MCPD
Public Health Implications

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Chloropropanols-tainted sauce faces Australia recall

January 28, 2002

Food Chemical News
Agribusiness intelligence | informa

NATURAL PRODUCTS INSIDER

Could EFSA's Warning About 3-MCPD in Edible Oils Affect the U.S. Food Industry?

August 1, 2016

https://www.naturalproductsinsider.com/articles/2016/08/could-efsa-s-warning-about-3-mcpd-in-edible-oils.aspx

Topics for Today's Discussion

- Review of the problem: the Science, the Realities and Perceptions – in Europe and in the United States
- Examine potential impact as a result of FDA priority. Note economic and legal/regulatory vulnerabilities for suppliers/oil producers
- Technical mitigation required: what are the best options?
- Consider franchising/licensing application of technology to other edible oil and biofuel producers

What is MCPD*?

- A contaminant first identified (1978) in acid-hydrolyzed vegetable proteins and soy sauce.
- It is the most commonly occurring of a group of contaminants known as chloropropanols.
- A food processing contaminant classified as a possible human carcinogen

* 3-Monochloropropane-1,2-diol

3-monochloropropane-1,2-diol or 3-chloropropane-1,2-diol [3-MCPD]

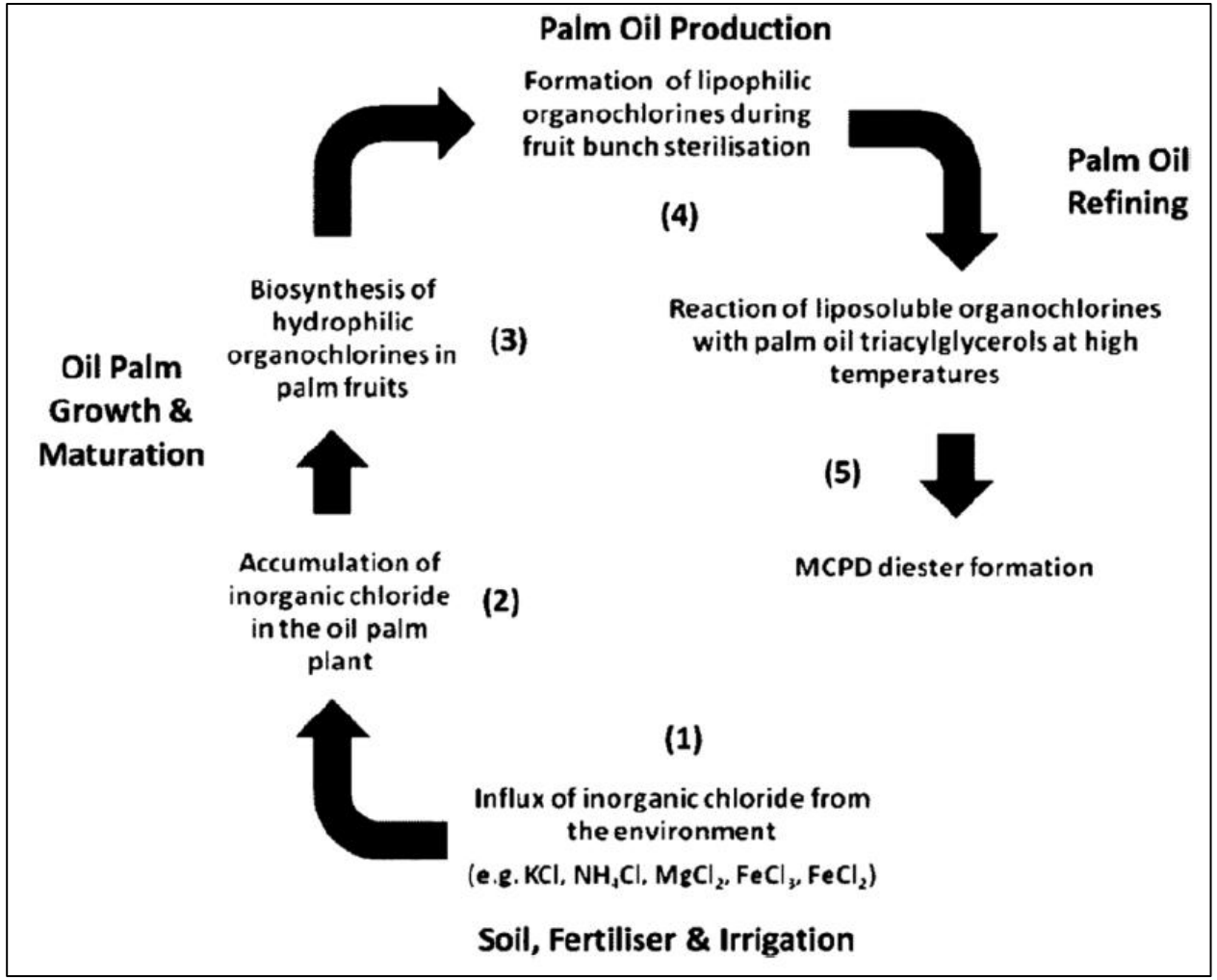
- Primarily created in foods by protein hydrolysis by adding hydrochloric acid at high temperature to speed up the breakdown of proteins
  - Chloride can react with glycerol backbone of lipids to produce 3-MCPD
  - 3-MCPD can also occur in foods which have been in contact with materials containing epichlorohydrin-based wet-strength resins which are used in production of some tea bags and sausage casings
- Found East Asian and Southeast Asian sauces such as oyster sauce, Hoisin sauce and soy sauce

Why are MCPDs in Foods?

- Formed during manufacturing or cooking from lipids and sodium chloride naturally present or added to the food
- Depending on the type of food it may occur as a free substance, in the form of an ester with fatty acids or in both forms

Svejkovská et al., Czech J Food Sci 2004;22: 190–96.

How MCPD in Palm Oil?



Root-cause analysis of the factors involved in the formation of MCPD diesters within the palm oil process chain.

(1) chlorine input into oil palm production
(2) accumulation of inorganic chloride in the plant
(3) bioconversion of inorganic chlorides to organochlorines in the fruits
(4) formation of liposoluble organochlorines during fruit bunch sterilization, and
(5) reaction of liposoluble organochlorines with palm oil TAG during oil refining and resulting in MCPD diesters.

Craft BD, Nagy K, Sandoz L, Destaillats F. Factors impacting the formation of monochloropropanediol (MCPD) fatty acid diesters during palm (Elaeis guineensis) oil production. Food Additives & Contaminants: Part A 2012;29(3):354-361

What is MCPD Exposure?

- General population (Europe)
  - < 1 μg/kg bw/day (94%)
- Toddlers and Other Children
  - 1 – 1.5 μg/kg bw/day
  - < 1 μg/kg bw/day (95%ile of 47% of population)
  - 1 to 2 μg/kg bw/day (95%ile of 41% of population)
- Toddlers, Other Children, Elderly
  - 2 to 3 μg/kg bw/day (95%ile for ~13% of population)

EFSA, 2016

Where are MCPDs in Foods?

Food Category	Mean; range (ppb)
Animal fats and Vegetable oils	1,020 (960 – 1,090)
Mixed fats/oils	1,230 (1,170 – 1,290)
Vegetable fats and oils	820 (740 – 890)
Grains and grain-based products	33 (26 – 39)
Smoked fish meat	37 (36 – 37)
Mixed spices	25 (23 – 26)
Infant formula powder (n=1)	300
Follow-on formula powder (n=2)	800, 1,200

EFSA, 2016
Mean; range

What is the MCPD Toxicology Profile?

- No human data
- Animal data (oral)
  - Mice: up to 31 mg/kg bw, 2 yrs → no neoplasms
  - Rats:
    - up to 400 ppm in drinking water, 2 yrs → increased various adenomas (NS) relative to controls
  - Genotoxicity (S. typhimurium): various doses up to equivalent to 100 mg/kg bw; not detected
  - Testicular toxicity: activity of all glycolytic enzymes reduced
  - Renal toxicity: chronic progressive nephropathy and renal tubule-cell lesions

IARC 3-MCPD Monograph 101, 2013

What is the MCPD Toxicology Profile?

- Animal data (oral)
  - Carcinogenicity
    - Rats:
      - possibly genotoxic; further research required; mechanism(s) of action remain unresolved
      - Renal lesions infrequent yet increased with intake
      - *In vitro* data suggest mutagenic; Limited *in vivo* data not support these findings
      - Evidence suggests nephrotoxicity, immunotoxicity, neurotoxicity, and testicular toxicity
    - Humans – no evidence
  - Classification – group 2B (*possibly carcinogenic to humans*)

IARC 3-MCPD Monograph 101, 2013

Why is There a Public Health Concern?

- Positive findings in *in vitro* genotoxicity test systems
- Malignant transformation of mammalian cells in culture
- Multiple studies in rats
  - Kidney tumors in male Fischer rats
  - Kidney tumors in male Sprague-Dawley rats
  - Kidney tumors in female Fischer rats
  - Kidney tumors in male Sprague-Dawley rats
  - Leydig cell tumors of the testes in male Fischer rats
  - Leydig cell tumors of the testes in male Sprague-Dawley rats
  - Mammary tumors in male Fischer rats

Toxicology → Public Policy?

- 2016 European Food Safety Authority report
  - Margarine, vegetable oils (excluding walnut oil), preserved meats, bread, and fine bakery wares as major sources in Europe
- Byproduct formed in foods [most commonly found member of chemical contaminants known as **chloropropanols**]
  - Carcinogenic [IARC]
  - Highly suspected to be genotoxic in humans
  - Has male anti-fertility effects

What is the Benchmark Dose?*

Reference	TDI (µg/kg bw/d)
Abraham et al., Eur J Lipid Sci Technol, 2012	2.7
EFSA, 2016	0.8
Hwang et al., Regul Toxicol Pharmacol, 2009	9
Reitjens et al., Eur J Lipid Sci Technol, 2012	7
Clemens et al., Toxicol Res Appl, 2017	9

TDI based on Benchmarking Dose (BMD)
BMD: A statistical model that estimates the dose that corresponds to a prescribed increase in the response (called the benchmark response or BMR) of a health effect.
Crump K Risk Anal 1995;15:79-89; an alternative to the traditional no-observed-adverse-effect level (NOAEL). Sand S et al., J Appl Toxicol 2008;28:405-21
* All TDIs, except the TDI calculated by Reitjens et al 2001 were based on the same data set for renal hyperplasia in male rats from Cho et al 2008.

What is the Regulatory Landscape of Chloropropanols?

- JECFA → TDI 2 μg/kg bw/d (based on limited carcinogenicity and genotoxicity studies among rodents)
- JECFA → intake regulatory limit of 20 μg/kg bw/d
- USA → not to exceed 1 ppm in foods (HVP, Asian-style sauces); market survey anticipated
  - Topic for imminent review by FDA
- Food Standards Australia New Zealand → < 0.2 ppm (assuming 40% dry weight)

Disruptive Technology: The Time is Now!

- "Disruptive technologies"
  - any innovation that disrupts conventional business models.
- Ripe for disruptive innovation

Take Away Messages

- Invoke and apply scientific imagination and technical expertise for:
  - **Mitigation** of contaminants/toxicants in edible oil and in biofuels
  - Develop **communications strategies** that demonstrate public health and environmental forethought and activism; own the real and perceived issues and leverage "fixes" before defensive posture damages image and profits