Food and Agriculture Organization of the United Nations

World Health Organization

JOINT FAO/WHO

LITERATURE REVIEW

Histamine in Salmonids

JOINT FAO/WHO

LITERATURE REVIEW

Histamine in Salmonids

2018

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
WORLD HEALTH ORGANIZATION

ISBN 978-92-5-130888-2 (FAO)
ISBN 978-92-4-151443-9 (WHO)

FAO information products are available on the FAO website (www.fao.org/publications) and can be purchased through publications-sales@fao.org

Photo cover: © FAOGlobefish

Contents

TABLES

FIGURES

Acknowledgements

The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) would like to express their appreciation to all those who contributed to the preparation of this document through provision of their time and expertise in writing or reviewing the document. A list of all contributors are included overleaf.

This work was coordinated by the FAO and WHO Secretariat: Sarah Cahill and Vittorio Fattori (Food Safety and Quality Unit, Agriculture and Consumer Protection Department, FAO), Esther Garrido Gamarro and John Ryder (Products, Trade and Marketing Branch, Fisheries and Aquaculture Department, FAO); and Angelika Tritscher and Rei Nakagawa (Department of Food Safety and Zoonoses, WHO).

Final language editing was undertaken by Thor Lawrence, and design and layout was provided by Joanne Morgante.

Contributors

PRIMARY AUTHOR

Dr Ian Goulding, Megapesca Lda., Portugal

REVIEWERS

Iddya Karunasagar, Nitte University, India

Masataka Satomi, National Research Institute of Fisheries Science, Fisheries Research Agency Japan

Hajime Toyofuku, Yamaguchi University, Japan

Ronald A. Benner, Jr, United States Food and Drug Administration, United States of America

Robert (Bob) Samuels, United States Food and Drug Administration, United States of America

Rogério Mendes, Portuguese Institute for the Sea and Atmosphere, IPMA, Portugal

Guillaume Dufllos, Agence nationale de securite sanitaire de l'alimentation, de l'environment et du travail, (ANSES), France

Mike Bolger, Consultant, United States of America

Tom Ross, Univeristy of Tasmania, Australia

Graham Fletcher, The New Zealand Institute for Plant and Food Research Limited, New Zealand

Abbreviations

ASFIS	Aquatic Sciences and Fisheries Information System
CCFH	Codex Committee on Food Hygiene
CDC	Centers for Disease Control
EU	European Union
GHP	good hygiene practice(s)
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration
HACCP	Hazard Analysis and Critical Control Points
LAB	Lactic Acid Bacteria
MAP	Modified Atmosphere Packaging
SFP	Scombrotoxin Fish Poisoning
WHO	World Health Organization

Executive summary

This report describes the methods and findings of a comprehensive literature review undertaken to assess the scientific evidence regarding the risk of histamine development in fish of the family Salmonidae and the potential impact for human health. Histamine is a naturally occurring substance which is derived from the decarboxylation of amino acids. It can be present in certain foods containing free histidine. Certain bacteria produce the enzyme histidine decarboxylase during growth. This enzyme reacts with free histidine, a naturally occurring amino acid that is present in higher proportions in certain species of fish, particularly those of the Scombridae and Scomberesocidae families. The result is the formation of histamine.

Histamine poisoning of humans is usually a mild disorder with a variety of symptoms which may be of a gastrointestinal, cardiovascular or neurological nature. Although symptoms may persist for several days there are no known long-term sequelae and the outcome is rarely if ever fatal. Histamine poisoning is often referred to as scombrotoxin fish poisoning (SFP) because of the frequent association of the illness with the consumption of spoiled scombroid fish.

SFP is most commonly linked to fish that have a high level of free histidine. Histamine formation is then dependent on the time/temperature conditions under which the fish is handled. The available data suggest that high histamine levels are as a result of gross time/temperature abuse during handling and storage, even in fish with high levels of free histidine. Compared with scombroid fish which have free histidine levels ranging from approximately 5 000 mg/kg to 20 000 mg/kg, most species in the Salmonidae family have less than 1 000 mg/kg histidine. Thus most members of the Salmonidae family have somewhere between 10 and 200 times less free histidine than scombroid fish.

There is evidence that under certain conditions the development of histamine can occur in at least two species of the Salmonidae family namely Atlantic salmon (Salmo salar) and rainbow trout (Oncorynchus mykiss). This is based on inoculation studies under laboratory controlled conditions. There is insufficient evidence regarding other genera within the family to indicate whether they are more or less susceptible to histamine development. Numerous storage trials on salmon and trout have sought to characterize the development of histamine during its shelf-life under different conditions. The available evidence indicates that whilst histamine can develop, in many trials it was not detected, or if it was, only in relatively low concentrations, well below current Codex limits set for other species such as tuna, and if at all towards the end or beyond limits of sensory acceptability. In only one of the 21 shelf-life studies reviewed was the Codex limit of 200 mg/kg exceeded, and then only after 2 weeks of storage after the detection of sensory spoilage.

Two market level surveys (Iran and Lithuania) found that 12.5% and 16% respectively of Salmonidae sampled had levels of histamine which exceeded regulatory limits and reference in the literature was also made to unpublished evidence that samples of salmon from the Danish market had been detected with high (but unspecified) levels of histamine. However, market sampling exercises in six other countries failed to detect histamine in Salmonidae, or if they did so, at levels below the Codex limit.

The evidence suggests that the typical bacterial flora associated with histamine development in fish, are not always present or dominant in the spoilage of fresh, smoked or salted Salmonidae, but that when they are, histamine can develop.

The epidemiological evidence for the pathogenesis of histamine in Salmonidae is scant. The review identified a small number (eleven) of documented confirmed cases of SFP-like syndrome linked to human consumption of Salmonidae over a span of 40 years. One of these involved low levels of histamine (mean 1.9 mg/kg) and another involved quite high levels (mean 434 mg/kg, in excess of regulatory limits set for tuna). There is no data on histamine levels in the other cases. An additional 46 suspected cases of histamine poisoning from salmon were reported between 1976 and 2015, two in the USA and 42 in the UK (some the latter involving canned and smoked fish). However, no further data on these are available. Also, one author has suggested that the low level of histamine in the implicated product in one of the documented cases suggests that other factors may also be involved in development of toxicity symptoms in humans and the recommendation of the FAO/WHO Expert meeting on biogenic amines (FAO/WHO, 2013) that "Studies are needed to investigate and clarify the SFP-like syndrome reported to be associated with consumption of salmonid species" is reiterated.

While more than eighty percent of global production of Salmonidae enters international trade there have been no reported cases of rejections of consignments traded internationally (although this could also reflect a low frequency of surveillance).

To conclude, based on the controlled spoilage studies it appears that histamine concentrations in Salmonidae in general seem to increase only after excessive storage times at the temperatures selected, and days to weeks past sensory shelf-life. With inoculation studies, histamine concentrations in Salmonidae did not appear to increase substantially until after extreme abuse conditions. Although extensively traded globally, there are no reports of Salmonidae being rejected based on histamine levels. Thus, while it is noted that under certain conditions histamine development can occur, the available evidence highlights that under appropriate time-temperature control, and within the sensory shelf-life of the product, histamine development in Salmonidae to the level that cause SFP is unlikely to occur.

The data on SFP-like illness associated with Salmonidae is not extensive. Histamine levels are only available for some of the cases and often at levels below that which has been seen to cause SFP. The low frequency of confirmed cases of toxicity in relation to the high volume of production, trade and consumption of Salmonidae suggests that the hazard is not a significant threat to human health.

The currently available evidence thus suggests that there is not a basis to include Salmonidae in the same risk category for SFP as other more commonly implicated species.

1

Introduction

This report describes the methods and findings of a comprehensive literature review undertaken to assess the scientific evidence regarding the risk of histamine development in fish of the family Salmonidae and the potential impact for human health. The review was undertaken to provide a scientific basis for the deliberations of the Codex Committee on Food Hygiene in relation to the development of new guidance on the control of histamine in fish.

Specifically, the work will contribute to the deliberations on the contents of a table therein aimed at providing a comprehensive list of fish species associated with Scombrotoxin Fish Poisoning (SFP) or high levels of free histidine, the precursor to histamine. Such a table can be applied as part of the hazard identification step of the risk assessment.

The Terms of Reference for the study were to undertake a review of both the peer-reviewed and grey literature on this issue of histamine in Salmonidae in order to get a better insight into the existence and extent of the problem of histamine in Salmonidae and Scombrotoxin (like) fish poisoning (SFP) associated with Salmonidae and the potential risk. The study aimed to collect and review the available and accessible information on SFP and SFP-like illness linked to Salmonidae, including experimental studies, details on any cases (including the potential reason for causing illness and in the case of mixed meals the degree of certainty/uncertainty that the Salmonidae was the source of the illness) and any other relevant information. It also aimed to consider aspects such as histidine levels in Salmonidae and how that relates to histamine formation, and the risk of histamine illness linked to Salmonidae, global production and trade in Salmonidae and any rejections linked to histamine and any other relevant issues in the discussion of the available information. This report therefore documents the approach, presents the key evidence and considers the strength/weaknesses of that evidence and draws conclusions.

2

Methodology

The study comprised four distinct components. The primary work was undertaken as a desk study during the period March to June 2017, and therefore reflects the state of published knowledge at that time. The paper was then subject to peer review by an international group of experts before finalization in September 2017.

2.1 CHARACTERIZATION OF THE SALMONIDAE FAMILY

Salmonidae are a family of bony fishes (teleosts), and the only family in the order Salmoniformes. They breed and spawn in fresh water, but many species also spend part of their life cycle at sea (i.e. they are anadromous). They feed on crustaceans, insects and their larva and small fish. The Family has a number of subfamilies, with the number of genera and species in each as indicated below, along with common names.

Subfamily: Coregoninae
- *Coregonus* - whitefishes (78 species)
- *Prosopium* - round whitefishes (six species)
- *Stenodus* - beloribitsa and nelma (one or two species)

Subfamily: Thymallinae
- *Thymallus* - graylings (14 species)

Subfamily: Salmoninae
- *Brachymystax* - lenoks (four species)
- *Hucho* (four species)
- *Oncorhynchus* - Pacific salmon and trout (12 species)
- *Parahucho* - Sakhalin taimen (one species)
- *Salmo* - Atlantic salmon and trout (47 species)
- *Salvelinus* - Char and trout (e.g. brook trout, lake trout) (51 species)
- *Salvethymus* - Long-finned char (one species)

Clear definition of the Salmonidae family is provided as it has been observed in the literature that there are other fish that may be commonly referred to as salmon but are not in fact members of the family Salmonidae (e.g. the fish commonly referred to as Australian salmon but which is a member of the family Arripidae). These are not included in this review.

2.2 CHARACTERIZATION OF PRODUCTION AND INTERNATIONAL TRADE IN SALMONIDAE

The main species of Salmonidae produced and entering commerce were identified using the ASFIS List of Species for Fishery Statistics Purposes[1] and the FAO Fishstat database[2].

Data on international trade was extracted from the ITC TradeMap Database[3] based on the Harmonized system (HS) Codes provided in Table 1.

TABLE 1. Harmonized system codes and descriptions for Salmonidae

HS Code	Description
030212	Pacific Salmon (*Oncorhynchus* spp.), Atlantic Salmon (*Salmo salar*) and Danube Salmon (*Hucho hucho*), Excluding Fillets, Liver and Roe, Fresh or Chilled
030213	Pacific Salmon (*O. nerka, gorbuscha, keta, tschawytscha, kisutch, masou and rhodurus*), Fresh or Chilled
030214	Atlantic Salmon (*Salmo salar)* and Danube Salmon (*Hucho hucho*), Fresh or Chilled
030219	Salmonidae, Excluding Fillets, Livers and Roes, Nes, Fresh or Chilled
030310	Pacific Salmon (*Oncorhynchus* spp.), Frozen (Excluding Head, Livers Roes and other fish meat of heading no 0304)
030311	Sockeye Salmon (Red Salmon) (*Oncorhynchus nerka*), Frozen
030312	Pacific Salmon (*Oncorhynchus gorbuscha, keta, tschawytscha, kisutch, masou and rhodurus*), Frozen, nes
030313	Atlantic Salmon (*Salmo salar*) and Danube Salmon (*Hucho hucho*), Frozen
030319	Salmonidae, Frozen, Nes
030322	Atlantic Salmon (*Salmo salar*) and Danube Salmon (*Hucho hucho*), Excluding Fillets, Livers and Roes, Frozen
030441	Pacific Salmon (*Oncorhynchus nerka, gorbuscha, keta*, etc.), Atlantic Salmon (*Salmo salar*) and Danube Salmon (*Hucho hucho*), Fillets, Fresh or Chilled
030452	Salmonidae Meat, Fresh or Chilled, Excluding Fillets and Steaks

1 Available at: http://www.fao.org/fishery/collection/asfis/en
2 Available at: http://www.fao.org/fishery/statistics/software/fishstat/en
3 Available at: http://www.intracen.org/itc/market-info-tools/trade-statistics/

030481	Pacific Salmon (*Oncorhynchus nerka, gorbuscha*, *keta*, Etc.), Atlantic Salmon (*Salmo salar*) and Danube Salmon (*Hucho hucho*), Fillets, Frozen
030541	Pacific Salmon (*Oncorhynchus* spp.), Atlantic Salmon (*Salmo salar*), and Danube Salmon (*Hucho hucho*), Including Fillets, Smoked
160411	Salmon, Prepared or Preserved, Whole or In Pieces, but not Minced

2.3 REVIEW OF REJECTIONS OF SALMONIDAE IN INTERNATIONAL TRADE

Rejections for the latest full year of data available from Competent Authorities of major fish trading nations or regions were reviewed (Table 2). This includes Australia, the European Union (EU), Japan, and the United States of America. Other major salmon consuming countries (China and the Russian Federation) do not publish these data.

TABLE 2. Sources of data on rejections of imported Salmonidae

Country/region	Authority	Data set/year
Australia	Department of Agriculture and Water Resources	Imported Food Inspection Scheme January-June 2016
EU	European Commission	Rapid Alert System for Feed and Food, 2016
Japan	Department of Environmental Health and Food Safety	Inspection Results of Imported Foods Monitoring and Guidance Plan for FY 2016
USA	Food and Drug Administration	Import Refusal Reports, October 2013 to present

2.4 REVIEW OF HISTAMINE-RELATED ILLNESSES ASSOCIATED WITH SALMONIDAE

A review of published and unpublished literature sources was conducted with a view to compiling the available evidence on the presence of the histamine hazard in fish of the family Salmonidae and any histamine-related illnesses associated with Salmonidae.

The literature review method employed searches of online databases of academic journals using a series of keywords. The five major academic databases used for this review were Google Scholar, Springer, Science Direct (Elsevier), Pubmed and Wiley.

Trial runs were undertaken based on a range of search terms such as salmonid, histamine, histidine, etc., with reviews of the first 200 references of each. Most references in the trial were identified as not relevant, with only 43 out of 6 000 articles identified as relevant to the study. Many articles returned by the search concerned the effects of histamine in fish feed on salmonid growth. Based on this trial, the search methodology was modified to exclude articles containing the term “feed”, since a large number of irrelevant articles would otherwise be returned. As a consequence, the search was conducted using the protocol and key words outlined in Table 3.

TABLE 3. Search protocol for the literature review

Primary search term (species)	Secondary search term (hazard)	Exclusion term
Salmonid Trout Oncorhynchus Salmon *Salmo* Char *Salvelinus* Grayling *Thymallinae* Whitefish *Coregonus*	Histamine Histidine Biogenic amine Scombroid poisoning Scombrotoxin	Feed

Note: searches with more than one term returned results containing one or other word

Relevant articles were extracted from the first 10 pages (approximately 200 articles) returned for each search. In total 16 320 articles were returned by the search over the five databases used (Table 4). Articles considered as relevant to the objectives of the study were those which considered:

- epidemiological evidence concerning the implication of fish of the family Salmonidae in cases of histamine poisoning;
- reports of studies based on sampling of fishery products from the market and testing for food safety conditions; or
- evidence of the presence of histamine or its precursor histidine in studies of the spoilage characteristics of fish of the family Salmonidae, including the possibility of potentiation by other biogenic amines.

Care was taken in the selection of reports of illnesses for risk assessment of fish toxicity, to ensure that only species from the family Salmonidae were selected. In some studies, non-salmonid species may be called by a common name suggesting links to Salmonidae. For example, Hungerford (2010) and Smart (1992) consider scombroid poisoning involving the Western Australian salmon (*Arripis truttaceus*) a marine fish of family *Arripidae*, not related to the *Salmonidae*. Knope, Sloan-Gardner and Stafford (2014) also refers to this species as salmon. Edmunds and Eitenmiller (1975) report studying histamine in speckled trout, which on closer reading concerns the marine croaker *Cynoscion nebulosus*. Only references concerning Salmonidae *sensu stricto* were selected for review.

In total 51 relevant articles were identified by the literature search (see Table 4), and these were subjected to a more detailed review of their content, which is reported below. Additional references, suggested by FAO and others, and including known non-academic and unpublished studies were also reviewed. These included reviews of national databases of foodborne diseases where they were publicly available.

It should be noted that histamine concentrations are reported differently in different studies. For example, concentrations may be expressed as mg%, mg/kg, mg/100g, µg/g and ppm. In this paper, for ease of comparison, all results quoted for histidine and histamine concentration have been converted to a consistent unit of concentration (mg/kg).

TABLE 4 Hits and relevant articles for keywords in academic database search

Keywords	No. of articles					
	Google Scholar	Springer	Science Direct	Pubmed	Wiley	No. Relevant
Salmonid Histamine Histidine	573	30	210	30	106	14
Salmonid Scombroid Poisoning	112	11	20	2	3	0
Salmonid Scombrotoxin	33	2	2	2	3	0
Oncorhynchus Histamine Histidine	620	251	128	0	174	12
Oncorhynchus Biogenic Amine	2400	143	281	226	254	9
Oncorhynchus Scombroid Poisoning	221	15	28	0	27	3
Trout Histamine Histidine	1740	233	486	2	361	2
Trout Biogenic Amine	5410	471	877	397	361	0
Trout Scombroid Poisoning	549	59	87	0	63	0
Trout Scombrotoxin	171	18	11	0	11	0
Salmon Salmo Histamine	1950	185	337	2	336	6
Salmon Salmo Biogenic Amines	1700	146	337	22	236	0

Salmon *Salmo* Scombroid Poisoning	261	21	30	0	33	4
Salmon *Salmo* Scombrotoxin	82	6	3	0	10	0
Char *Salvelinus* Histamine Histidine	52	6	8	2	10	1
Char *Salvelinus* Biogenic Amine	255	21	10	397	24	0
Char *Salvelinus* Scombroid Poisoning	17	2	6	0	2	0
Char *Salvelinus* Scombrotoxin	17	2	6	0	2	0
Grayling *Thymallinae* Histamine Histidine	0	0	0	0	0	0
Grayling *Thymallinae* Biogenic Amine	0	0	0	0	0	0
Grayling *Thymallinae* Scombrotoxin	0	0	0	0	0	0
Grayling *Thymallinae* Scombroid Poisoning	0	0	0	0	0	0
Whitefish *Coregonus* Histamine Histidine	35	5	5	0	8	0
Whitefish *Coregonus* Biogenic Amine	145	12	16	3	22	0
Whitefish *Coregonus* Scombroid Poisoning	24	3	1	0	1	0
Whitefish *Coregonus* Scombrotoxin	3	1	1	0	0	0
Totals	16 370	1 643	2 890	1 085	2 047	51

3

Review of literature on histamine in Salmonidae

3.1 THE HISTAMINE HAZARD

Histamine is a naturally occurring substance which is derived from the decarboxylation of amino acids. It can be present in certain foods containing free histidine. Certain bacteria produce the enzyme histidine decarboxylase during growth. This enzyme reacts with free histidine, a naturally occurring amino acid that is present in higher proportions in certain species of fish, particularly those of the Scombridae and Scomberesocidae families. The result is the formation of histamine.

Histamine poisoning of humans is a chemical intoxication occurring a few minutes to several hours after ingestion of foods that contain unusually high levels of histamine (Huss, Ababouch and Gram, 2003). It is usually a mild disorder with a variety of symptoms that may be of a gastrointestinal (e.g. cramps, diarrhoea, vomiting), cardiovascular (e.g. flushing, rash, headache, etc.) or neurological (pain, itching) nature (FAO/WHO, 2013). Although symptoms may persist for several days there are no known long-term sequelae and the outcome is rarely if ever fatal. Histamine poisoning is often referred to as scombrotoxin fish poisoning (SFP) because of the frequent association of the illness with the consumption of spoiled scombroid fish. Further details on SFP are available in Section 2.3.4 – Histamine as the causative toxin of SFP and in Annex 3 (Section 1.1.6) of the Joint FAO/WHO Expert meeting report on public health risks of histamine and other biogenic amines from fish and fishery products (FAO/WHO, 2013) [4].

4 . Available at: http://www.fao.org/fileadmin/user_upload/agns/pdf/Histamine/Histamine_AdHocfinal.pdf

SFP is most commonly linked to fish that have a high level of free histidine. Histamine formation is then dependent on the time×temperature conditions under which the fish is handled. The available data suggest that high histamine levels are as a result of gross time×temperature abuse during handling and storage, even in fish with high levels of free histidine (FAO/WHO, 2013). Compared with scombroid fish which have free histidine levels ranging from approximately 5 000 mg/kg to 20 000 mg/kg, most species in the Salmonidae family have less than 1 000 mg/kg histidine (Table 5) (FAO/WHO, 2013). Thus most members of the Salmonidae family have somewhere between 10 and 200 times less free histidine than scombroid fish.

Many countries have passed regulations defining maximum limits for histamine in fishery products. These are commonly based on the Codex standard which indicates that histamine levels should not exceed 200 mg/kg[5]. This is supported by a risk assessment undertaken by FAO/WHO, where it was concluded that a dose of 50 mg would not be expected to induce any symptoms in healthy humans (FAO/WHO, 2013). Considering an average serving size of 250 g of fish, the risk assessment concluded that the maximum concentration in fish should not be greater than 200 mg/kg. In terms of regulations at national level, several approaches have been taken with some countries using the 200 mg/kg limit and others setting lower limits, such as 50 mg/kg or 100 mg/kg which may also take other aspects into consideration such as quality. A short summary of regulatory approaches is provided in Annex 1 to this report. Irrespective of the regulatory limit, it should be noted that with the application of good hygienic practices (GHP), and hazard analysis and critical control point (HACCP) systems, it has been reported that histamine levels of less than 15 mg/kg in fish are achievable (FAO/WHO, 2013).

Further information of the nature of the hazard, factors which give rise to its presence in fish and fishery products, and control options are provided in the FAO/WHO expert meeting report on biogenic amines (FAO/WHO, 2013).

---

[5] Standard for Quick Frozen Finfish, Uneviscerated and Eviscerated (CODEX STAN 36-1981)
Standard for Canned Tuna and Bonito (CODEX STAN 70-1981)
Standard for Canned Sardines and Sardine-Type Products (CODEX STAN 94- 1981)
Standard for Canned Finfish (CODEX STAN 119-1981)
Standard for Quick Frozen Blocks of Fish Fillet, Minced Fish Flesh and Mixtures of Fillets and Minced Fish Flesh (CODEX STAN 165-1989)
Standard for Quick Frozen Fish Sticks (Fish Fingers), Fish Portions and Fish Fillets - Breaded or in Batter (CODEX STAN 166-1989)
Standard for Quick Frozen Fish Fillets (CODEX STAN 190-1995)
Standard for Boiled Dried Salted Anchovies (CODEX STAN 236-2003)
Standard for Salted Atlantic Herring and Salted Sprat (CODEX STAN 244-2004)
Standard for Fish Sauce (CODEX STAN 302-2011)
Standard for Smoked Fish, Smoke-Flavoured Fish and Smoke-Dried Fish (CODEX STAN 311-2013)

TABLE 5. Free histidine levels in members of the Family Salmonidae (based on FAO/WHO, 2013)

Genus and species	Reported free histidine levels (mg/kg)	Reference
Salmo salar	130–300	Emborg *et al.*, 2002; Espe *et al.*, 1993 Murata *et al.*, 1998
Oncorhynchus tshawytscha	70–288	Murata *et al.*, 1998; Shirai *et al.*, 1983
Oncorhynchus keta	70–670	Murata *et al.*, 1998; Konso *et al.*, 1998
Oncorhynchus kisutch	219–970	Murata *et al.*, 1998; Shirai *et al.*, 1983
Oncorhynchus macrostomus	188–441	Murata *et al.*, 1998;
Oncorhynchus masou	387–2362	Murata *et al.*, 1998;
Oncorhynchus nerka	240–590	Murata *et al.*, 1998; Shirai *et al.*, 1983
Oncorhynchus gorbusvha	408–1557	Murata *et al.*, 1998; Shirai *et al.*, 1983 Murata *et al.*, 1998; Shirai *et al.*, 1983 Murata *et al.*, 1998; Shirai *et al.*, 1983

3.2 PREVIOUS REVIEWS

A number of studies have reviewed the incidence of histamine in fishery products. Between 1976 and 1986, 258 incidents of suspected histamine fish poisoning were reported in an extensive review of cases in Britain (Bartholomew *et al.*, 1987). The majority of these incidents involved mackerel (111, 43%, mainly smoked mackerel), followed by tuna (73, 28%) and sardines (37, 14%). Ten incidents (4%) involved herring (pickled or kippered). There were a total of 12 incidences of suspected histamine poisoning linked to salmon consumption. The authors noted that although there had been six incidents linked to consumption of canned salmon, five of these involved fish with less than 10 mg/kg histamine, despite the presence of characteristic symptoms. Salmon from the sixth episode had 170 mg/kg of histamine. Since histamine levels were relatively low and salmon had not been widely associated with scombrotoxic poisoning, the authors postulated that another toxin could have contributed to the symptoms.

Scoging (1991) as described by Lehane and Olley (2000) identified 441 suspected incidents of "scombrotoxic fish poisoning" in the United Kingdom (UK) between 1976 and 1990, involving 962 cases. Scoging (1998) also investigated 405 incidents between 1987 and 1996 which included 243 sporadic incidents (60%), 105 general outbreaks (26%) and 56 family outbreaks (14%). Tuna (fresh/ frozen and canned) and mackerel were most commonly implicated in both suspected and confirmed (elevated histamine) incidents. Salmon was involved in 30 suspected incidents during this period, but only one incident was investigated with an analysis of a sample, and found to contain slightly elevated histamine levels (51 mg/kg).

An extensive review of the histamine hazard in United Kingdom (UK) fishery products, commissioned by the UK Food Standards Agency considered *inter alia* the risk of the histamine hazard being present in salmonids on the UK market (James *et al*., 2013). The study concluded that at the time of writing there had been no reported incidents of elevated histidine or histamine in fresh North Atlantic salmon (*Salmo salar*), either wild caught or farmed. The review quoted the studies of de la Hoz *et al*. (2000) and Emborg *et al*. (2002) which both showed that although histamine can be formed in Atlantic salmon (*Salmo salar*) during storage, the rate of accumulation is slow and high levels are not formed before the fish spoils.

In the publication "Improving Seafood Products for the Consumer", the authors of the chapter on histamine and biogenic amines (Dalgaard and Emborg, 2008), noted that salmon has been reported to cause histamine poisoning. Highlighting, that flesh contains little free histidine (130–1 090 mg/kg), they noted that these levels can correspond to low histamine (less than 10–170 mg/kg) levels in fish when other conditions conducive to histamine formation are also present. However, it was noted that histamine and histidine degradation products had not been measured in blood or urine of affected patients and therefore other toxins could not be excluded as the cause of symptoms.

In a review of Scombroid poisoning by Hungerford (2010), two references are made to salmon containing histamine; one considers Western Australian salmon (*Arripis truttaceus*) and the other sockeye salmon (*Oncorhynchus nerka*). In the former reference, the species is not a member of the family Salmonidae. In the latter case the reference is made to Gessner, Hokama and Isto (1996) which is further described below.

Huss, Embarek and Jeppesen (1995) reviewed the control of biological hazards in cold smoked salmon production. Whilst salmon was not a species recognised as being implicated in histamine poisoning, the authors noted that salmon does contain considerable amounts of the amino acids which by decarboxylation may give rise to formulation of a range of biogenic amines, including histamine. Quoting Møller (1989) and Sidwell (1981) the concentration of the precursor histidine in salmon muscle was found to be 4 100 mg/kg (accounting for 2.2-2.9% of the protein) although not all of this is necessarily bio-available. The authors also report that high levels of histamine have been found in routine control of smoked salmon in Denmark, although these findings are unpublished.

3.3 REPORTS OF ILLNESS

Gessner, Hokama and Isto (1996) characterized a scombrotoxicosis-like illness in a single patient following the ingestion of home smoked sockeye salmon (*Oncorhynchus nerka*). Toxicity was confirmed via mouse bioassay, but mean histamine levels were only 1.9 mg/kg (range, 0.3-2.4). Putrescine and cadaverine levels were similarly low. The authors observed that the implicated salmon had histamine levels 25-fold less than the United States Food and Drug Administrations' (FDA) action level for tuna (50 mg/kg histamine), and the patient ate an estimated 0.0006 mg of histamine per kg of body weight, well below the estimated 1 mg of histamine per kg of body weight reported to cause human illness. They consider the possibility that the toxicity was potentiated by the presence of putrescine and cadaverine and suggest that "*some cases of scombrotoxicosis do not result from exogenous histamine exposure*".

A follow up to a case of an allergic reaction linked to salmon consumption in Italy was reported by Muscarella *et al.* (2013), with a finding of 434 ±34 mg/kg of histamine, suggesting that this was the responsible agent. However, no further details on the case were available.

Feng, Teuber and Gershwin, in their 2016 review of histamine fish poisoning quote the United States of America Centers for Disease Control (CDC) as reporting that between 1998 and 2012, the fish most frequently involved in histamine fish poisoning reactions in the United States of America, according to the CDC, are tuna, mahi-mahi, escolar, marlin, and salmon, with the last-named accounting for

TABLE 6 Histamine food poisoning involving salmon and trout in the United States of America 1998 to 2015

Year	State	Status	Cases/ illnesses	Establishment
1999	Florida	Suspected	2	Restaurant - other or unknown type
2003	Florida	Confirmed	4	Restaurant - other or unknown type
2009*	Washington	Confirmed	3	Private home
2012	Illinois	Confirmed	2	Restaurant - Sit-down dining
2015	Iowa	Suspected	2	Private home/residence

Notes: *These cases specifically referred to salted salmon
Source: Centers for Disease Prevention and Control (CDC) Foodborne Outbreak Online Database (FOOD Tool) https://wwwn.cdc.gov/foodborneoutbreaks/

only 1.8% of reported cases during this period. A re-assessment of the data by the authors of the present review identified five reported food poisoning incidents involving salmon and trout, of which three were confirmed and two suspected (see Table 6). Unfortunately no biogenic amine data were presented by Feng, Teuber and Gershwin, in their 2016 review.

Mäkinen-Kiljunen, Kiistala and Varjonen, (2003) reported a strong allergic reaction to a skin prick test using the roe of rainbow trout (*Oncorhynchus mykiss*) in patients who had exhibited local symptoms and anaphylaxis following ingestion of roe. Anaphylactic symptoms after initial salmon roe consumption were also reported by Flais (2004). However, in neither case was the role of histamine considered.

Lavon, Lurie and Bentur (2008) reviewed 21 events of scombroid poisoning involving 46 patients recorded in Israel during 2005–2007. Tuna was the commonest fish consumed (84.7%) and no Salmonidae products were implicated in the remainder.

3.4 CONTROLLED SPOILAGE STUDIES

Given the limited data on reports of illness attributed to histamine poisoning in Salmonidae, the review also considered the potential for the development of histamine in relevant species. The review therefore sought to identify studies that measured the level of histamine and/or its precursor histidine, in relevant species.

The authors identified twenty-one spoilage and shelf-life studies involving Salmonidae that measured histamine development under different storage conditions of temperature, time, process (salted/smoked) and storage atmosphere. All of these measured quality parameters during spoilage caused by naturally occurring microbiological flora (as against inoculation studies, which are considered below). Rainbow trout and Atlantic salmon are the most researched species. Eleven studies involved rainbow trout, six with Atlantic salmon and one of each pink salmon, coho salmon and Arctic char.

Microbiological activity in farmed Coho salmon (*Oncorhynchus kisutch*) during chilled storage, was studied by Aubourg *et al.* (2007). Spoilage was assessed by a range of parameters, including histamine and microbial indicators. Histamine levels were reported to increase after the end of the microbial lag phase (12–17 days), but levels remained below acceptable safety limits (maximum 28.8 mg/kg) throughout the period.

Leisner *et al.* (1994) investigated the incidence of histamine- or tyramine-producing lactic acid bacteria in vacuum-packed sugar-salted fish (including salmon and mackerel). No histamine-producing isolates were observed, suggesting that the nature of this product suppresses bacterial activity associated with the enzyme histidine decarboxylase.

Shumilina *et al.* (2015) used High Resolution Nuclear Magnetic Resonance (NMR) spectroscopy to monitor post-mortem changes in thirty-one different fish metabolites in Atlantic salmon fillets stored at 0°C and 4°C. The formation of the biogenic amines tyramine and cadaverine was observed only during storage at 4°C after about 7 days of storage. Histamine formation was not observed in this study. Neither was it observed in a similar study by Shumilina *et al.* (2016) in which NMR spectroscopy was used to monitor changes in the composition of trichloroacetic acid extracts of Atlantic salmon (*Salmo salar*) backbones, heads and viscera stored at 4°C and 10°C. Again, only the formation of tyramine and cadaverine was observed, after 7 days of storage at 4°C.

Matějková *et al*. (2013) investigated the effect of vacuum packaging followed by high-pressure treatment on formation of biogenic amines in vacuum-packed trout flesh (*Oncorhynchus mykiss)*. Whilst the rate of development of biogenic amines such as putrescine, cadaverine and tyramine showed good correspondence with the level of applied pressure and organoleptic properties, tryptamine, phenylethylamine and histamine were not detected in any of the spoiled samples stored at 3.5°C (with the single exception of a sample stored for 70 days).

Křížek *et al*. (2012a) studied the effect of low-dose high-energy electron beam irradiation on biogenic amines formation in vacuum-packed trout flesh (*Oncorhynchus mykiss*) stored at 3.5°C. Putrescine, cadaverine and tyramine developed and correlated with the irradiation dose and organoleptic properties. Tryptamine was not detected in any of the samples. Histamine was detected at <1 mg/kg in untreated samples after 7 days rising to a mean of 103 mg/kg after 28 days storage.

Chytiri *et al.* (2004) considered the usefulness of biogenic amines as indicators of microbial and sensory changes in freshwater rainbow trout (*Onchorynchus mykiss*) stored on ice. The concentration of putrescine, cadaverine, spermidine, tryptamine, and beta-phenylethylamine increased significantly in both whole and filleted trout between days 15 and 18 of storage. Other biogenic amines (tyramine, histamine, and spermine) only developed towards the end of the storage period, and the maximum concentration of histamine was 1.6 mg/kg after 8 days. The authors considered that the low count of Enterobacteriaceae (below 10^6 cfu/g) accounted for the lower production of histamine. Tryptamine, beta-phenylethylamine, histamine, and cadaverine were not considered to be appropriate as spoilage indicators.

In another storage trial, Emborg *et al.* (2002) investigated the development of microbial spoilage, formation of biogenic amines and shelf-life of chilled fresh and frozen/thawed salmon packed in a modified atmosphere (MAP) and stored at 2°C. Despite the high levels of *Photobacterium phosphoreum,* less than 20 mg/kg of histamine was observed in fresh MAP salmon prior to its sensory spoilage (at circa 14 days in the case of chilled fresh and 21 days in frozen/thawed MAP salmon).

The biogenic amine content and associated bacterial changes (*Pseudomonas* spp., psychrotrophic and mesophilic counts) in whole, farmed rainbow trout (*Oncorhynchus mykiss*) were monitored by Rezaei *et al.* (2007) during ice storage for 18 days. Levels of putrescine, cadaverine and histamine, and bacterial loads all increased significantly during storage, but histamine was detected only at the later stages of storage (1.6 mg/kg after 18 days) and was considered to be less suitable than the other biogenic amines as freshness indicator.

In another chilled storage trial of rainbow trout (*Oncorhynchus mykiss*), Hosseini, Rahimi and Mirghaed (2014) showed that although it was not detected on the first and third day of storage, the concentration of histamine increased linearly during ice storage over 18 days, rising from 1.09 mg/kg to 4.30 mg/kg.

Özogul, Kus and Kuley (2013) assessed the comparative quality loss in wild and cultured rainbow trout (*Oncorhynchus mykiss*) during chilled storage. The fish became unacceptable after 14 days. Histamine was detected in only one sample throughout the storage period (at a level of 0.5 mg/kg in wild rainbow trout at 7 days of chilled storage). Histamine was not detected in samples tested after 19 days.

Özogul, *et al.* (2013) also studied the impact of strawflower and mistletoe extract on quality properties of rainbow trout fillets, finding that histamine accumulated only at low levels (<2 mg per 100 g) and that these plant extracts were able to suppress the development of biogenic amines. The untreated control developed 9.6 mg/kg of histamine after 20 days of chilled storage.

Peiretti *et al.* (2012) studied the effects of rosemary oil (*Rosmarinus officinalis*), a common, ”natural” preservative, on the shelf-life of minced rainbow trout (*Oncorhynchus mykiss*) during refrigerated storage. The study found that histamine development was inhibited by the use of rosemary oil, but over the duration of the trial (9 days) histamine levels (including in the untreated control) did not exceed 0.32 mg/kg, well within the limits considered to be safe for human consumption.

Dawood *et al*. (1988) also studied the occurrence of non-volatile amines in chilled-stored rainbow trout (Salmo irideus, later reclassified as *Oncorhynchus mykiss*) following a period of chilled storage after initial temperature abuse (6 hours at 30°C). The concentrations of putrescine, cadaverine and histamine increased during storage, while those of spermidine and spermine decreased after an initial rise during the first 4 days. Histamine levels detected averaged 13 mg/kg after 14 days. The authors suggest that the concentration of putrescine, and possibly that of cadaverine and histamine, in the flesh of chilled-stored rainbow trout, can be used as a criterion for the assessment of the freshness of the fish.

Grotta *et al*. (2016) assessed the chemical and nutritional characteristics of rainbow trout affected by the "Red-Mouth Disease", a bacterial infection of freshwater and marine fish caused by the pathogen *Yersinia ruckeri*. The characterization included testing for histamine using HPLC with a limit of detection of 4 mg/kg. Histamine levels were measured after 5 days at 0-4°C and found to be 5.35 (±0.55) mg/kg in healthy fish and 6.6 (±0.63) mg/kg in unhealthy fish.

De la Hoz *et al*. (2000) studied the microbial counts, biochemical parameters (including non-volatile amines) and sensory attributes (colour and odour) of refrigerated (2°C) salmon (*Salmo salar*) steaks stored under different CO_2-enriched and air atmospheres. It was noted that histamine levels were non-detectable at the outset and controls increased to 15 mg/kg by days 7-9 which is when the fish was considered spoiled. In the modified atmosphere packages these levels were not reached until days 13-17 of storage. Even after 22 days the modified atmosphere packaged fish did not exceed 100 mg/kg.

Self and Wu (2012) determined eight biogenic amines in selected seafood products, including salmon using ultra-high performance hydrophilic interaction chromatography. Method applicability was tested in a sample of a non-scombroid species, Sockeye salmon, in which no histamine was detected.

Křížek *et al*. (2012b) studied the formation of biogenic amines in fillets and minced flesh of three freshwater fish species: common carp (*Cyprinus carpio*), rainbow trout (*Oncorhynchus mykiss*) and perch (*Perca fluviatilis*) stored at 3°C and 15°C. They found that content of putrescine appeared to be a good quality indicator for all examined fish species. The fish species and the method of flesh processing did not have a significant influence on the putrescine formation. Tyramine was formed mainly in carp and trout mince at 15°C. Histamine was not detected in trout after 10 days at 3°C, and rose to a maximum of 0.32 mg/kg after 16 days. However, at 15°C histamine levels reached 79.7mg/kg after 7 days.

Simsek & Kilic (2013) also investigated the effects of marination, cooking and storage on physico-chemical and microbiological properties of raw ready-to-eat trout döner kebab stored at 4°C and -18°C. Content of biogenic amine was low throughout with a highest recorded level of 44.1 ± 3.8 mg/kg after 30 days storage at 4°C.

Crapo and Himelbloom (1999) characterized spoilage features and histamine development in whole Pacific herring (*Clupea harengus pallasi*) and pink salmon (*Oncorhynchus gorbuscha*) fillets when held for two weeks at 10°C. At the end of this period, although the salmon was spoiled, histamine was not detected. Herring was considered spoiled by day 6, and histamine concentrations in this species reached 54.9 mg/kg at day 14.

Jørgensen, *et al.* (2000a) developed a multiple compound quality index for cold-smoked Atlantic salmon (*Salmo salar*) by applying multivariate regression at different stages of spoilage. The quality index was based on concentrations of cadaverine, histamine, putrescine, and tyramine and pH and showed good correlation with sensory assessments. Different biogenic amine profiles were found to be related to the differences in the spoilage microflora. Two weeks after sensory spoilage was first detected, samples were tested and histamine was detected at concentrations between 3 mg/kg to 240 mg/kg.

There are very few studies on histamine development in members of the Salmonidae family other than *Oncorynchus* spp. and *Salmo* spp. Synowiecki *et al.* (1994) studied the nutrient composition, including amino acids, of Artic Char (*Savelinus alpinus*) fed on a diet with a high carotenoid content. Total free amino acid content in Char samples varied between 295 and 364 mg/100g but no histamine was detected in any of the samples. No studies were identified on Whitefish (*Coregoninae)* and Grayling (*Thymallinae).*

3.5 INOCULATION STUDIES

A small number of studies have investigated the development of biogenic amines in Salmonidae when intentionally inoculated with different species of bacteria.

Histamine production in coho salmon muscle (and mackerel, albacore, mahi-mahi) after inoculation with an isolate of *Morganella morganii* was studied by Kim *et* *al*. (2002). All fish species, supported growth of *M. morganii* at temperatures above 15°C. At elevated temperatures (optimally 25°C), histamine was shown to be produced to levels of 2.4 to 2.3 mg/kg. Histamine did not develop during frozen storage, but developed rapidly in fish that had been previously frozen when subsequently thawed and stored at 25°C.

In a study of the spoilage characteristics of vacuum-packed rainbow trout (*Oncorhynchus mykiss*) where fillets were inoculated with two different *Lactobacillus* strains, Katikou *et al*. (2006) sought to correlate the development of biogenic amines with microbiological and sensory attributes. In all cases the development of biogenic amines was suppressed by the treatment with *Lactobacillus*. Putrescine and cadaverine, were the main biogenic amines formed, and were correlated with both spoilage bacterial counts and off-odour. After sensory rejection (20 days at 4°C), the histamine concentration was 6.11 mg/kg.

Jørgensen, Huss and Dalgaard (2000b) identified the spoilage microflora from cold-smoked salmon and determined biogenic amine production of single and co-cultures in this product. *Photobacterium phosphoreum* and *Lactobacillus curvatus* were identified as the specific spoilage organisms in cold-smoked salmon, but the former was the only species that produced histamine when inoculated on sterile cold-smoked salmon. Production of putrescine was enhanced 10–15 times when cultures of *Serratia liquefaciens* or *Hafnia alvei* were grown with *Carnobacterium divergens* or *Lactobacillus sakei* subsp. *carnosus*. This phenomenon was explained by interspecies microbial metabolism of arginine, i.e., metabiosis, suggesting the possibility of potentiation in cases of contamination with specific cocktails of microflora species.

Kuley (2011) investigated the influence of brine solutions on biogenic amine formation in fermented trout fillets inoculated with lactic acid bacteria. The histamine content in the untreated control rose to a mean of 100 mg/kg after 35 days (one sample had a concentration of 333 mg/kg), while the treated groups contained less than 75 mg/kg. The study concluded that the biogenic amine production was dependent on the microbial flora, availability of precursors and physicochemical factors, such as temperature, pH, salt, oxygen and sugar concentration, and that lactic acid bacteria did not appear to play an important role in biogenic amine production.

Katikou *et al.* (2006) also studied the development of biogenic amines in *Lactobacillus*-inoculated vacuum-packed rainbow trout (*Oncorhynchus mykiss*) fillets, over a 20 day refrigerated period. The authors found that concentrations of putrescine and cadaverine correlated well with both spoilage bacterial counts and off-odour scores. Spermine and spermidine contents decreased during storage, and levels of the other biogenic amines determined, including histamine, remained below 10 mg/kg even after sensory rejection.

The development of biogenic amines in cold-smoked rainbow trout fermented with lactic acid bacteria (LAB) was also studied by Petäjä, Eerola and Petäjä (2000). Throughout, the products contained low amounts of biogenic amines, with the exception of cadaverine, histamine and tyramine, which increased in all product groups in one experimental series out of three. The highest concentrations of histamine was in the control products without any LAB inoculation, with levels of 7.4, 78 and 10 mg/kg after storage of 1 week at 8°C plus 35 days at 4°C.

Smoked salmon and trout products have been shown to contain microbial flora capable of histidine decarboxylase production. Da Silva *et al.* (2002) reported a study in which strains of *Pseudomonas*, and *Acinetobacter* spp., isolated from commercial samples of smoked salmon demonstrated significant histidine decarboxylase activity *in vitro*. da Silva and Gibbs (2015) studied the microbial characteristics of cold-smoked salmon and salmon trout on the Portuguese market, and identified the presence of bacteria capable of producing histamine when isolated and cultivated on appropriate media; growth of these bacteria was much weaker at 5°C than 25°C, where 41% of samples demonstrated this potential.

3.6 TESTS ON SAMPLES TAKEN FROM MARKETS

Several studies report the results of testing for histamine in fish samples selected from retail markets or food service providers and a number have included Salmonidae.

A study undertaken by Mashak, Moradi and Moradi (2011) evaluated psychrophilic and mesophilic aerobic bacteria and also histamine levels in 60 samples of rainbow trout (*Oncorhynchus mykiss*) purchased from fish markets in Tehran. The testing method employed used the ELISA method (Rida Screen Histamine Kits). The range of histamine contents identified was 40 to 280 mg/kg (mean 41.8 mg/kg), with 12.5% of samples falling above the maximum limit of 200 mg/kg. Histamine levels were highly correlated with bacterial enumeration ($P<0.01$). Lower concentrations were reported by Emir-Çoban, Özlem, and Bahri Patir (2008) in fresh rainbow trout samples taken from the Turkish market, with seasonal variations between 7.7 and 16.4 mg/kg.

Evangelista *et al.* (2016) reported on analytical methodology for histamine in fresh and canned fish, using as substrates fresh tuna steaks, fillets of Nile tilapia and three samples of rainbow trout sampled from fish farms within the state of Minas Gerais, Brazil. The study could not detect histamine in the trout samples.

Kim *et al.* (2009) studied biogenic amine development in forty-one species of fish, squid and shellfish selected from retail markets in the Republic of Korea including 5 samples of chum salmon (*Oncorhynchus keta*). The dominant microbial group was *Enterobacteria* throughout the storage period. The salmon samples had a mean of 1.4 mg/kg of histamine (max: 6–8 mg/kg).

The histamine concentrations in 146 samples of fishery products purchased from supermarkets in Lithuania was assessed by Garmienė, Zaborskienė and Šalaševičienė (2014). Histamine was determined by High Performance Liquid Chromatography (HPLC). Histamine levels in salmon varied from 5.00 mg/kg (the detection limit) up to 240.78 mg/kg. Marinated salmon samples contained 48 times less histamine compared to those of cold smoked salmon products and 23 times less, compared with those of chilled salmon products. The authors calculated that histamine levels in 16% of salmon samples analysed exceeded the limits defined in Regulation (EC) 2073/2005, although this is was not evident from the data presented. Furthermore, without the details on storage conditions, and a sensory evaluation at the time of testing it is unclear what the results truly mean.

Auerswald *et al.* (2006) reported on histamine levels in seventeen species of fresh and processed South African seafood, purchased from different outlets, including one sample of Atlantic salmon from Norway and two of salmon trout (*Salmo trutta*). In the salmon, the reported level of histamine was 2.8 mg/kg, while the trout ranged between 3.8 and 48.4 mg/kg. Samples were also taken of the Cape salmon (*Atractoscion aequidens*) which is not a member of the salmonid family.

Rodrigues *et al.* (2012) reported on the histamine content of 54 samples of sushi and sashimi collected from 19 restaurants in Brazil. The mean histamine content of 18 samples of salmon sushi was 0.6 mg/kg (±0.24) and of 14 samples of salmon sashimi was 3.6 mg/kg (±13.4). .

Pawul-Gruba, Michalski and Osek (2014) measured histamine levels in 93 samples of fresh and smoked fish commercially available in Poland, including 10 samples of salmon and 7 of brown trout (*Salmo trutta*). Histamine was detected in two samples of fresh salmon (1.5 mg/kg) and one sample of smoked salmon (2.7 mg/kg). In all fresh and smoked brown trout, histamine levels were below the limit of detection. The highest concentrations of the compound were found in smoked herring and smoked sprat (17.7 mg/kg and 24.1 mg/kg, respectively).

Piersanti *et al.* (2014) reported the results of a four-year programme of screening and confirmatory testing for histamine in fish products in the frame of official controls in Italy. A total of five hundred and ninety batches of fish products (3129 determinations), including 10 samples of Atlantic salmon (*Salmo salar*), were analysed between 2008 and 2012. Only a small percentage of batches analysed (4.9%) was judged non-compliant, none of which were salmon.

Muscarella *et al.* (2013) also reported on a survey of histamine levels in 311 samples of fresh fish and fish products collected in Puglia (Italy) between 2009 and 2011, with testing by ELISA and HPLC with fluorimetric detection. Non-compliance rates of 5%, similar to those reported by Piersanti *et al.* (2014) were noted. Some of the samples were taken from local restaurants in follow-up to reported cases of allergic reaction. In one case, a salmon steak (the only salmon sample tested in the study) showed a histamine concentration level of 434 ±34 mg/kg of histamine. However, no further details or contextual information such as storage conditions were included in the report.

A survey of fish meat from restaurants in the Czech Republic included Atlantic salmon, brown trout and rainbow trout (Buňka *et al*., 2013). Histamine was detected in eight of the 20 Atlantic salmon samples with levels ranging from <10mg/kg to between 50 and 100 mg/kg. Samples were either frozen or stored on ice. While specific storage information was not available for the salmon the authors noted that there were no significant difference in results based on storage conditions.

While other surveys on the biogenic amine and/or histamine content in fish have been undertaken, it was observed that these did not include information on histamine on Salmonidae and therefore they have not been considered here.

4

Global Production and trade in Salmonidae

4.1 PRODUCTION

The main species of Salmonidae produced and entering commerce, and their common names, are shown in Table 7.

TABLE 7. Main species produced and their common names

Common name	Latin name
Atlantic salmon	*Salmo Salar*
Rainbow trout	*Oncorhynchus mykiss*
Pink (=Humpback) salmon	*Oncorhynchus gorbuscha*
Chum(=Keta=Dog) salmon	*Oncorhynchus keta*
Sockeye(=Red) salmon	*Oncorhynchus nerka*
Coho(=Silver) salmon	*Oncorhynchus kisutsh*
Chinook(=Spring=King) salmon	*Oncorhynchus tshawytscha*
Sea trout	*Salmo trutta*
Brook trout	*Salvelinus fontinalis*
Lake trout(=Char)	*Salvelinus* spp.
Masu(=Cherry) salmon	*Oncorhynchus masou*
Sevan trout	*Salmo ischchan*

Global production of these species of Salmonidae as reported to the FAO Fishstat Database was 4 335 597 tonne in 2015 (see Table 8).

Capture fisheries supplied 1 029 989 tonne in 2015 (24%) and aquaculture (marine and freshwater) provided the balance. The major producers are also indicated in Table 8: Norway (32%), Chile (19%), the USA (12%) and the Russian Federation (9%) are the largest producers of salmonids.

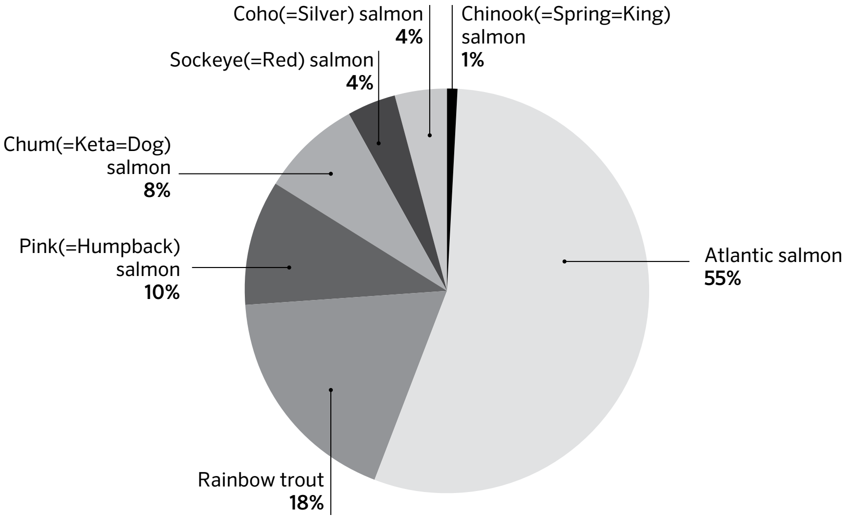
TABLE 8. Major producers of Salmonidae 2015

Producer	Production (tonnes)
Norway	1 376 760
Chile	830 279
United States of America	523 819
Russian Federation	407 374
United Kingdom	184 906
Japan	167 181
Iran (Islamic Rep. of)	140 632
Canada	139 929
Turkey	106 969
Faroe Islands	80 600
Australia	48 336
Peru	41 238
France	37 766
Denmark	33 230
Others	216 579
Total	4 335 597

Source: FAO Fishstat 2017

Figure 1. shows the global production by species in 2015, of which 55% was Atlantic salmon (*Salmo salar*) and 18% was rainbow trout (*Oncorhynchus mykiss*). Pacific salmons (other *Onchorynchus* spp.) accounted for 27% of production. Other species of Salmonidae, notably chars (*Salvelinus* spp.), whitefish (*Coregonus* spp.) and grayling (*Thymallus* spp.) and highly localized species such as the Danube salmon (*Hucho* spp.), have negligible production

FIGURE 1. Global Production of Salmonids, 2015



Source: FAO Fishstat 2017

reported in the Fishstat database[6]. If they enter international trade at all they are recorded as "not elsewhere indicated". Annual trade figures for each year 2006 to 2015 are shown in Annex 2.

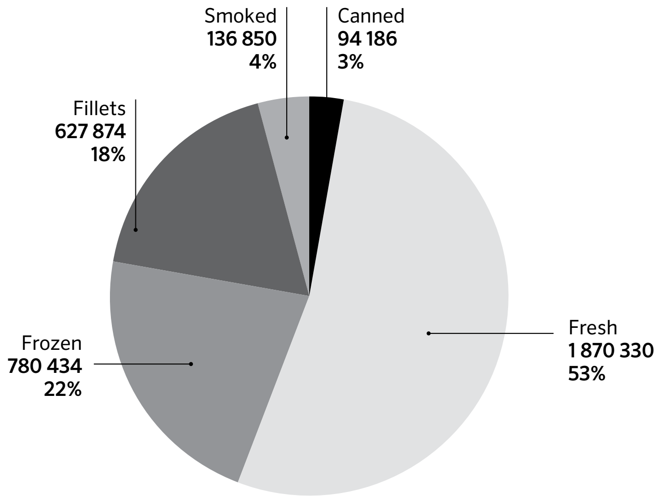
4.2 TRADE

Salmonids are widely traded, either in fresh, smoked or frozen form, and in the case of Pacific salmons, also in canned form. Gross global exports were in the region of 3 509 674 tonnes in 2015, some 81% of global production. Figure 2 provides an overview of the nature of the products traded internationally.

About 53% of the trade volume is in the form of fresh products and the most traded product is fresh or chilled Atlantic salmon *Salmo salar* (47% of trade). Around 23% is traded in frozen form, 18% as fresh or frozen fillets, 4% smoked and 3% canned. According to the FAO FishStat Database, the major exporting countries (by volume) are the large producers (Norway, Chile, United States of America, Russian Federation, Denmark and the United Kingdom) which account for an estimated 63% of exports. The main importers are China, the United States of America, Japan, Russian Federation and several European Union countries (Sweden, Denmark,

[6] Available at http://www.fao.org/fishery/statistics/software/fishstat/en

FIGURE 2. Global Exports in Salmonids by type of product (tonnes and %)



Source: ITC TradeMap

Germany and Poland) which account for 61% of imports. More detailed data on international trade for the period 2012 to 2015 is shown in Annex 2.

4.3 REVIEW OF REJECTIONS IN INTERNATIONAL TRADE

4.3.1 Australia

Australia applies border controls on imported food products under the Imported Food Control Order 2001, based on the advice from Food Standards Australia New Zealand.

The species on which histamine controls are applied was subject to a reclassification from the 4 January 2017[7]. The following fish and fish products have been classified as risk foods for histamine (FSANZ, 2016), which means they are subject to 100% inspection until 5 consecutive consignments have passes inspection. With continuing compliance the inspection rate is progressively reduced.

Fish of the family:
  Scombridae (for example, tuna, mackerel and bonito);
  Coryphaenidae (for example, mahi-mahi);

[7] Based on Australian Government IFN 21-16 – Histamine susceptible fish. Issued: 21 December 2016. Available at http://www.agriculture.gov.au/import/goods/food/notices/ifn-21-16

Pomatomidae (for example, bluefish);
Carangidae (for example, trevallies, jacks and pompanos);
Clupeidae (for example, herrings, sardines);
Engraulidae (for example, anchovy);
Scomberesocidae (for example, king gars and saury); and
fish products containing more than 300 g/kg of all or any of the fish named above.

The food will not be released if it is found to contain more than 200 mg/kg of histamine. Other fish, which are considered a low risk, are referred to as surveillance food, and have only a 5% chance of being referred for inspection.

According to the Imported Food Inspection Scheme of the Australian Department of Agriculture and Water Resources[8] for the period October 2005 - August 2013 of the 11 897 samples tested for histamine in fish and fish products, there were 173 non-compliant consignments, a 1.5 % failure rate.

The fish types reported to have failed to comply with the Maximum Limits for histamine in the Code include mackerel, tuna, bonito, anchovy, seer fish, sprats, salmon, and sardines. No specific data is provided for the case of salmon. However, given that Knope, Sloan-Gardener Stafford (2014), in their review of histamine fish poisoning in Australia, 2001 to 2013, also refer to West Australian Salmon (*Arripis* spp.), these border rejections cannot be definitively identified as fish of the Salmonidae family.

Under the Imported Food Inspection Scheme, 1 074 samples of imported fishery products were tested for histamine during the period January to June 2016, and 10 were found to be non-compliant. There were no rejections of Salmonidae for this hazard.

4.3.2 European Union

European Union (EU) Member States which operate EU border inspection posts, implement Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs, which sets out histamine limits for different species of fish. Criteria are applied to:

- Fishery products from fish species associated with a high amount of histidine;

[8] Imported Food Inspection Scheme 2016, Imported food inspection data report for January to June 2016, Department of Agriculture and Water Resources, Canberra, December. CC BY 3.0. Available at: http://www.agriculture.gov.au/import/goods/food/inspection-compliance/inspection-data#2016

- Fishery products which have undergone enzyme maturation treatment in brine, manufactured from fish species associated with a high amount of histidine; and
- Fish sauce produced by fermentation of fishery products

Fish species associated with a high amount of histidine are defined as "particularly fish species of the families: Scombridae, Clupeidae, Engraulidae, Coryfenidae, Pomatomidae, Scombresosidae".

There are no data on sampling, but within notifications of 326 consignments of hazardous fishery products made to the EU's Rapid Alert System for Feed and Food[9] of fishery products in 2016, there were 42 reports of non-compliance with limits for histamine in fish and fishery products. None of these involved salmonids.

4.3.3 United States of America

Imports of fishery products to the United States of America are controlled by the United States Food and Drug Administration (FDA). FDA's seafood Hazard Analysis Critical Control Point (HACCP) rule, under Title 21 of the Code of Federal Regulations, Part 123 Fish and Fishery Products, defines scombroid toxin-forming species as tuna, bluefish, mahi mahi, and other species, whether or not in the family Scombridae, in which significant levels of histamine may be produced in the fish flesh by decarboxylation of free histidine as a result of exposure of the fish after capture to temperatures that permit the growth of mesophilic bacteria. Implementation regulations published by the FDA[10] indicate that processors must assess the potential of other species to produce histamine. Failure to properly control and identified hazard could cause a manufacturer's seafood to be refused entry into the United States of America.

In addition, FDA can refuse consignments of seafood in which contaminants, such as elevated histamine, are detected. A survey of the Import Refusal Reports[11] published by the United States Food and Drug Administration during the period from 1 October 2013 to present (as of this writing), shows that approximately 75 non-compliant consignments of salmon were refused entry, none as a consequence of elevated histamine in the affected product (albeit, few, if any, of the salmon products were tested for histamine).

[9] See https://ec.europa.eu/food/safety/rasff/portal_en

[10] Food and Drug Administration 21 CFR Parts 123 and 1240, Docket No. 93N–0195, RIN 0910–AA10, Procedures for the Safe and Sanitary Processing and Importing of Fish and Fishery Products see: https://www.gpo.gov/fdsys/search/pagedetails.action?st=95-30332&granuleId=95-30332&packageId=FR-1995-12-18

[11] See https://www.accessdata.fda.gov/scripts/importrefusals/

4.3.4 Japan

Food safety requirements are defined under the Food Safety Basic Act (Act No.48 of 2003), and import controls implemented under the Imported Foods Monitoring and Guidance Plan. This includes checks on histamine in fish and fishery products. However, the precise targeting is not specified.

In its annual reports[12] of the results of the import monitoring by the Department of Environmental Health and Food Safety of the Ministry of Health, Labour and Welfare, there are no specific data published on the rejections of import consignments due to this hazard.

[12] Inspection Results of Imported Foods Monitoring and Guidance Plan for FY 2016 Interim Report December 2016. See: http://www.mhlw.go.jp/english/topics/importedfoods/16/16-06.html

5

Summary of findings

5.1 OVERVIEW OF ILLNESSES

The review found very limited evidence of SFP and SFP-like illnesses linked to Salmonidae. Over a period of 40 years, a handful of papers indicated there may have been about 55 cases but the majority of these were only suspected as being linked to Salmonidae (Table 9). Only 11 of these cases were actually confirmed. In a few cases the product was tested but the results are somewhat inconsistent. Some indicate very low levels of histamine (<10 mg/kg) in which cases the authors suggest that there may have been something else which contributed to the illness. On a couple of occasions when fish samples were available histamine was found at levels that may cause illness. In general, cases or incidents seem to be isolated or linked to small groups or family settings. Much of the data on illness is historical in nature and only 8 cases linked with salmon, 6 of which were confirmed, actually occurred in the last decade. The historical nature of much of this data when techniques were not available to confirm species, and the observation that salmon may be used as a common name for species that are not a member of the family Salmonidae, also raises questions as to whether in suspected cases, the implicated fish was indeed a member of the family Salmonidae.

TABLE 9. Summary of the findings of the review for data on SFP or SFP-like illness linked to Salmonidae

Country	Year	Status	Number of illnesses	Product	Establishment	Level of histamine mg/kg	Reference
Italy	-	Confirmed	1	Salmon steak	Restaurant	434 mg/kg	Muscarella et al., 2013
UK	1987-1996	Suspected	30	Salmon	Not available	51 mg/kg (sample only available from one incident)	Scoging, 1991
UK	1976-1986	Suspected	12	Salmon (6 were canned salmon)	Not available	Five samples - <10 mg/kg One sample: 170 mg/kg	Bartholomew et al., 1987
USA	2015	Suspected	2	Salmon	Private home/ residence	Not available	CDC, 2017
USA	2012	Confirmed	2	Salmon	Restaurant - Sit-down dining	Not available	CDC, 2017
USA	2009	Confirmed	3	Salted salmon	Private home/ residence	Not available	CDC, 2017
USA	2003	Confirmed	4	Salmon	Restaurant - other or unknown	Not available	CDC, 2017
USA	1999	Suspected	2	Salmon	Restaurant - other or unknown	Not available	CDC, 2017
USA	-	Confirmed	1	Home-smoked sockeye salmon	Private residence / home	1.9mg/kg	Gessner, Hokama and Isto, 1996

5.2 DEVELOPMENT OF HISTAMINE IN SALMONIDAE

A tabulated summary of the main findings regarding the development of histamine in Salmonidae is shown in Table 10. The shelf-life studies indicated that histamine development in Salmonidae is not detected or very low within the shelf-life period. While higher levels were observed in a couple studies, these were associated with extended storage time or an increase in ambient temperature (Křížek *et al.*, 2012a, b; Simsek & Kilic; 2013), but in these cases levels still remained at or below 100 mg/kg. Levels of histamine greater than 100 mg/kg were reported in only a few studies, one study looking at the impact of brine on biogenic amine formation and three of the thirteen market surveys identified. In the first study, levels only exceeded 200 mg/kg after 4 weeks of storage. It was also noted that the bacterial counts were very high at this point but no sensory analysis data were available. Of the market studies, one study reported one salmon sample that was analysed as part of a larger survey in southern Italy, and in this case the sample was related to a reported incident of histamine poisoning. A survey of fish markets in Tehran reported 12.5% of samples above 200 mg/kg and a similar one in Lithuania indicated 16% above this limit. But there was not adequate information to conclude what may have contributed to these levels (ambient temperature, storage conditions, etc.).

TABLE 10. Summary of the findings of a literature review on histamine levels in Salmonidae

Species	Conditions	Reported histamine level	Reference
Shelf life studies (naturally occurring spoilage bacteria):			
Atlantic salmon heads and viscera	4°C	Not detected after 7 days	Shumilina *et al.*, 2016
Atlantic salmon	4°C	Not detected after 7 days	Shumilina *et al.*, 2015
Coho salmon	Chilled	Negligible (12 days) 28.8 mg/kg at 17 days (mean n=5; SD 11.7:)	Aubourg *et al.*, 2007
Fresh and frozen/ thawed salmon	Modified atmosphere at 2°C Vacuum packed and frozen at 2°C	11.3 (± 4.9) mg/kg at 14 days (fresh) Not detected in frozen/ thawed salmon at 28 days	Emborg *et al.*, 2002
Salted/brined cold-smoked salmon	Storage for 2 weeks at 5°C after sensory spoilage	3±3 to 240 ±64 mg/kg	Jørgensen, *et al.* (2000a)
Pink Salmon	10°C	Not detected after 2 weeks	Crapo and Himelbloom (1999)
Salmon	15 days at 20% and 40% CO_2-atmosphere	Not detected	de la Hoz *et al.*, 2000
Salmon (not specified)	Vacuum packed, salted	No histamine producing isolates were detected	Leisner *et al.*, 1994
Rainbow trout	0-4°C diseased and healthy fish	5.35 (±0.55) mg/kg (5 days) (healthy fish) 6.6 (±0.63) mg/kg (5 days) (unhealthy (red-mouth disease) fish)	Grotta *et al.*, 2016

Rainbow trout	Vacuum packed 3.5°C	Not detected (except after 70 days)	Matějková *et al.*, 2015
Rainbow trout	Ice storage	4.30 mg/kg after 18 days	Hosseini, Rahimi and Mirghaed, 2014
Rainbow trout	Chilled storage	<0.5mg/kg at 7 days Not detected at 19 days	Özogul *et al.*, 2013
Rainbow trout	Chilled storage	8.1 mg/kg at 20 days (untreated control) (mean: n=3)	Özogul, Kus and Kuley, 2013
Rainbow trout döner kebab	4°C	44.1 ± 3.8 mg/kg after 30 days storage	Simsek & Kilic, 2013
Rainbow trout mince	Refrigerated	0.32 mg/kg after 9 days	Peiretti *et al.*, 2012
Rainbow trout	7 days @15°C 10 days @3°C	79.7 mg/kg Histamine not detected	Křížek *et al.*, 2012b
Rainbow trout	Ice storage	1.6 mg/kg after 18 days (mean: n=3; SD: 0.28)	Rezaei *et al.*, 2007
Rainbow trout (whole)	Ice	1.6 mg/kg at 18 days (mean: 2(n=3); SD: 0.0015)	Chytiri *et al.*, 2004
Rainbow trout	6 hours @ 30°C plus 14 days at 0°C	13 mg/kg after 14 days	Dawood *et al.*, 1988
Trout	Vacuum-packed 3.5°C	0.77 mg/kg after 7 days (mean n=3; SD:1.88); 103 mg/kg after 28 days (mean n=3; SD:85)	Křížek *et al.*, 2012a
Arctic Char	Fresh	No histamine detected	Synowiecki *et al.*, 1994
Shelf Life studies (inoculation)			
Coho salmon	Inoculation with *Morganella morganii* Storage at 4°, 15°, 25°, and 37°C for up to 60 hours	Max levels reported: 2.4 mg/kg @ 15 °C 2.5 mg/kg, @ 25 °C 2.3 mg/kg @ 37°C	Kim *et al.*, 2002
Rainbow trout Vacuum-packed	20 days storage at 4 ± 0.5°C	Maximum 6.11 ± 0.2 mg/kg in non-inoculated control	Katikou *et al.*, 2006
Rainbow trout fillets (lactic fermentation)	35 days at 4 °C	Max level 333 ± 5.1 mg/kg after 35 days (untreated control)	Kuley, 2011
Cold-smoked rainbow trout (lactic fermentation)	ripened at 7–8°C for 1 week and 4 °C for 35 days	7.4, 78.0, and 10 mg/kg in non-inoculated control after 35 days	Petäjä, Eerola and Petäjä (2000)

Studies on samples taken from markets			
Atlantic salmon	Lithuania	5.00 mg/kg to 240.78 mg/kg 16% exceeded the EU limits	Garmienė, Zaborskienė and Šalaševičienė, 2014
Atlantic salmon	Italy	No samples (out of 10) reported with histamine	Piersanti *et al*., 2014
Atlantic salmon	Czech Republic	<10mg/kg to 50 – 100 mg/kg (8/20 samples)	Buňka *et al*., 2013
Atlantic salmon	Brazil	Salmon sushi 0.6 mg/kg (±0.24) Salmon sashimi 0.36 mg/kg (±1.34).	Rodrigues *et al*., 2012
Atlantic salmon	South Africa	2.8 mg/kg	Auerswald *et al*., 2006
Chum Salmon	the Republic of Korea	Mean 1.4 mg/kg Range ND – 6.8mg/kg	Kim *et al*., 2009
Fresh salmon Smoked salmon	Poland	1.5 mg/kg 2.7 mg/kg	Pawul-Gruba, Michalski and Osek, 2014
Salmon	Puglia (Italy)	One sample reported 434 ±34 mg/kg (linked to an allergic reaction)	Muscarella *et al*., 2013
Rainbow trout	the Islamic Republic of Iran	40 to 280 mg/kg (mean 41.8 mg/kg) 12.5% of samples above 200 mg/kg	Mashak, Moradi and Moradi, 2011
Rainbow trout	Turkey	7.7 to 16.4 mg/kg depending on season	Emir Çoban, Özlem, and Bahri Patir, 2008
Rainbow trout	Brazil	Not detected	Evangelista *et al*., 2016
Brown trout	South Africa	3.8 to 48.4mg/kg	Auerswald *et al*., 2006
Brown trout	Poland	Not detected	Pawul-Gruba, Michalski and Osek, 2014

6

Conclusions

There is clear evidence that under certain conditions the development of histamine can occur in at least two species of the Salmonidae family. Several inoculation studies on sterile Atlantic salmon (*Salmo salar*) and rainbow trout (*Oncorynchus mykiss*) with known bacterial producers of histidine decarboxylase have clearly demonstrated that there can be present sufficient histidine in the muscle of these species to generate measurable quantities of histamine. Most of the research has been conducted on Atlantic salmon and rainbow trout. There is insufficient evidence regarding other genera within the family to indicate whether they are more or less susceptible to histamine development.

Numerous storage trials on salmon and trout have sought to characterize the development of histamine during its shelf life under different conditions. Evidence from 21 spoilage trials show that whilst histamine can develop, in many trials it is not detected, or if it is, only in relatively low concentrations, well below current regulatory limits set for other species such as tuna, and if at all towards the end or beyond limits of sensory acceptability. In only one of the shelf-life studies reviewed (Jorgensen *et al.*, 2000a) was the Codex limit of 200 mg/kg exceeded, but only after 2 weeks of storage after the detection of sensory spoilage.

At the same time, studies in the Islamic Republic of Iran and Lithuania found that 12.5% and 16% respectively of Salmonidae sampled from the market had levels of histamine that exceeded regulatory limits (Mashak, Moradi and Moradi, 2011, Garmienė, Zaborskienė and Šalaševičienė, 2014). Huss, Embarek and Jeppesen (1995) also reported unpublished evidence that samples of salmon from the Danish market had been detected with high (but unspecified) levels of histamine. Other market sampling exercises in six different countries failed to detect histamine, or if they did so, at levels below the limits set for other fish species.

The evidence suggests that the typical bacterial flora associated with histamine development in fish, are not always present or dominant in the spoilage of fresh, smoked or salted Salmonidae, but that when they are, histamine can develop.

However, the epidemiological evidence for the pathogenesis of histamine in Salmonidae is scant. The review has been able to identify only a small number (eleven) of documented cases of SFP-like syndrome linked to human consumption of Salmonidae over a span of 40 years, as reported by Gessner, Hokama and Isto (1996), Muscarella *et al.* (2013) and the CDC Foodborne Outbreak Online Database. One of these involved low levels of histamine (mean 1.9 mg/kg) and another involved quite high levels (mean 434 mg/kg, in excess of regulatory limits set for tuna). There is no data on histamine levels in the other cases. An additional 46 suspected cases of histamine poisoning from salmon were reported between 1976 and 2015, two in the United States of America and 42 in the United Kingdom (some of the latter involving canned and smoked fish). However, as no further data on these is available, these remain unconfirmed, and a more recent review from the United Kingdom indicated no reported incidents of elevated histidine or histamine in fresh North Atlantic salmon (James *et al.,* 2013).

Furthermore, the low level of histamine in the implicated product in one of the documented cases suggests that other factors may also be involved in development of toxicity symptoms in humans, which could include potentiation by other biogenic amines (although there is conflicting evidence for this), as well as endogenous variables such as individual susceptibility, and previous exposure. However, the evidential basis is insufficient for a full assessment.

The low frequency of confirmed cases of toxicity in relation to the high volume of production, trade and consumption of Salmonidae suggests that the hazard is not a significant threat to human health. Although more than eighty percent of global production of Salmonidae enters international trade (with the major exporters being Norway, Chile, United States of America and the Russian Federation) there have been no reported cases of rejections of consignments traded internationally (although this could also reflect a low frequency of surveillance). To put this in context, in 2017 alone there have been 37 RASFF notifications related to histamine in tuna and at least 72 cases of histamine-related illness linked to tuna consumption in in two European countries alone (EFSA, 2017).

Most Atlantic salmon consumed is derived from marine aquaculture; rainbow trout comes mostly from fresh water aquaculture; and Pacific salmon of all species is derived (with minor exceptions) from capture fisheries. The influence of salinity, species and production method, in terms of histidine levels, natural microbial flora and histamine development have not been investigated.

All studies reviewed have concluded that due to the non-linear development of histamine, this compound is not a good indicator of spoilage (unlike other biogenic amines such as cadaverine and putrescine which correlate well with observable sensory changes). This finding of histamine as a poor indicator of spoilage is in line with the report of the FAO/WHO expert meeting on biogenic amines (FAO/WHO, 2013)

To conclude, based on the controlled spoilage studies it appears that histamine concentrations in Salmonidae seemed to increase only after excessive storage times at the temperatures selected, and days to weeks past sensory shelf-life. With inoculation studies, histamine concentrations in Salmonidae did not appear to increase substantially until after extreme abuse conditions. Although extensively traded globally, there are no reports of Salmonidae being rejected based on histamine levels. Thus, while it is noted that under certain conditions histamine development can occur, the available evidence highlights that under appropriate time×temperature control, and within the sensory shelf-life of the product, histamine development in Salmonidae to the levels that cause SFP is unlikely to occur .

The data on SFP-like illness associated with Salmonidae is not extensive. Histamine levels are only available for some of the cases and often are at levels below that which has been seen to cause SFP. This has led some authors to question whether indeed illness was related to histamine. In this context it is worthwhile to reiterate the recommendation of the FAO/WHO Expert meeting on biogenic amines (FAO/WHO, 2013) which states that "*Studies are needed to investigate and clarify the SFP-like syndrome reported to be associated with consumption of salmonid species. These studies should establish whether the syndrome is SFP and, if it is not, the exact nature of the syndrome should be characterized*." In the literature, evidence on SFP overwhelmingly relates to species other than Salmonidae (FAO/WHO, 2013; Lehane and Olley, 2000; EFSA, 2017; Feng, Teuber and Gershwin, 2016).

The currently available evidence thus suggests that there is not a basis to include Salmonidae in the same risk category for SFP as other more commonly implicated species.

7

References

Aubourg, S.P., Quitral, V., Larraín, M.A., Rodríguez, A., Gómez, J., Maier, L. & Vinagre, J. 2007. Autolytic degradation and microbiological activity in farmed Coho salmon (*Oncorhynchus kisutch*) during chilled storage. *Food Chemistry,* 104(1): 369–375.

Auerswald, L., Morren, C. & Lopata, A.L. 2006. Histamine levels in seventeen species of fresh and processed South African seafood. *Food Chemistry*, 98(2): 231–239.

Bartholomew, B.A., Berry, P.R., Rodhouse, J.C., Gilbert, R.J. & Murray, C.K. 1987. Scombrotoxic fish poisoning in Britain: features of over 250 suspected incidents from 1976 to 1986. *Epidemiology and Infection,* 99(03): 775–782.

Buňka, F., Budinský, P., Zimáková, B., Merhaut, M., Flasarová, R., Pachlová, V., Kubáň, V. & Buňková, L. 2013. Biogenic amines occurrence in fish meat sampled from restaurants in region of Czech Republic. *Food Control*, 31(1): 49–52

Chytiri, S., Paleologos, E., Savvaidis, I. & Kontominas, M.G. 2004. Relation of biogenic amines with microbial and sensory changes of whole and filleted freshwater rainbow trout (*Onchorynchus mykiss*) stored on ice. *Journal of Food Protection*, 67(5): 960–965.

Crapo, C. & Himelbloom, B. 1999. Spoilage and histamine in whole Pacific herring (*Clupea harengus pallasi*) and pink salmon (*Oncorhynchus gorbuscha*) fillets. *Journal of Food Safety,* 19(1): 45–55.

da Silva, M.V. & Gibbs, P. 2015. Significance of biogenic amines in cold-smoked fish and their relation to microbiological characteristics of products available in Portuguese retail markets. *Journal of Toxicology and Environmental Health, Part A,* 78(13-14):945–957.

da Silva, M.V., Pinho, O., Ferreira, I., Plestilová, L. & Gibbs, P.A., 2002. Production of histamine and tyramine by bacteria isolated from Portuguese vacuum-packed cold-smoked fish. *Food Control,* 13(6): 457–461.

Dalgaard, P. & Emborg, J. 2008. Histamine and biogenic amines; formation and importance in seafood. (*Ch 15, pp. 292–326*) *In:* Torger Børresen (ed.) Improving Seafood Products for the Consumer. Woodhead Publishing Ltd. Cambridge, England.

Dawood, A.A., Karkalas, J., Roy, R.N. & Williams, C.S. 1988. The occurrence of non-volatile amines in chilled-stored rainbow trout (*Salmo irideus*). *Food Chemistry,* 27(1): 33–45.

de la Hoz, L., López-Gálvez, D.E., Fernández, M., Hierro, E. & Ordóñez, J.A. 2000. Use of carbon dioxide enriched atmospheres in the refrigerated storage (2°C) of salmon (*Salmo salar*) steaks. *European Food Research and Technology,* 210: 79–188.

Edmunds, W. J. & Eitenmiller, R.R. 1975. Effect of storage time and temperature on histamine content and histidine decarboxylase activity of aquatic species. *Journal of Food Science,* 40(3): 516–519.

EFSA[European Food Safety Agency]. 2017. Assessment of the incidents of histamine intoxication in some EU countries. Available at: http://onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2017.EN-1301/epdf

Emborg, J., Laursen, B.G., Rathjen, T. & Dalgaard, P. 2002. Microbial spoilage and formation of biogenic amines in fresh and thawed modified atmosphere-packed salmon (*Salmo salar*) at 2°C. *Journal of Applied Microbiology,* 92(4): 790–799.

Emir Çoban, Ö., & Patir, B. 2008. Investigation of histamine level and some chemical quality parameters in fish consumed in Elazig City. *International Journal of Science and Technology*, 3(1): 59–65.

Espe, M., Lied, E. & Torrissen, K.R. 1993. Changes in plasma and muscle free amino-acids in Atlantic salmon (Salmo salar) during absorption of diets containing different amounts of hydrolyzed cod muscle protein. *Comparative Biochemistry and Physiology Part A: Physiology,* 105: 555–562.

Evangelista, W.P., Silva, T.M., Guidi, L.R., Tette, P.A., Byrro, R.M., Santiago-Silva, P., Fernandes, C. & Gloria, M.B.A. 2016. Quality assurance of histamine analysis in fresh and canned fish. *Food chemistry,* 211: 100–106.

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.

Feng, C., Teuber, S. & Gershwin, M.E. 2016. Histamine (scombroid) fish poisoning: a comprehensive review. *Clinical Reviews in Allergy and Immunology*, 50(1): 64–69.

Flais, M.J., Kim, S.S., Harris, K.E. & Greenberger, P.A. 2004. Salmon caviar-induced anaphylactic shock. *Allergy and Asthma Proceedings*, 25(4): 233–236).

FSANZ [Food Safety Australia New Zealand], 2016. Imported food risk statement: Fish and fish products from the families specified and histamine. Available at: https://www.foodstandards.gov.au/consumer/importedfoods/Documents/Fish%20and%20fish%20products%20and%20histamine.pdf

Garmienė, G., Zaborskienė, G. & Šalaševičienė, A. 2014. Fish product safety in Lithuania: Assessment of histamine levels. *Annals of Food Science and Technology,* 15(2): 353–360.

Gessner, B.D., Hokama, Y. & Isto, S. 1996. Scombrotoxicosis-like illness following the ingestion of smoked salmon that demonstrated low histamine levels and high toxicity on mouse bioassay. *Clinical Infectious Diseases,* 23(6): 1316–1318.

Grotta, L., Marchetti, S., Buccella, F., Castellani, F., Zitti, G. & Martino, G. 2016. Evaluation of Chemical-Nutritional Characteristics of Rainbow Trout Samples Affected by the "Red-Mouth Disease" Compared to healthy trout samples. *Animal Review*, 3(3): 59–65.

Hosseini, A.R., Rahimi, R. & Mirghaed, A.T. 2014. Determination of histamine content in muscle tissue of rainbow trout (*Oncorhynchus mykiss*) during ice storage. *Comparative Clinical Pathology,* 23(3): 775–778.

Hungerford, J.M. 2010. Scombroid poisoning: a review. *Toxicon*, 56(2): 231–243.

Huss, H.H., Ababouch, L. & Gram, L., 2003, Assessment and management of seafood safety and quality. *FAO Fisheries Technical Paper*, 444. FAO, Rome.

Huss, H.H., Embarek, P.K.B. & Jeppesen, V.F. 1995. Control of biological hazards in cold smoked salmon production. *Food Control,* 6(6): 335–340.

James, C., Derrick, S., Purnell, G. & James, S.J. 2013. Review of the risk management practices employed throughout the fish processing chain in relation to controlling histamine formation in at-risk fish species (FS241055).

Jørgensen, L.V., Dalgaard, P. & Huss, H.H. 2000a. Multiple compound quality index for cold-smoked salmon (*Salmo salar*) developed by multivariate regression of biogenic amines and pH. *Journal of Agricultural and Food Chemistry,* 48(6): 2448–2453.

Jørgensen, L.V., Huss, H.H. & Dalgaard, P. 2000b. The effect of biogenic amine production by single bacterial cultures and metabiosis on cold-smoked salmon. *Journal of Applied Microbiology,* 89(6): 920–934.

Katikou, P., Georgantelis, D., Paleologos, E.K., Ambrosiadis, I. and Kontominas, M.G. 2006. Relation of biogenic amines' formation with microbiological and sensory attributes in *Lactobacillus*-inoculated vacuum-packed rainbow trout (*Oncorhynchus mykiss*) fillets. *Journal of Agricultural and Food Chemistry,* 54(12): 4277–4283.

Kim, M.K., Mah, J.H. & Hwang, H.J. 2009. Biogenic amine formation and bacterial contribution in fish, squid and shellfish. *Food Chemistry,* 116(1): 87–95.

Kim, S.H., Price, R.J., Morrissey, M.T., Field, K.G., Wei, C.I. & An, H. 2002. Histamine production by *Morganella morganii* in Mackerel, Albacore, Mahi-mahi, and salmon at various storage temperatures. *Journal of Food Science,* 67(4): 1522–1528.

Knope, K.E., Sloan-Gardner, T.S. & Stafford, R.J. 2014. Histamine fish poisoning in Australia, 2001 to 2013. *Communicable diseases intelligence quarterly report,* 38(4): E285–293.

Konso, S., Yamaguchi, Y., Fuke, S. & Shirai, T. 1983. Amino acids and related compounds in the extracts of different parts of the muscleof chum salmon. *Bulletin of the Japanese Society for the Science of Fish*, 49(2): 301–304.

Křížek, M., Matějková, K., Vácha, F. & Dadáková, E. 2012a. Effect of low-dose irradiation on biogenic amines formation in vacuum-packed trout flesh (*Oncorhynchus mykiss). Food chemistry,* 132(1): 367–372.

Křížek, M., Vácha, F., Vejsada, P. & Pelikánová, T. 2012b. Formation of biogenic amines in fillets and minced flesh of three freshwater fish species stored at 3°C and 15°C. *Acta Veterinaria Brno,* 80(4): 365–372.

Kuley, E., Özogul, F., Özogul, Y. & Akyol, I. 2011. The function of lactic acid bacteria and brine solutions on biogenic amine formation by foodborne pathogens in trout fillets. *Food chemistry,* 129(3): 1211–1216.

Lavon, O., Lurie, Y. & Bentur, Y. 2008. Scombroid fish poisoning in Israel, 2005–2007. The *Israel Medical Association Journal*, 10(11): 789–792.

Lehane, L. & Olley, J. 2000. Histamine fish poisoning revisited. *International journal of food microbiology,* 58(1): 1–37.

Leisner, J.J., Millan, J.C., Huss, H.H. & Larsen, L.M. 1994. Production of histamine and tyramine by lactic acid bacteria isolated from vacuum-packed sugar-salted fish. *Journal of Applied Bacteriology,* 76(5): 417–423.

Mäkinen-Kiljunen, S., Kiistala, R. & Varjonen, E. 2003. Severe reactions from roe without concomitant fish allergy. *Annals of Allergy, Asthma and Immunology,* 91(4): 413–416.

Mashak, Z., Moradi, B. & Moradi, B. 2011. Preliminary study of histamine in rainbow trout (*Oncorhynchus mykiss*) samples from fish markets in Tehran. *Journal of Food Hygiene.* 1(2): 39–47.

Matějková, K., Křížek, M., Vácha, F. & Dadáková, E. 2013. Effect of high-pressure treatment on biogenic amines formation in vacuum-packed trout flesh (*Oncorhynchus mykiss*). *Food chemistry,* 137(1): 31–36.

Møller, A. 1989. Food Composition Tables Nutrient Composition of Danish Foods, Storkøkkencentret, Levnedsmiddelstyrelsen, Søborg, Danmark

Murata, Y., Kaneniwa, M. & Yamashita, Y. 1998. Composition of free amino acids and related compounds in the edible portion of ten salmonid species. *Bulletin of the National Research Institute of Fisheries Science*, 10(2): 65–73

Muscarella, M., Magro, S.L., Campaniello, M., Armentano, A. & Stacchini, P. 2013. Survey of histamine levels in fresh fish and fish products collected in Puglia (Italy) by ELISA and HPLC with fluorimetric detection. *Food Control,* 31(1): 211–217.

Özogul, F., Kus, B. & Kuley, E. 2013. The impact of strawflower and mistletoe extract on quality properties of rainbow trout fillets. *International Journal of Food Science & Technology*, 48(11): 2228–2238.

Özogul, F., Yavuzer, E., Özogul, Y. & Kuley, E. 2013. Comparative quality loss in wild and cultured rainbow trout (*Oncorhynchus mykiss*) during chilling storage. *Food Science and Technology Research,* 19(3): 445–454.

Pawul-Gruba, M., Michalski, M. & Osek, J. 2014. Determination of histamine in fresh and smoked fish commercially available in Poland. *Bulletin of the Veterinary Institute in Pulawy,* 58(2): 301–304.

Peiretti, P.G., Gai, F., Ortoffi, M., Aigotti, R. & Medana, C. 2012. Effects of rosemary oil (*Rosmarinus officinalis*) on the shelf-life of minced rainbow trout (*Oncorhynchus mykiss*) during refrigerated storage. *Foods,* 1(1): 28–39.

Petäjä, E., Eerola, S. & Petäjä, P. 2000. Biogenic amines in cold-smoked fish fermented with lactic acid bacteria. *European Food Research and Technology,* 210(4): 280–285.

Piersanti, A., Tavoloni, T., Lestingi, C. & Galarini, R. 2014. High-throughput histamine analysis approach in an official control laboratory: Analytical methods and four years fish products results. *Food chemistry,* 153: 437–443.

Rezaei, M., Montazeri, N., Langrudi, H.E., Mokhayer, B., Parviz, M. & Nazarinia, A. 2007. The biogenic amines and bacterial changes of farmed rainbow trout (*Oncorhynchus mykiss*) stored in ice. *Food Chemistry,* 103(1): 150–154.

Rodrigues, B.L., Santos, L.R., Mársico, E.T., Camarinha, C.C., Mano, S.B. & Conte Junior, C.A. 2012. Qualidade físico-química do pescado utilizado na elaboração de sushis e sashimis de atum e salmão comercializados no município do Rio de Janeiro, Brasil. *Ciências Agrárias,* 33: 1849–1856.

Scoging, A.C. 1991. Illness associated with seafood. CDR (London England Reviews) 1, R117–122.

Scoging, A.C. 1998. Scombrotoxic (histamine) fish poisoning in the United Kingdom. *Communicable Disease and Public Health,* 1(3): 204–205.

Self, R.L. & Wu, W.H. 2012. Determination of eight biogenic amines in selected seafood products by MSPD extraction followed by UHPLC-Orbitrap MS. *Journal of Food Composition and Analysis,* 27(2): 169–173.

Shirai, T., Fuke, S., Yamaguchi, K. & Konosu, S. 1983. Amino acids and related compounds in the extracts of heated muscles of four species of salmon. *Bulletin of the Japanese Society for the Science of Fish*, 49: 765–768.

Shumilina, E., Ciampa, A., Capozzi, F., Rustad, T. & Dikiy, A. 2015. NMR approach for monitoring post-mortem changes in Atlantic salmon fillets stored at 0°C and 4°C. *Food chemistry,* 184: 12–22.

Shumilina, E., Slizyte, R., Mozuraityte, R., Dykyy, A., Stein, T.A. & Dikiy, A. 2016. Quality changes of salmon by-products during storage: Assessment and quantification by NMR. *Food chemistry*, 211: 803–811.

Sidwell, V.D. 1981. Chemical and Nutritional Composition of Finfishes, Whales, Crustaceans, Molluscs and their Products. National Marine Fisheries Service, Washington, DC

Simsek, A. & Kilic, B. 2013. Effects of marination, cooking and storage on physico-chemical and microbiological properties of ready-to-eat trout döner kebab. *Journal für Verbraucherschutz und Lebensmittelsicherheit,* 8(3): 165–174.

Smart, D.R. 1992. Scombroid poisoning. A report of seven cases involving the Western Australian salmon, *Arripis truttaceus*. *The Medical journal of Australia,* 157(11-12): 748–751.

Synowiecki, J., Shahidi, F. & Penney, R.W. 1994. Nutrient Composition of Meat and Uptake of Carotenoids by Artic Char (*Savelinus alpinus*). *Journal of Aquatic Food Product Technology,* 2(3): 37–58.

ANNEX 1

Regulatory Histamine Limits

A1.1 CODEX ALIMENTARIUS

Codex Alimentarius limits histamine in fish and fishery products. Provisions relating to histamine are currently located in 11 specific standards rather than in an overarching document (Table A1.1). With the exception of fish sauce the provisions are similar in all standards. In terms of hygiene the standards require that "no sample unit shall contain histamine that exceeds 20 mg per 100 g". Specific reference is made to the families Scombridae, Scombresocidae, Clupeidae, Coryphaenidae and Pomatomidae. In addition, the Codex Code of Practice for Fish and Fishery Products (CAC/RCP 52-2003) identifies histamine as a hazard, noting the need for control measures and indicating in some cases what such measures may include.

A1.2 UNITED STATES FOOD AND DRUG ADMINISTRATION

In 1995, the United States Food and Drug Administration (FDA) issued revised policy guidance identifying articles of scombrotoxin-forming fish or fishery products containing 2 or more sample units greater than or equal to 50 mg/kg of histamine, or 1 or more sample units greater than 500 mg/kg of histamine, to be adulterated. In addition, in 1997, FDA's seafood Hazard Analysis and Critical Control Point (HACCP) regulation went into effect and FDA recommended that processors implement controls to prevent scombrotoxin-forming fish or fishery products from exceeding 50 mg/kg.

[As of this writing, these levels are under review by FDA and likely to be adjusted based on current knowledge.]

A1.3 CANADA

Canada has established a maximum contaminant concentration of 200 mg/kg of histamine in enzyme ripened products (e.g. anchovies, anchovy paste, and fish sauce). For all other fish and fish products (e.g. canned or fresh or frozen fish), the maximum concentration is 100 mg/kg (Health Canada 2012).

A1.4 EUROPEAN UNION

European Commission Regulation 2073/2005 on microbiological criteria for foodstuffs limits histamine content in fish and products, from species associated with a high amount of histidine, to 200 mg/kg, with decision making based on a three-class attributes sampling plan. It specifies that a high-performance liquid chromatography (HPLC) method must be used for analysis.

A1.5 AUSTRALIA AND NEW ZEALAND

In Australia and New Zealand Schedule S19—6 Maximum levels of contaminants and natural toxicants, of the Australia New Zealand Food Standards Code, currently specifies a Unit of histamine in fish and fish products of 200 mg/kg.

TABLE A1.1 Codex standards for fish and fishery products that include a specific limit for histamine

Standard*	Reference and year	Decomposition	Hygiene	Determination of histamine
Standard for quick frozen finfish, uneviscerated and eviscerated	CODEX STAN 36-1981 Adopted in 1981. Revised in 1995, 2017. Amended in 2013	The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested. This shall apply only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families.	No sample unit shall not contain histamine that exceeds 20 mg/100 g. This applies only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families.	Performance criteria for methods for determination of histamine are provided.
Standard for canned tuna and bonito	CODEX STAN 70-1981 - Adopted in 1981. Revision: 1995. Amendments: 2011, 2013, 2016.)	The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested.	no sample unit shall contain histamine that exceeds 20 mg per 100 g;	Performance criteria for methods for determination of histamine are provided.
Standard for canned sardines and sardine-type products	CODEX STAN 94 – 1981 Formerly CAC/RS 94-1978. Adopted 1981. Revisions: 1995, 2007. Amendments: 1979, 1989, 2011, 2013, 2016	The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested.	no sample unit shall contain histamine that exceeds 20 mg per 100 g	Performance criteria for methods for determination of histamine are provided.
Standard for canned finfish	CODEX STAN 119 - 1981 Adopted 1981. Revision: 1995. Amendment: 2011, 2013, 2016.	Canned finfish of the families Scombridae, Scombresocidae, Clupeidae, Coryphaenidae and Pomatomidae shall not contain more than 10 mg/100 g of histamine based on the average of the sample units tested.	No sample unit shall contain histamine that exceeds 20 mg per 100 g. This applies only to species of the families Scombridae, Clupeidae, Coryphaenidae, Scombresocidae and Pomatomidae.	Performance criteria for methods for determination of histamine are provided.

Standard*	Reference and year	Decomposition	Hygiene	Determination of histamine
Standard for quick frozen blocks of fish fillet, minced fish flesh and mixtures of fillets and minced fish flesh	CODEX STAN 165-1989 Adopted in 1989. Revised in 1995, 2017. Amended in 2011, 2013, 2014, 2016	The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested. This shall apply only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families.	No sample unit shall not contain histamine that exceeds 20 mg/100 g in any sample unit. This applies only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families;	Performance criteria for methods for determination of histamine are provided.
Standard for quick frozen fish sticks (fish fingers), fish portions and fish fillets - breaded or in batter	CODEX STAN 166 – 1989 Adopted in 1989. Revised in 1995, 2004, 2017. Amended in 2011, 2013, 2014, and 2016.	The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested. This shall apply only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families.	No sample unit shall not contain histamine that exceeds 20 mg/100 g. This applies only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families;	Performance criteria for methods for determination of histamine are provided.
Standard for quick frozen fish fillets	CODEX STAN 190 -1995 Adopted in 1995. Revised in 2017. Amended in 2011, 2013, 2014.	The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested. This shall apply only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families.	No sample unit shall not contain histamine that exceeds 20 mg/100 g. This applies only to species of Clupeidae, Scombridae, Scombresocidae, Pomatomidae and Coryphaenedae families;	Performance criteria for methods for determination of histamine are provided.
Standard for boiled dried salted anchovies	CODEX STAN 236-2003	The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested.	No sample unit shall contain histamine that exceeds 20 mg/100 g.	Performance criteria for methods for determination of histamine are provided.

Standard*	Reference and year	Decomposition	Hygiene	Determination of histamine
Standard for salted Atlantic herring and salted sprat	CODEX STAN 244-2004 Adopted in 2004. Amendments 2011, 2013, 2016.	The products shall not contain more than 10 mg of histamine per 100 g fish flesh based on the average of the sample unit tested.	No sample unit shall contain histamine that exceeds 20 mg per 100 g fish muscle.	Performance criteria for methods for determination of histamine are provided.
Standard for fish sauce	CODEX STAN 302-2011		The product shall not contain more than 40 mg histamine /100 g of fish sauce in any sample unit tested.	See AOAC 977.13.
Standard for smoked fish, smoke-flavoured fish and smoke-dried fish	CODEX STAN 311- 2013 Adopted in 2013. Amended in 2016	The product of susceptible species shall not contain more than 10 mg of histamine per 100 g fish flesh based on the average of the sample unit tested and all products in this Standard shall be free from persistent and objectionable odours and flavours characteristic of decomposition	The product shall not contain histamine that exceeds 20 mg/100g fish flesh in any sample unit tested. This applies only to susceptible species (e.g. Scombridae, Clupeidae, Engraulidae, Coryphaenidae, Pomatomidae, Scombere-socidae). Lot Acceptance For histamine no sample unit shall exceed 20 mg/100 g of fish flesh as per the sampling plan chosen.	Performance criteria for methods for determination of histamine are provided.

All standards are available online at http://www.fao.org/fao-who-codexalimentarius/committees/committee-detail/en/?committee=ccffp

ANNEX 2 Salmonid production and trade

TABLE A2.1 Global production of Salmonidae 2006-2015

Species (ASFIS species)	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
	tonnes									
TOTAL	2 946 349	3 225 829	3 019 147	3 539 081	3 267 989	3 771 739	4 060 345	4 206 961	4 228 314	4 335 597
Atlantic salmon *Salmo salar*	1 321 788	1 381 461	1 453 886	1 454 008	1 439 287	1 737 760	2 076 729	2 096 306	2 350 618	2 383 926
Rainbow trout *Oncorhynchus mykiss*	612 460	669 149	676 801	754 757	754 701	795 244	885 665	819 510	807 494	762 843
Pink (=Humpback) salmon *Oncorhynchus gorbuscha*	316 205	506 343	294 876	591 654	384 473	585 355	406 085	570 352	297 882	444 230
Chum (=Keta=Dog) salmon *Oncorhynchus keta*	361 561	331 266	295 819	359 908	318 175	276 451	316 110	357 958	336 677	350 726
Sockeye (=Red) salmon *Oncorhynchus nerka*	151 523	164 609	138 896	150 040	173 811	158 581	151 293	138 758	186 925	187 538
Coho (=Silver) salmon *Oncorhynchus kisutsh*	148 542	136 272	126 406	192 455	158 323	179 753	187 602	185 780	208 998	167 711
Others	28 877	30 367	27 006	31 120	33 817	35 353	32 079	33 748	35 305	34 907

Source: FAO Fishstat 2017

TABLE A2.2 Global Trade in Salmonidae, 2012-2015

HS Code	Product Label	Global trade (tonnes)			
		2012	2013	2014	2015
030214	Fresh or chilled Atlantic salmon Salmo salar and Danube salmon *Hucho hucho*	1 513 801	1 497 636	1 614 205	1 665 649
030211	Fresh or chilled trout Salmo trutta, *Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache* and *Oncorhynchus chrysogaster*	79 366	76 563	73 750	80 310
030219	Fresh or chilled salmonidae (excluding trout *Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache and Oncorhynchus chrysogaster,* Pacific salmon *Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou and Oncorhynchus rhodurus*, Atlantic salmon *Salmo salar* and Danube salmon *Hucho hucho*)	94 543	109 702	114 776	108 007
030213	Fresh or chilled Pacific salmon *Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou* and *Oncorhynchus rhodurus*	25 319	30 873	27 713	16 362
030212	Fresh or chilled Pacific salmon *Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou* and *Oncorhynchus rhodurus*, Atlantic salmon *Salmo salar* and Danube salmon *Hucho hucho*	642	1 264	26	2
030319	Frozen salmonidae (excluding trout and Pacific, Atlantic and Danube salmon)	-	136 038	137 477	114 399
030312	Frozen Pacific salmon (excluding sockeye salmon "red salmon")	288 252	379 605	307 591	326 708
030313	Frozen, Atlantic salmon Salmo salar and Danube salmon *Hucho hucho*	125 841	156 165	196 380	191 080
030314	Frozen trout *Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache* and *Oncorhynchus chrysogaster*	126 260	111 707	83 653	77 009
030311	Frozen sockeye salmon [red salmon] *Oncorhynchus nerka*	59 284	65 275	51 463	71 034

030321	Frozen trout (*Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache* and *Oncorhynchus chrysogaster*)	21 278	14 262	23	204
030322	Frozen Atlantic salmon (*Salmo salar*) and Danube salmon (*Hucho hucho*)	1 619	1 227	105	
030310	Frozen Pacific salmon *Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou* and *Oncorhynchus rhodurus*		-	-	
030481	Frozen fillets of Pacific salmon *Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou and Oncorhynchus rhodurus,* Atlantic salmon *Salmo salar* and Danube salmon *Hucho hucho*	219 769	268 236	303 183	270 180
030441	Fresh or chilled fillets of Pacific salmon *Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou and Oncorhynchus rhodurus,* Atlantic salmon *Salmo sala* and Danube salmon *Hucho hucho*	242 036	255 200	270 687	280 077
030482	Frozen fillets of trout *Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache* and *Oncorhynchus chrysogaster*	-	48 272	38 984	34 943
030494	Frozen meat, whether or not minced, of Alaska pollack *Theragra chalcogramma* (excluding fillets)	18 440	20 301	24 106	24 644
030442	Fresh or chilled fillets of trout *Salmo trutta, Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache* and *Oncorhynchus chrysogaster*	13 863	14 914	13 580	14 908
030452	Fresh or chilled meat, whether or not minced, of salmonidae (excluding fillets)	-	2 853	3 264	3 122
030541	Smoked Pacific salmon *Oncorhynchus nerka, Oncorhynchus gorbuscha, Oncorhynchus keta, Oncorhynchus tschawytscha, Oncorhynchus kisutch, Oncorhynchus masou* and *Oncorhynchus rhodurus*, Atlantic salmon *Salmo salar* and Danube salmon *Hucho hucho*, incl. fillets (excluding offal)	97 025	104 108	107 652	115 314
030543	Smoked trout Salmo trutta, *Oncorhynchus mykiss, Oncorhynchus clarki, Oncorhynchus aguabonita, Oncorhynchus gilae, Oncorhynchus apache* and *Oncorhynchus chrysogaster*, incl. fillets (excluding offal)	20 868	23 214	23 255	21 536
160411	Prepared or preserved salmon, whole or in pieces (excluding minced)	91 226	100 266	96 589	94 186
Totals		3 039 432	3 417 681	3 488 462	3 509 674

Source: ITC Trade Map Database

Histamine is a naturally occurring substance that is derived from the decarboxylation of amino acids. It can be present in certain foods containing free histidine. Certain bacteria produce the enzyme histidine decarboxylase during growth. This enzyme reacts with free histidine, a naturally occurring amino acid that is present in higher proportions in certain species of fish, particularly those of the Scombridae and Scomberesocidae families. The result is the formation of histamine.

Histamine poisoning is often referred to as scombrotoxin fish poisoning (SFP) because of the frequent association of the illness with the consumption of spoiled scombroid fish. SFP is most commonly linked to fish that have a high level of free histidine. Histamine formation is then dependent on the time/temperature conditions under which the fish is handled. Even in fish with high levels of free histidine, the available data suggest that high histamine levels are as a result of gross time/temperature abuse during handling and storage.

Compared with scombroid fish, which have free histidine levels ranging from approximately 5 000 mg/kg to 20 000 mg/kg, most species in the Salmonidae family have less than 1000 mg/kg histidine. Nevertheless some concerns have been raised about the potential risk of SFP or SFP-like illness linked to Salmonidae, considering these fish are globally traded with 80% of global production entering international trade.

This report describes the methods and findings of a comprehensive literature review undertaken to assess the scientific evidence regarding the risk of histamine development in fish of the family Salmonidae and the potential impact for human health.

FOR MORE INFORMATION CONTACT:
Food-Quality@fao.org
www.fao.org/food/food-safety-quality/home-page/en/

ISBN 978-92-5-130888-2
9 789251 308882
CA1207EN/1/08.18