^{10}\)         | Chlordane:  
  - ≥ 0.3 ppm (edible portion) | Sec. 575.100 Compliance Policy Guide                 |

Appendix 5: FDA and EPA Safety Levels in Regulations and Guidance

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### TABLE A-5
**FDA AND EPA SAFETY LEVELS IN REGULATIONS AND GUIDANCE**

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
</table>
| 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 and shellfish[^13] | Diquat[^1]:  
• Fish > 2.0 ppm;  
• Shellfish > 20.0 ppm | 40 CFR 180.226 |
• > 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 |
| Crayfish, and Fish[^13] | Fluridone[^1]:  
• > 0.5 ppm | 40 CFR 180.420 |
• > 0.01 ppm | 40 CFR 180.666 |

[^10]: All fish
[^13]: Fish and shellfish
[^1]: Fish – freshwater finfish, farm raised

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Appendix 5: FDA and EPA Safety Levels in Regulations and Guidance
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<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish – freshwater finfish,</td>
<td>Florpyrauxifen-benzyl:(^1):</td>
<td>40 CFR 180.695</td>
</tr>
<tr>
<td>Fish – shellfish, crustacean, and</td>
<td>• Freshwater Finfish &gt; 2.0 ppm;</td>
<td></td>
</tr>
<tr>
<td>Fish – shellfish, mollusc(^13)</td>
<td>• Shellfish, crustacean &gt; 0.5 ppm;</td>
<td></td>
</tr>
<tr>
<td>Fish, and shellfish(^13)</td>
<td>• Shellfish, mollusc &gt; 20.0 ppm</td>
<td></td>
</tr>
<tr>
<td>All fish(^10)</td>
<td>Glyphosate(^1):</td>
<td>40 CFR 180.364</td>
</tr>
<tr>
<td></td>
<td>• Fish &gt; 0.25 ppm;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Shellfish &gt; 3.0 ppm</td>
<td></td>
</tr>
<tr>
<td>Scombrotxin-forming fish, e.g., Tuna, mahimahi, and related fish</td>
<td>Histamine:</td>
<td>Sec. 540.525 Compliance Policy Guide</td>
</tr>
<tr>
<td></td>
<td>• ≥ 500 ppm - toxic;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ≥ 50 ppm - decomposed</td>
<td></td>
</tr>
<tr>
<td>Fish and shellfish(^13)</td>
<td>Imazapyr(^1):</td>
<td>40 CFR 180.500</td>
</tr>
<tr>
<td></td>
<td>• Fish &gt; 1.0 ppm;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Shellfish &gt; 0.1 ppm</td>
<td></td>
</tr>
<tr>
<td>All fish(^10)</td>
<td>Methylmercury(^2):</td>
<td>Sec. 540.600 Compliance Policy Guide</td>
</tr>
<tr>
<td></td>
<td>• ≥ 1.0 ppm</td>
<td></td>
</tr>
<tr>
<td>All fish(^10)</td>
<td>Mirex:</td>
<td>Sec. 575.100 Compliance Policy Guide</td>
</tr>
<tr>
<td></td>
<td>• ≥ 0.1 ppm (edible portion)</td>
<td></td>
</tr>
<tr>
<td>Products</td>
<td>Levels</td>
<td>References</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>------------</td>
</tr>
<tr>
<td>Fish, Fish – shellfish, crustacean, and Fish – shellfish, mollusc¹³</td>
<td>Penoxsulam¹:\n- Fish &gt; 0.01 ppm;\n- Shellfish, crustacean &gt; 0.01 ppm;\n- Shellfish, mollusc &gt; 0.02 ppm</td>
<td>40 CFR 180.605</td>
</tr>
<tr>
<td>All fish¹⁰</td>
<td>Polychlorinated Biphenyls¹ (PCBs):\n- ≥ 2.0 ppm (edible portion)</td>
<td>21 CFR 109.30</td>
</tr>
<tr>
<td>Fish – freshwater finfish, and Fish – shellfish, crustacean¹³</td>
<td>Saflufenacil¹:\n- &gt; 0.01 ppm</td>
<td>40 CFR 180.649</td>
</tr>
<tr>
<td>Fish, Fish – shellfish, crustacean, and Fish – shellfish, mollusc¹³</td>
<td>Spinosad¹:\n- &gt; 4.0 ppm</td>
<td>40 CFR 180.495</td>
</tr>
<tr>
<td>Fish¹³</td>
<td>Triclopyr and its metabolites and degradates¹:\n- &gt; 3.0 ppm</td>
<td>40 CFR 180.417</td>
</tr>
<tr>
<td>Fish – freshwater finfish, Fish – saltwater finfish, Fish – shellfish, crustacean, and Fish – shellfish mollusc¹³</td>
<td>Topramezone¹:\n- &gt; 0.05 ppm</td>
<td>40 CFR 180.612</td>
</tr>
</tbody>
</table>
### TABLE A-5
FDA AND EPA SAFETY LEVELS IN REGULATIONS AND GUIDANCE

<table>
<thead>
<tr>
<th>Products.</th>
<th>Levels.</th>
<th>References.</th>
</tr>
</thead>
</table>
| **Bivalve shellfish**

  **Azaspiracid**\(^7,8\) (Azaspiracid Shellfish Poisoning (AZP)):

  • ≥ 0.16 mg/kg azaspiracid-1 equivalents (i.e., combined azaspiracid-1, -2, and -3).

| **Clams, mussels, oysters, and whole and roe-on scallops, fresh, frozen, or canned**

  **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.


| **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.


| **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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### TABLE A-5
FDA AND EPA SAFETY LEVELS IN REGULATIONS AND GUIDANCE

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>All fish&lt;br&gt;10</td>
<td>Saxitoxin&lt;sup&gt;3, 6&lt;/sup&gt; (Paralytic Shellfish Poisoning (PSP)):&lt;br&gt;• ≥ 0.8 mg/kg saxitoxin equivalent (80 µg/100 g)</td>
<td>Sec. 540.250 Compliance Policy Guide&lt;br&gt;Compliance Program 7303.842</td>
</tr>
</tbody>
</table>

#### PHYSICAL

<table>
<thead>
<tr>
<th>Products</th>
<th>Levels</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>All fish&lt;br&gt;10</td>
<td>Hard or sharp foreign object:&lt;br&gt;• Generally 0.3 (7 mm) – 1.0 (25 mm) in length</td>
<td>Sec. 555.425 Compliance Policy Guide</td>
</tr>
</tbody>
</table>

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

**FOOTNOTES:**

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](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](https://www.fda.gov/animalveterinary/products/importexports/ucm315830.htm)).

Appendix 5: FDA and EPA Safety Levels in Regulations and Guidance
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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.


13. Products and “fish” are defined through EPA’s References. Refer to the EPA for explanation.
Appendix 5: FDA and EPA Safety Levels in Regulations and Guidance

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