



SIDE EVENT:

Histamine

CCFH 2016



Part 1. Background and Importance of Work on Histamine

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Histamine is not a new issue for CCFH Report of 19th CCFH, 1983

codex alimentarius commission

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CODEX ALIMENTARIUS COMMISSION

Sixteenth Session 1985

REPORT OF THE NINETEENTH SESSION OF THE
CODEX COMMITTEE ON FOOD HYGIENE

Washington, D.C., 26-30 September 1983



WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

VPH/FOS/85.1

ENGLISH ONLY

HISTAMINE POISONING
ASSOCIATED WITH FISH, CHEESE, AND OTHER FOODS

Prepared for World Health Organization

by

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Report of 19th CCFH

140. The Committee recognized that at the present time it would be too premature to elaborate any internationally acceptable regulatory limits within the framework of FAO/WHO Food Standard Programme on histamine in foods as well as to make recommendation on how to prevent and control such intoxications.

Report of 20th CCFFP 1992

- It was agreed to incorporate histamine safety limit in the Standard of canned sardine and sardine type product (Stan 94-1984).
- Original proposed limit: **20mg/100g**
- One delegation felt that the proposed level is too high, and could not reach consensus, therefore put square blanket around 200ppm.

Report of 21st CCFFP, 1994

- DRAFT REVISED STANDARD FOR CANNED FINFISH
- Codex secretariat informed: No JECFA evaluation
- Extensive discussion: **20mg/100g VS 10 mg/100g**
- Finally, based on a suggestion from one member country, CCFFP agreed to adopt **the level of 20mg/100g in the Section on Hygiene, as related to the safety aspects involved**, and to refer to a **level of 10mg/100g** as an indicator of **decomposition**.

History of Histamine Discussions at CCFFP (1)

- Codex Alimentarius established several standards that include maximum levels for histamine in different fish and fishery products.
- Different limits have been established:
 - indicators of decomposition (100 ppm) and
 - indicators of hygiene and handling (200 ppm).
- However, the associated guidance on the relevant sampling plans and other aspects of sampling is limited or even non-existent.
- Furthermore, many of these limits were established in an era before risk assessment and the scientific basis for the limits is unclear.

History of Histamine Discussions at CCFFP (2)

- As food safety management moves towards more risk- and evidence-based approaches, there is a need to review existing limits in the light of the most up-to-date scientific information and to ensure that there is a robust scientific basis for any limits recommended by Codex.

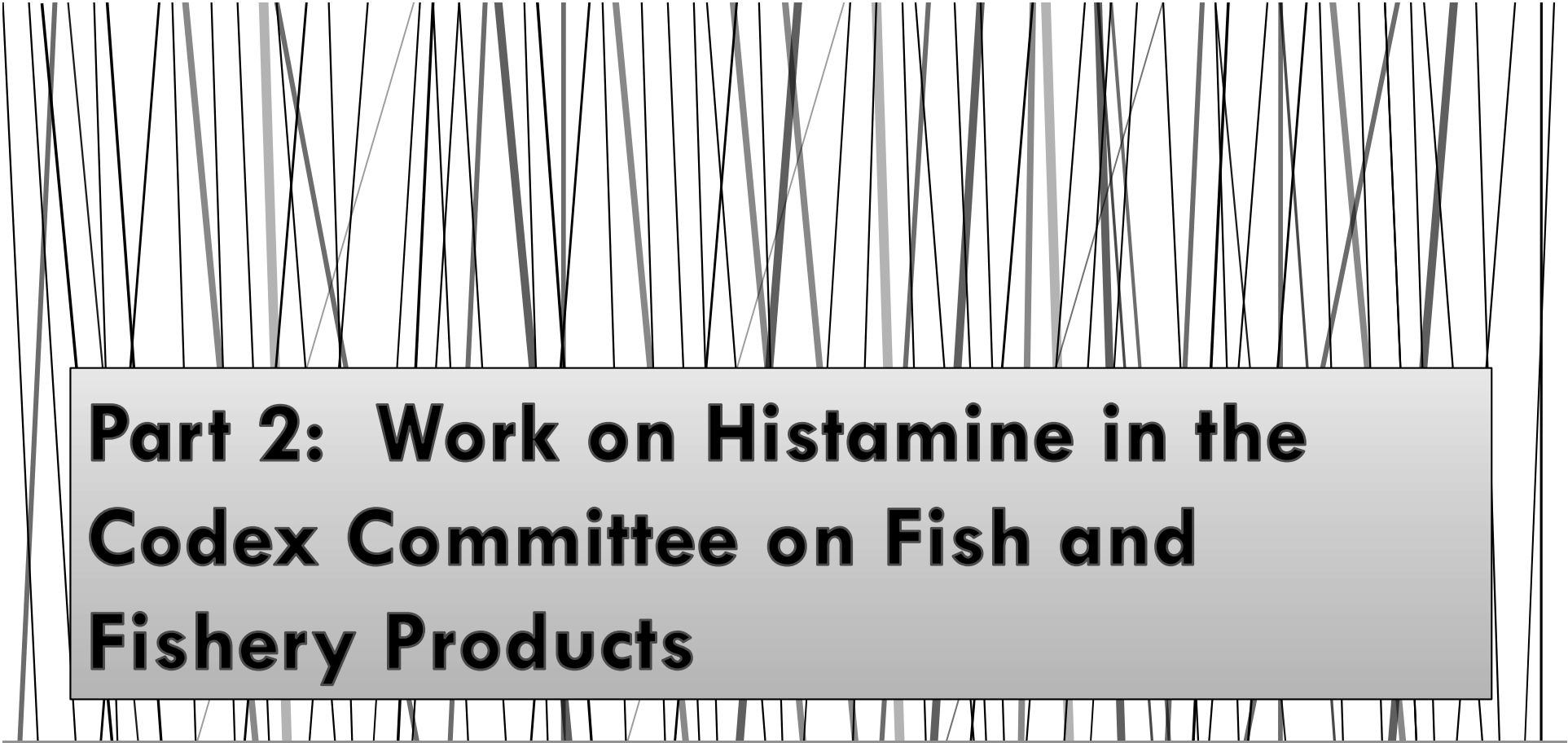
Histamine Limits and Sampling Plans in Codex Standards

Codex Standards	Histamine Limits	Sampling plan
<p>Codex Standard for sardines and sardine-type products (Codex Stan 94–1981,Rev 2007)</p> <p>Codex Standard for canned tuna and bonito (Codex Stan 70–1981,Rev 1995)</p> <p>Codex Standard for canned finfish (Codex Stan 119–1981,Rev 1995.)</p> <p>Standard for salted Atlantic herring and salted sprat (Codex Stan 244–2004)</p>	<p>3. Essential composition and quality factors</p> <p>3.3. Decomposition</p> <p>The products shall not contain more than 10 mg/100 g of histamine based on the average of the sample unit tested</p> <p>5. Hygiene and handling</p> <p>No sample unit shall contain histamine that exceeds 20 mg per 100 g</p>	<p>Sampling of lots for examination of the final product as prescribed in Section 3.3 shall be in accordance with the FAO/WHO Codex Alimentarius Sampling Plans for Prepackaged Foods (AQL-6.5) (CODEX STAN233-1969)</p>
<p>Codex Standard for fish Sauce (Codex Stan 302–2011)</p>	<p>6. Hygiene and handling</p> <p>The product shall not contain more than 40 mg histamine/100g of fish sauce in any sample unit tested</p>	<p>Sampling of lots for examination of the final product shall be in accordance with the <i>General Guidelines on Sampling</i> (CAC/GL 50-2004).</p> <p>A sample unit is the individually packed product (bottle) or a 1 l portion from bulk containers</p>

31st CCFFP (Summary From The Report)

- After the finalization of the fish sauce standard, the Delegation of Japan proposed to consider issues related to histamine from a more general perspective,
 - to review public health risk of histamine from fish and fishery products,
 - taking into account existing sampling plans, different levels of protection at the national level, and
 - noted this work should be considered in conjunction with the work on MC revision in the CCFH.
- **The Representative of FAO**
 - supported this initiative and,
 - FAO was prepared to contribute to such work, and
 - noted the need to consider trade implications and food safety issues related to histamine. →

- **The CCFFP agreed to establish an e WG to prepare a discussion paper to consider:**
 - Review epidemiological data to estimate public health risk of histamine in fish and fishery products
 - Review existing sampling plans in different countries/regions
 - Evaluate how the sampling plans and the histamine maximum limits work for risk reduction and consumer health protection
 - Review any trade implication/problem associated with histamine controls including sampling plans
 - take into account the work of the CCFH WG on the revision of the Principles for the Establishment of Application of MC related to Foods.
- **The need for scientific advice from FAO/WHO was pointed out and countries need to participate by providing data required for this work.**



Part 2: Work on Histamine in the Codex Committee on Fish and Fishery Products

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codex alimentarius commission

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CODEX COMMITTEE ON FOOD HYGIENE

Nineteenth Session
Washington, D.C., 26-30 September 1983

MONOGRAPH ON HISTAMINE POISONING

Prepared

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TOP 5

Food-Pathogen Pairs
Responsible for
Outbreaks and
Outbreak-Associated
Illnesses in 2014

Outbreaks: Top 5 Food-Pathogen Pairs

Pathogen	Food category	Number of Outbreaks	Number of Outbreak-Associated Illnesses
Ciguatoxin	 FISH	19	72
Scombroid toxin	 FISH	16	38
Salmonella	 CHICKEN	11	227
Campylobacter	 DAIRY	8	144
<i>Vibrio parahaemolyticus</i>	 MOLLUSKS	8	28

Commodity Standards

Minimum quality and safety requirements for traded commodity

- End Product lot examination
- Contains provisions and methods to determine if lot meets standard

Code of Practice for Fish and Fishery Products

- Guidance for industry/regulators for use during production
- How to produce product that meets the commodity standard
- HACCP and DAP (Defect Action Point) based

Histamine Work in Committee on Fish and Fishery Products

- **31st Session**, April 2011 – Japan recommended work
- **32nd Session**, October 2012 – Starting Discussion Paper
- 2012 Joint FAO/WHO Expert Meeting on Public Health Risks of Histamine and Other Biogenic Amines from Fish and Fishery Products
- **33rd Session**, February 2014 – EWG reviews FAO/WHO Expert Report and makes recommendations for changes in standards.
- **34th Session**, October 2015 – EWG Discussion Paper on Histamine is basis for current work in CCFH.

Main Topics Discussed

1. Updating the histamine safety limit in commodity standards
2. Revising histamine sampling guidance for commodity standards
3. Revising histamine guidance in the code of practice for fish and fishery products

Histamine Safety Limit

- NOAEL corresponds to 200 mg histamine/kg in fish (is also current safety limit)
- 200 mg/kg in fish is near level where illness symptoms can begin to occur for 95th percentile portion size
- Committee considered an Uncertainty/Safety Factor (2X – 10X) to reduce limit (100 mg/kg – 20 mg/kg)
- No decision made – Safety limit remains same, pending availability of further scientific data
- Decomposition/quality limit untouched
 - Outside scope of health hazard work
 - Possible future work on indicators of decomposition

Sampling Plan Guidance

Inconsistencies in standards

- References to appropriate guidance documents lacking
- Appears that acceptable quality level (AQL) of 6.5% applies to a histamine safety limit

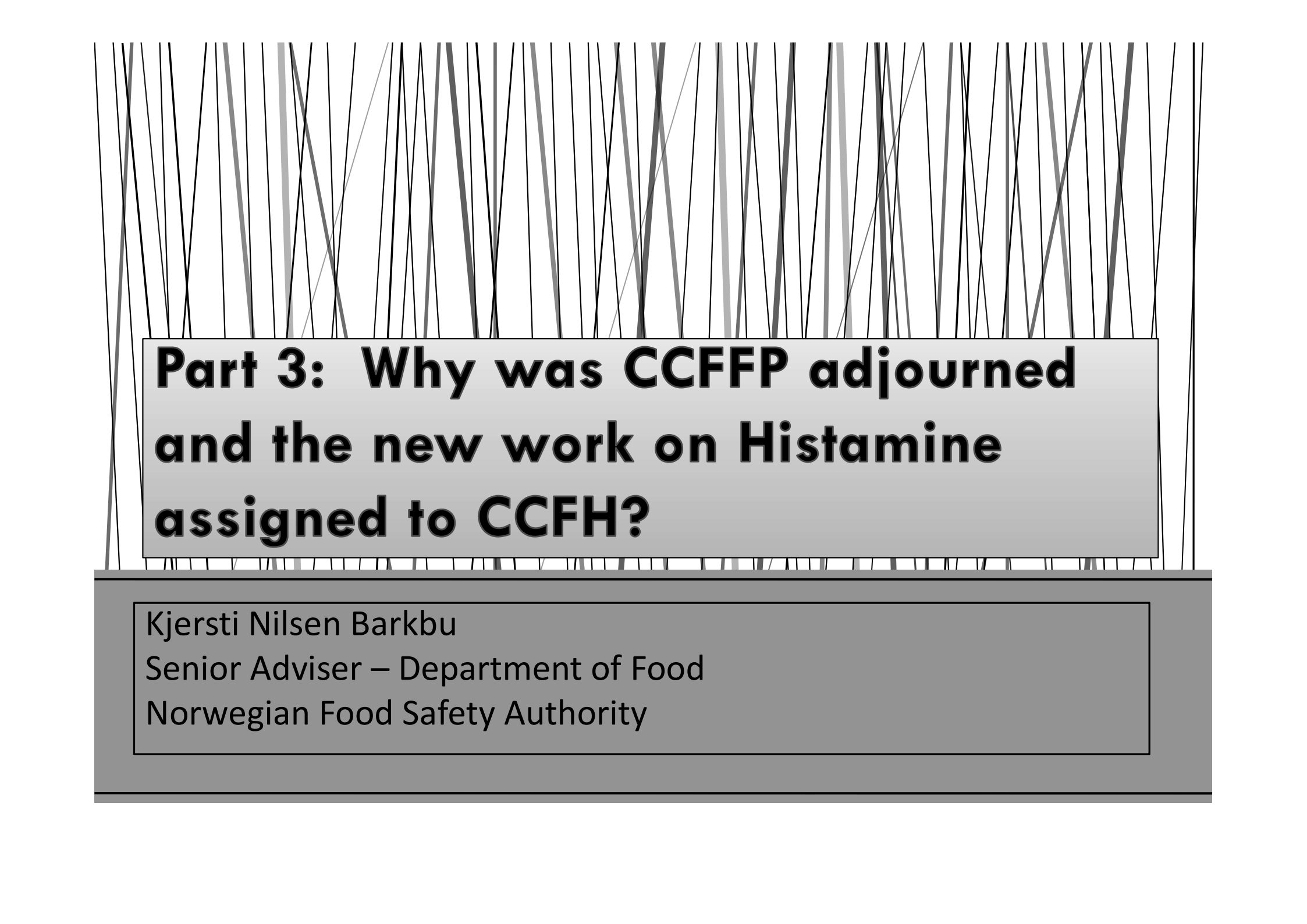
Options

- A) Better qualitative guidelines, uniformity, references
- B) Quantitative performance parameters
 - Level of protection
 - Confidence limit
 - General Guidelines on Sampling
 - WHO/FAO Histamine Sampling Tool
- C) Fixed sampling plan(s) based on quantitative performance parameters

Histamine Control Guidance

- Histamine easily controlled with HACCP time/temperature controls
- Skipjack tuna stored at 31°C (88°F) - Histamine stays under 10 mg/kg for up to 8 hours
- Improve histamine control guidance in the Code of Practice for Fish and Fishery Products
- Code is particularly lacking in harvest vessel guidance





Part 3: Why was CCFFP adjourned and the new work on Histamine assigned to CCFH?

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Overview

- Why was Codex Committee on Fish and Fishery Products (CCFFP) adjourned?
 - **I – summary and conclusion from CCFFP34**
 - **II – discussions on the future of CCFFP**
- Why was new work on Histamine assigned to the Codex Committee on Food hygiene (CCFH)?
 - **I – rationale**
 - **II – discussions before CCEXEC and CAC**

Why was Codex Committee on Fish and Fishery Products (CCFFP) adjourned? (I)

- In 2015, at their last session, CCFFP34 finalized their work on all items in the Step Procedure.
 - There was only one proposal for new work.
 - CCFFP advanced the following sections on processing to Step 8 or 5/8:
 - (i) fish sauce
 - (ii) fresh and quick frozen raw scallop products and
 - (iii) sturgeon
- for inclusion in *Code of Practice for Fish and Fishery Products (CAC/RCP 52-2003)*

Work of CCFFP

- CCFFP forwarded:
 - (i) sampling plans and amendments to the food additive provisions of several standards for fish and fishery products
 - (ii) Section 7.4 - Estimation of fish content of the *Standard for Quick Frozen Fish Sticks (Fish Fingers), Fish Portions and Fish Fillets – Breaded or in Batter* (CODEX STAN 166-1989) and
 - (iii) Section 11 – *Processing of salted and dried salted fish of the Code of Practice for Fish and Fishery Products* (CAC/RCP 52-2003)

New Work

CCFFP agreed to start new work on:

specific guidance on histamine control in the *Code of Practice for Fish and Fishery Products* (CAC/RCP 52-2003) and sampling plans for histamine in relevant standards for fish and fishery products

Why was Codex Committee on Fish and Fishery Products (CCFFP) adjourned? (II)

CCFFP34 discussed the future of the committee and agreed to:

- (1) continue working by correspondence, as the amount of outstanding work did not warrant physical sessions of CCFFP

Why was Codex Committee on Fish and Fishery Products (CCFFP) adjourned? (II)

- (2) forward new work on histamine - specific guidance on histamine control and to develop new sampling plans for histamine
 - Japan and the United States were requested to prepare a project document for the new work for submission to the Executive Committee (CCEXEC) and Codex Alimentarius Commission (CAC) via the Codex Secretariat
 - CCFFP established an EWG, led by Japan and the United States, working in English only. The EWG, subject to the approval of new work, would develop the specific guidance and new sampling plans for histamine.

Why assign new work on Histamine to the Codex Committee on Food hygiene (CCFH)? (I)

- Judging from the complexity of issues, it will be a challenge to bring this work forward in the step procedure based on consensus
- Working only by correspondence should not be the approach when more efficient working methods are at hand
- There is a lack of Codex procedures for working by correspondence...

- The work will be resource demanding for the Codex Secretariat when handled outside an active committee
- It is against Codex strategic goals to plan for work to be done in a way that could be foreseen as being neither efficient nor cost effective
- When a committee has finalized its main work, it is not justified convening a committee for a matter that can be solved in another ongoing active committee

Why assign new work on Histamine to the Codex Committee on Food hygiene (CCFH)? (II)

The CCFFP Chair in close collaboration with delegates, the Codex Secretariat and the Chair of Codex Committee on Food Hygiene (CCFH) discussed how Codex best could work on this new work in the future after the CCFFP.

Decision

It was suggested to CCEXEC and CAC, to continue with the remaining work under the umbrella of an existing committee holding physical sessions, namely the CCFH. This would facilitate:

- progress on the remaining issue by normal working procedures and priorities
- an effective, efficient, transparent and consensus based standard development in line with Codex strategic goals



Codex Procedures and Critical Review

Verna Carolissen
Codex Secretariat

Histamine – CAC39 decision

- Agreed to assign work to CCFH
- Based on critical review recommendation of CCEXEC
- Why?
 - ✓ Appropriate action as opposed to working by correspondence
 - ✓ Efficient way of working and using Codex resources

Procedure for elaboration of Codex standards and related texts

CAC takes into account outcome of critical review conducted by CCEXEC that a standard should be elaborated and also which subsidiary body should undertake the work

Critical review

- Undertaken by CCEXEC
- Examines proposal taking into account the “criteria for the establishment of work priorities; the strategic plan of the Commission...”

Critical Review

- CCEXEC considered new work proposal from CCFFP
- Took into account recommendation of chair of the CCFFP that work be undertaken by CCFH
 - Would facilitate progress by normal working procedures and priorities



Public Health Risks of Histamine and other Biogenic Amines from Fish and Fishery Products

Dr. Sarah Cahill

FAO

Focus of meeting – Scombrototoxin fish poisoning (SFP)

Common symptoms of scombrototoxin fish poisoning

Type	Symptoms
Cardiovascular	Flushing, rash, hypotension, headache, tachycardia
Gastrointestinal	Abdominal cramps, diarrhoea, vomiting
Neurological	Pain, itching
Other	Oral burning sensation, peppery taste, nausea, swelling of tongue

Symptoms develop rapidly, Last 8-12 hours, rarely fatal

•Hazard identification

- Evidence that histamine is the most significant causative agent of SFP
- Others include cadacerine and putrescine (histamine potentiators), tryamine
- Use histamine as an indicator of SFP (easy to analyse, several methods available)

Hazard Identification – Fish Species

- Comprehensive list of fish spp. that had been associated with SFP to date
- Both market name and scientific names included
- Histidine levels (2600 – 20,070 mg/kg)
- Annual production – important to ranking risk locally
- Salmonidae included due to reported illnesses of SFP –like intoxication (70 – 2362mg/kg histidine)

Table 2.3

Risk characterization

Hazard Characterization:
NOAEL and BMD: 50mg histamine
(healthy individuals not be expected
to suffer any symptoms)
No cumulative effect expected

Exposure assessment: serving
size – 250g at a single eating
event

Risk characterization

200mg/kg

max concentration in a serving that
would not cause an adverse effect

Risk management options

- Histamine formation and SFP can be easily controlled applying good hygienic practices (GHP) and hazard analysis critical control point (HACCP). ($<15\text{mg/kg}$ is achievable based on industry data)
- What would lead to high levels ($>200\text{mg/kg}$)
 - Sufficient free histidine
 - Presence of histamine producing bacteria
 - Conditions to support their growth and production of histidine decarboxylase enzymes
 - Conditions that allow of histidine decarboxylase to convert histidine to histamine

Risk management options

- GHP and HACCP can interrupt one or more of these conditions
- Report considers a number of the intervention options including:
 - Chilling
 - Gutting and gilling of susceptible fish
 - Refrigerated storage and freezing
 - Heating to destroy bacteria and the enzymes
 - High hydrostatic pressure
 - pH
 - Salt
 - Modified atmosphere and vacuum packaging
 - Additives
 - Starter cultures/enzymes for fermented products

Risk management options

- Appropriate sampling plans should be used to validate the HACCP systems, verify the effectiveness of control measures, and detect failures in the system.
- The meeting analyzed a range of sampling plans under different scenarios of histamine.
- Acknowledged the utility of having access to the mathematical tools used in the meeting to develop different sampling plans, and therefore recommended that FAO/WHO find ways to make these available in an easy to use format.
- FAO and WHO have subsequently developed a publicly available tool (www.fstools.org/histamine)

The Histamine Sampling tool

- The FAO/WHO provides support in the decision-making related to the establishment and/or use of sampling plans for detection of histamine.
- The tool provides support in two main areas related to sampling for histamine:
 - ***Designing a Sampling Plan***

This tool function attempts to find sampling plans which meet user-defined objectives, by searching for combinations of the number of samples (n) and a concentration threshold (m).
 - ***Analyzing the performance of a Sampling Plan***

This tool function estimates the probability of accepting lots of product tested according to a user-defined sampling plan.
- Living tool – can be updated and revised as feedback comes in from users (one revision has already been completed)

Conclusions

- Histamine can be controlled – GHP and HACCP
- Range of test methods available and easily accessible
- Sampling plans are important in monitoring – these will vary depending on where they are applied
- Histamine was considered the most appropriate marker although other biogenic amines may be a role in SFP
- Exact mechanisms of toxicity still not clear
- For healthy individuals, adverse effect only when dose exceeds 50mg/kg
- But may not be appropriate for other segments of the population who may have increased sensitivity (metabolic differences, drug therapies)
- Wide range of fish have been associated with SFP – need consideration in risk management (Table 2.3)