An Update on Acrylamide in Food

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Acrylamide in Food Workshop

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Acrylamide in So Many Foods?

- Global "shock wave" surprise came from Sweden, April 24, 2002 press conference.
- But, in so many foods, at those high ppb levels???
- Within weeks, other labs showed it's really true!!!
- Why did it take us so long to discover it???
- What is the real health risk to humans???
- What do we do now???

Outline…

- Focus on update of post-WHO developments.
- Comparison with other “cooked food” carcinogens.
- Brief mention of advances in formation & analysis.
- What have various countries and public health authorities been doing since the WHO Group met?
- What is happening with California Proposition 65?
- This Workshop is the next step…and we all have an important role to play.

Comparison with other "Cooked Food" Carcinogens and Mutagens

- Late 60's/early 1970's gave us our first reported food concerns about carcinogenic/mutagenic polycyclic aromatic hydrocarbons in grilled meats, N-nitroso compounds in cured meats and beer.
- Late 1970's gave us the first wave of reports about heat-induced, Maillard (carbonyl-amine) browning reaction products and also the heterocyclic amines (Trp-P1 & 2, Glu-P1 & 2, IQ, MeIQ, PhIP, etc).
- These results came about from advances in GC-MS techniques; volatiles, not non-volatiles, were measured more easily.
- Even though these compounds were found to be mutagens and animal carcinogens, their levels in foods were routinely very low ppb.

Tareke et al., "Analysis of Acrylamide, a Cooking Carcinogen Formed in Heated Foodstuffs"

J. Agric. Food Chem. (Aug. 14) 50:4998-5006 (2002)

- AA in foodstuffs measured by two methods:
  - LC-MS-MS detection of underivatized AA [LD of 10 µg/kg]
  - GC-MS detection of brominated derivative [LD of 5 µg/kg]

- Temperature dependence of AA formation was shown:
  - Higher levels in carbohydrate-rich foods [150 – 4,000 µg/kg]
  - Moderate levels in protein-rich foods [5 - 50 µg/kg]
  - AA not detected in unheated control or boiled foods
  - Higher surface area foods had higher levels.

- Swedish adults AA intake estimated to be 100 µg/day.

- Rosen & Hellenas [Swedish NFA] further described the LC-MS-MS method, *Analyst* (July) 127:880-882 (2002).

Joint Food and Agriculture Organization/ World Health Organization Consultation

Geneva, June 25-27, 2002

- Conclusion: the presence of AA in food is "a major concern in humans based on the ability to induce cancer and heritable mutations in laboratory animals."
- Potential neurotoxic effects in workers and effects on fertility that have been observed in animals were both thought to occur at levels much higher than would be possible through dietary intake.
- Research recommendations included:
  - Need for inter-laboratory validation of test methods and fuller assessment of total dietary intakes
  - Need for chemical mechanistic studies on the modes of formation and fate of AA in food, and efforts to minimize AA
  - Toxicological research focused on studies to determine the relevance and significance of the observed rat tumors to human health risk.

Final Report issued Sept 17:
http://www.who.int/fsf/Acrylamide_report.pdf

FAO/WHO International Network on Acrylamide in Food

- October 18 Press Release announced the Network's formation and launch of the Website:

  http://www.who.int/fsf/Acrylamide/research.htm

- Network will be operated with the Joint Institute for Food Safety and Applied Nutrition (JIFSAN), a collaborative research and education program between the FDA and the University of Maryland; Director Dr. David Lineback.

- Network Goals:
  - Database of researchers and data providers
  - References for published papers
  - Updates on current research
  - FAO/WHO updates on health risk of AA in foods
  - Discussion forum for researchers.

European Activities on Acrylamide

- Several governments have reported additional AA data generated since May (UK, Germany, Switzerland, Belgium, Sweden, Norway); analytical proficiency testing is underway.

- European Commission's Scientific Committee on Food expressed its Opinion on July 3; Recommendations:
  - Reduce levels to "as low as reasonably achievable" [ALARA Principle]
  - Endorsed FAO/WHO Consultation's interim guidance on dietary practices and healthy eating
  - Called for urgent research on lowering AA formation and understanding its human health implications.

- European Commission held a Contaminants Working Group meeting October 16 in Brussels; member states and industry participated; no EU "action" levels foreseeable.

European Activities on Acrylamide

- German BgVV will establish “signal” levels for each product group; proposed 1,000 ppb “action” level in August.
- UK Food Standards Agency issued in September a “Research Requirements Document” on AA, requesting that “expressions of interest” be submitted on research proposals for key aspects.
- Swiss Federal Office of Public Health, Food Safety Division, met with stakeholders September 16; Swiss see no need for action levels.
- Sweden leading the Nordic Council of Ministers AA coordination project.
- Norway expected to test all potato products on the market; no action levels foreseen.

Dietary Exposure Assessment in Europe

International Agency for Research on Cancer's (IARC) Working Group on "Nutrition and Cancer Diseases," within the EPIC framework:

- Recently surveyed eating habits of thousands of middle-aged European adults (around age 55):
- German BgVV reported at August 29 information seminar that the IARC results for about 4,500 Germans showed:
  - Males: 0.15 µg/kg b.w./day [10.5 µg/day]
  - Females: 0.14 µg/kg b.w./day [8.4 µg/day]
- These intakes are considerably lower than FAO/WHO estimates, but data may be limited by the range of foods surveyed and our knowledge of AA in foods.
- In the German subset, potato products accounted for about 50% of the AA exposure, while bakery products and breads accounted for about 20%.

FDA's Draft "Action Plan" on Acrylamide

Released Sept. 20 in advance of the Sept. 30 Public Meeting:

http://www.cfsan.fda.gov/~dms/acryplan.html

- Earlier released (July 23) their "Detection and Quantitation of Acrylamide in Foods" Draft methods paper; LC/MS/MS method:

  http://www.cfsan.fda.gov/~dms/acrylami.html

- Held interagency roundtable of federal public health agencies involved in AA research on September 24.

- Major Goals of Action Plan:
  - Assess U.S. dietary exposure; develop rapid screening methods and validate confirmatory analysis methods
  - Assess potential risks via toxicology evaluation and research
  - With partners, identify formation and mitigation mechanisms
  - Inform and educate consumers and processors
  - Foster public/private partnerships to gather data for assessing the human risk.

FDA Research Activities

- National food survey of AA levels in FY03, plus Total Diet Study market basket samples; to date, more than 150 food samples analyzed out of 600-sample goal; continuing efforts on analytical methods; limit of quantitation is 10 ppb using LC-MS-MS method.
- Research collaboration on formation and mitigation mechanisms.
- Toxicology studies will be conducted on: (1) bioavailability of AA from foods; (2) identity of DNA and protein adducts as biomarkers of exposure and as clues to toxicity mechanisms.
- AA and glycidamide (its metabolite) will be nominated for the full testing regimen to the National Toxicology Program (NTP), including chronic carcinogenicity and mechanistic studies, as FDA's "high priority" chemical selections for FY 2003; FDA's National Center for Toxicological Research (NCTR) will conduct these studies for NTP.
- Collaborate with the Centers for Disease Control to evaluate use of protein adducts to monitor AA exposures in humans.

FDA's Future Meetings and Collaborations

- Food Advisory Committee's (FAC) Subcommittee on Contaminants and Natural Toxicants will meet in early December: revised Action Plan, preliminary data on AA levels in foods, and research and analysis needs as well as exposure and toxicology issues.
- Full FAC will meet in March 2003.
- Participation at meeting of Codex Committee on Food Additives and Contaminants, March 17-21, 2003.
- Participation at meeting of FAO/WHO Joint Expert Committee on Food Additives and Contaminants (JECFA), winter/spring 2004.

Asparagine Linked to Acrylamide Formation

- In September, Asparagine was conclusively shown by at least 5 research groups to react with glucose to form AA:
  - Health Canada and P&G at AOAC Symposium in LA
  - Nestle and University of Reading (UK) published in *Nature*
  - Australians have also confirmed this.
- The 3-carbon, 1-nitrogen structural backbone of AA was shown to come completely from asparagine by elegant labeling studies.
- Highest level amino acid found in potatoes in free form; there may be opportunities to find low asparagine potato cultivars; but glucose levels are also important.
- I believe many other AA formation mechanisms will eventually be uncovered, including complex free radical reactions:
  - Other Maillard carbonyl-amine reactions
  - Acrolein → Acrylic acid → AA pathways
  - Heat degradation reactions further along Maillard pathways
  - Oxidized fats/oils can provide carbonyl reactants.
  - ???

California Proposition 65

- Acrylamide added to Prop 65 List of Carcinogens on January 1, 1990; a No Significant Risk Level (NSRL) was set at 0.2 μg/day.
- Cancer warning label is required if the average daily consumption (calculated over a 70-year lifetime) of a listed chemical in a food product exceeds this NSRL.
- 60-Day Notices were sent by two plaintiffs' groups to McDonald's and Burger King because of French fries, and later to several other food companies for various products tested by the Center for Science in the Public Interest.
- Attorney General issued an Opinion Letter in July to both plaintiffs' groups urging them not to sue, but in September one group did sue McDonald's and Burger King anyway for failure to warn consumers about AA.
- Note: Food products manufactured anywhere in the world and sold in California are subject to Prop 65 requirements.

Summary of Global Activities Needed

- The "Acrylamide Solution" [if there is one!!] will require the global cooperative and continuing efforts of toxicologists, epidemiologists, risk assessors/managers, analytical and mechanistic chemists, agricultural scientists, food product developers, government regulatory experts and risk communicators.

- Analytical chemists will fill the data gaps in our knowledge base of AA's global occurrence/concentration in foods and beverages, and can also assist in unraveling both formation and mitigation mechanisms.

- Toxicologists and risk assessors/managers in many countries will carefully evaluate current data and future research results to determine the true public health consequences of acrylamide dietary exposure.

- Food processor/food service companies will need to examine their product lines for AA assessment and management.

The Dose Makes the Poison!

"All things are poison and there is none which is not a poison. Solely the dose differentiates a poison from a remedy."

Paracelsus

(1493-1541)