

Sec. 540.525 Scombrototoxin (Histamine)-forming Fish and Fishery Products – Decomposition and Histamine (CPG 7108.24) Draft Compliance Policy Guide Guidance for FDA Staff

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Guidance for FDA Staff

This draft compliance policy guide, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or we) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guide at the phone number listed on the title page.

I. Introduction

The purpose of this compliance policy guide (CPG) is to provide guidance for FDA staff on adulteration associated with decomposition and/or histamine identified during surveillance sampling and testing of fish and fishery products susceptible to histamine formation. This CPG is being revised to update FDA regulatory action guidance for sensory analysis and histamine levels in scombrototoxin-forming fish and fishery products.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this CPG, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidances means that something is suggested or recommended, but not required.

II. Background

The composition of the muscle tissue in certain fish species, such as tuna and mahi-mahi, can cause histamine, among other spoilage compounds, to form due to the activity of

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enzymes produced by spoilage bacteria after the fish die. Unless these particular fish are properly chilled promptly after death and maintained in a chilled state, or are otherwise treated or processed to prevent further microbial activity, histamine can accumulate in the edible muscle of these fish. Once formed, histamine cannot reliably be removed by subsequent activities, such as washing, freezing, or heating.

Properly harvested and handled fish and fishery products have little to no detectable histamine. The presence of 35 ppm or more histamine in fish is evidence of considerable and avoidable time and temperature exposures resulting in microbial-induced decomposition (i.e., the conversion of histidine to histamine in the fish muscle by bacterial enzymes) whether or not the decomposition is detected by sensory examination.¹

Elevated histamine can be prevented in fish by adherence to Current Good Manufacturing Practices (CGMPs) (21 CFR Part 117, Subpart B) and Hazard Analysis Critical Control Point (HACCP) principles required by FDA's Fish and Fishery Products regulation (21 CFR Part 123) by each processor in the distribution chain. It is important to control the time and temperature of fish at each point in the distribution chain beginning with harvesters and the first receivers of fish from harvest vessels, along with the use of proper precautions by retailers and consumers. Therefore, testing that reveals elevated histamine in FDA's surveillance samples is indicative of improper harvesting, processing, and/or storage of the sampled lot or shipment. Additional information about scombrototoxin (histamine) formation in fish and the scombrototoxin hazard and its controls can be found in FDA's Fish and Fishery Products Hazards and Controls Guidance² and FDA's Bad Bug Book.³

In addition, scombrototoxin fish poisoning (sometimes also referred to as scombroid poisoning or histamine poisoning) continues to represent the highest number of illnesses associated with finfish in the United States.⁴ Adoption of a 200-ppm histamine level based on the possibility of human illness at or above that level is consistent with a conclusion of an international group of histamine and risk assessment experts convened by the Food and Agriculture Organization of the United Nations and World Health

¹ Staruszkiewicz, W.F., J.D. Barnett, P.L. Rogers, R.A. Benner, Jr., L.L. Wong, and J. Cook. 2004. Effects of on-board and dockside handling on the formation of biogenic amines in mahimahi (*Coryphaena hippurus*), skipjack tuna (*Katsuwonus pelamis*), and yellowfin tuna (*Thunnus albacares*). *J. Food Prot.* 67(1):134-141.

² FDA. Fish and Fishery Products Hazards and Controls Guidance, Fourth Edition. March 2020. Available at: <https://www.fda.gov/food/seafood-guidance-documents-regulatory-information/fish-and-fishery-products-hazards-and-controls>.

³ FDA. Bad Bug Book, Foodborne Pathogenic Microorganisms and Natural Toxins. 2012. Available at: <https://www.fda.gov/food/foodborne-pathogens/bad-bug-book-second-edition>.

⁴ Centers for Disease Control and Prevention. 2017. Surveillance for Foodborne Disease Outbreaks. Annual Report. Available at: https://www.cdc.gov/fdoss/pdf/2017_FoodBorneOutbreaks_508.pdf.

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Organization (FAO/WHO) and reported in 2013,⁵ and aligns the U.S. with other nations.⁶ In addition, the Codex Alimentarius standards⁷ also identify 200 ppm as a health-related threshold.

III. Policy

FDA may regard scombrototoxin-forming fish or fishery products to be adulterated within the meaning of section 402(a)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 342(a)(1)) in that they bear or contain a poisonous or deleterious substance which may render them injurious to health, when histamine is present at or above 200 ppm, as established by testing.

FDA may regard scombrototoxin-forming fish or fishery products to be adulterated within the meaning of section 402(a)(3) of the FD&C Act (21 U.S.C. 342(a)(3)) in that they consist in whole or in part of any filthy, putrid, or decomposed substance, when histamine is present at or above 35 ppm or when evidence of decomposition is detected by sensory analysis.

FDA may regard scombrototoxin-forming fish or fishery products to be adulterated within the meaning of section 402(a)(4) of the FD&C Act (21 U.S.C. 342(a)(4)) in that they have been prepared, packed, or held under insanitary conditions whereby they may have become contaminated with filth, or whereby they may have been rendered injurious to health, when histamine is present at or above 35 ppm.

IV. Regulatory Action Guidance

The following regulatory action guidance is applicable to FDA's surveillance sample test results for all fish and fishery products that are associated with scombrototoxin (histamine) formation except dried fish and fermented fish sauce/paste products that are intended for use only as condiments or as minor flavoring ingredients in other food products. Fish species associated with histamine formation and scombrototoxin (histamine) fish poisoning are listed in FDA's Fish and Fishery Products Hazards and Controls Guidance, Chapter 3, Table 3-2. Decomposition in non-scombrototoxin-forming fish and fishery products is addressed in CPG Sec. 540.370 Fish and Fishery Products – Decomposition.⁸

⁵ FAO/WHO [Food and Agriculture Organization of the United Nations/World Health Organization]. 2013. Public Health Risks of Histamine and other Biogenic Amines from Fish and Fishery Products. Meeting Report. Available at: https://www.who.int/foodsafety/publications/histamine_risk/en/.

⁶ For example, the European Commission has had this threshold since 2005. See Commission Regulation No 2073/2005.

⁷ See e.g., Codex STAN 36-1981, Standard for Quick Frozen Finfish, Uneviscerated and Eviscerated, Codex STAN 94-1981, Standard for Canned Sardines and Sardine-Type Products, Codex STAN 119-1981, Standard for Canned Finfish, Codex STAN 190-1995, Standard for Quick Frozen Fish Fillets; Codex STAN 236-2003, Standard for Boiled Dried Salted Anchovies, Codex STAN 244-2004, Standard for Salted Atlantic Herring and Salted Sprat.

⁸ FDA. CPG Sec. 540.370 Fish and Fishery Products – Decomposition. 2009. Available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cpg-sec-540370-fish-and-fishery-products-decomposition>.

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An appropriate ORA Program Field Office may initiate an enforcement action involving any of the violative situations described in the preceding section, provided at least one of the three following general requirements is met:

A. Decomposed

An article of scombrototoxin-forming fish or fishery products meets criterion 1. or 2. (below)

1. Sensory evidence of decomposition

Using a two-class, pass/fail evaluation approach, the presence of decomposition is detected in:

- a. a minimum of two (2) subsamples from a lot when up to 30 subsamples are examined from the lot; or
- b. a minimum of one (1) subsample from a lot when the lot consists of fewer than 30 units (fish or cartons of fish) and subsamples were collected and examined from all available units.

The presence of decomposition is detected in a subsample, i.e., the subsample “fails” the decomposition evaluation, when:

- a. 20% or more of the edible portion, or portions/pieces within a subsample, contains definite and persistent sensory attributes indicative of decomposition; and/or
- b. in the case of canned tuna, honeycombing of the tuna is observed;

as determined by qualified FDA seafood sensory analysts (a current list of qualified FDA seafood sensory analysts may be obtained from ORA, Office of Regulatory Science).

2. Histamine levels as evidence of decomposition

A histamine level equal to or greater than 35 ppm is detected by original and check analysis in one (1) or more subsamples from a lot when up to 30 subsamples are analyzed from the lot. The analytical method(s) identified for histamine detection in the applicable Compliance Program (CP) (CP 7303.842 or CP 7303.844) should be used.

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B. Bears or Contains a Deleterious Substance

For an article of scombrototoxin-forming fish or fishery products, a histamine level equal to or greater than 200 ppm is detected by original and check analysis in one (1) or more subsamples from a lot when up to 30 subsamples are examined from the lot.

The analytical method(s) identified for histamine detection in the applicable CP (CP 7303.842 or CP 7303.844) should be used.

Documented evidence of a scombrototoxin fish poisoning associated with an article of fish, irrespective of histamine content, should be reported to the Office of the Commissioner's (OC) Office of Emergency Operations (OEO), and CFSAN's Coordinated Outbreak Response and Evaluation Network (CORE).

C. Prepared, Packed, or Held Under Insanitary Conditions

For an article of scombrototoxin-forming fish or fishery products, a histamine level equal to or greater than 35 ppm is detected by original and check analysis in one (1) or more subsamples from a lot when up to 30 subsamples are examined from the lot.

The analytical method(s) identified for histamine detection in the applicable CP (CP 7303.842 or CP 7303.844) should be used.

Other Considerations

The criteria in this guidance do not establish an acceptable level of decomposition or histamine in food. Processors and owners of scombrototoxin-forming fish and fishery products are responsible for ensuring that the food complies with the FD&C Act. FDA may choose to take regulatory action against adulterated food within the meaning of the FD&C Act that does not meet the direct reference criteria in this guidance.

V. Specimen Charges

Domestic Action

A. Decomposed

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate commerce, within the meaning of section 402(a)(3) of the FD&C Act (21 U.S.C. 342(a)(3)) in that it consists in whole or in part of a decomposed substance.

B. Bears or Contains a Deleterious Substance

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate

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commerce, within the meaning of section 402(a)(1) of the FD&C Act (21 U.S.C. 342(a)(1)) in that it bears or contains a poisonous or deleterious substance, namely histamine, which may render it injurious to health.

C. Prepared, Packed, or Held Under Insanitary Conditions

The article of food was adulterated when introduced into and while in interstate commerce and is adulterated while held for sale after shipment in interstate commerce, within the meaning of section 402(a)(4) of the FD&C Act (21 U.S.C. 342(a)(4)) in that it 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.⁹

Import Refusal

A. Decomposed

The article of food is subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act (21 U.S.C. 381(a)(3)) in that it appears to be adulterated within the meaning of section 402(a)(3) of the FD&C Act (21 U.S.C. 342(a)(3)) in that it consists in whole or in part of a decomposed substance.

B. Bears or Contains a Deleterious Substance

The article of food is subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act (21 U.S.C. 381(a)(3)) in that it appears to be adulterated within the meaning of section 402(a)(1) of the FD&C Act (21 U.S.C. 342(a)(1)) in that it bears or contains a poisonous or deleterious substance, namely histamine, which may render it injurious to health.

C. Prepared, Packed, or Held Under Insanitary Conditions

The article of food is subject to refusal of admission pursuant to section 801(a)(1) of the FD&C Act (21 U.S.C. 381(a)(1)) in that it appears to be adulterated within the meaning of section 402(a)(4) of the FD&C Act (21 U.S.C. 342(a)(4)) in that it 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.⁹

An import shipment offered for entry may be detained and subject to refusal if one or more like product forms of the same commodity in the entry appears to be adulterated (e.g., tuna sold as loins, saku blocks, steaks, cubes, poke, or ground; or one product form

⁹ Note, the insanitary conditions led to a histamine level greater than or equal to 35 ppm and may contribute to levels greater than or equal to 200 ppm if appropriate CGMPs and HACCP controls are not maintained.

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packaged in varying product sizes such as tuna steaks packaged as individual 4 oz., 6 oz., and 8 oz. steaks).

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