Components of an Effective Allergen Plan: Cleaning Control and Validation Strategies

Joe L. Baumert, Ph.D.
University of Nebraska
Food Allergy Research & Resource Program
jbaumert2@unl.edu

Why Are Allergens Now a Key Issue?

- Increased Awareness
  - Medical Journal Publications 1988, 1992
  - Advocacy Support Groups
- Trend toward "Value Added" Products including gluten-free, dairy-free, peanut-free, allergen-free
- Improvements in Detection
- Company Liability
  - Negative Publicity/Financial Impact

Increased Consumer Awareness

- Inquiries and complaints to food companies increasing
- Complaints from consumers and physicians
- Food companies more alert to such complaints
- Media coverage (Canada, U.K.)
- Consumer Groups
  - Food Allergy and Anaphylaxis Network (U.S.)
  - Anaphylaxis Canada
  - Anaphylaxis Campaign (U.K.)

THE TIMES - 22nd December, 1993

Peanuts in lemon pie killed allergy girl

Why the Increased Interest in Food Allergies?

Clinical

- Increased prevalence of food allergies
- Increased consumer awareness of food allergies
- Increased prevalence of severe reactions

Fatal Food-Induced Anaphylaxis

John W. Yunginger, MD; Kristin G. Sweeney, MD; William Q. Sturner, MD; Leigh A. Giannandrea, MD; Joel D. Teigland, MD; Michael Bray, MD; Peter A. Benson, MD; James A. York; Lynda Biedrzycki, MD; Diane L. Squillace; Ricki M. Helm, PhD

Fatal food-induced anaphylaxis is rarely reported. In 16 months, we identified seven such cases involving five males and two females, aged 11 to 43 years. All victims were atopic with multiple prior anaphylactic episodes after ingestion of the incriminated food (peanut, four; pecan, one; crab, one; fish, one). In six cases the allergenic food was ingested away from home. Factors contributing to the severity of individual reactions included denial of symptoms, concomitant intake of alcohol, reliance on oral antihistamines alone to treat symptoms, and adrenal suppression by chronic glucocorticoid therapy for coexisting asthma. In no case was epinephrine administered immediately after onset of symptoms. Premortem or postmortem serum samples were available from six victims; in each case elevated levels of IgE antibodies to the incriminated food were demonstrated. Food-sensitive individuals must self-administer epinephrine promptly at the first sign of systemic reaction. Emergency care providers should be aware of cricothyrotomy as a life-saving procedure.

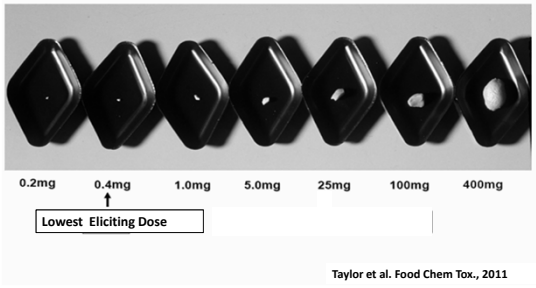
(*JAMA* 1988;260:1450-1452)

Why the Increased Interest in Food Allergies?

Food Industry

- Increased consumer awareness
- Potential impact of severe reactions
- Increased number of product recalls
- Increased attention by governmental regulatory agencies
- Threshold dose is very low

Dose of Peanuts Causing Reactions in Highly Sensitized Subjects

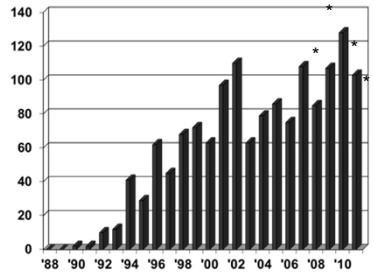


Taylor et al. Food Chem Tox., 2011

Key Food Industry Lessons

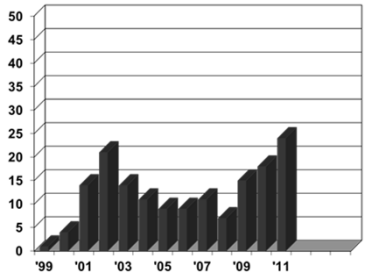
- Major company recalls
  - Rework
  - Inadequate cleaning of shared equipment
  - Line cross-overs
  - Packaging errors
  - Ingredient suppliers
  - Custom processors

U.S. FDA Food Allergen Recall Incidents
1988-2011

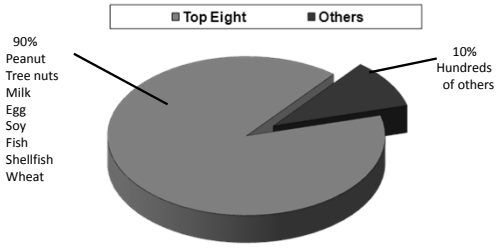


*includes FDA recalls and alerts

FSIS/ USDA Food Allergen Recalls
Calendar Years 1999-2011



Food Allergies Prevalence: The "Big Eight"



Allergenic Foods Important in Other Geographical Areas

- Celery (Europe)
- Mustard (Europe and Canada)
- Molluscan shelllfish (Europe and Canada)
- Lupine (Europe)
- Buckwheat (SE Asia)
- Sesame seed (Europe, Canada, Australia/NZ)

Where Risks Occur

- Research and Development
- Engineering and System Design
- Raw Materials/Suppliers/Co-Packers/Purchasing
- Operations/Manufacturing
- Packaging and Labeling
- Sanitation
- Human Error/Training

Allergen Management

- Form an allergen control team
- Conduct a quantitative risk assessment
- Develop an allergen process flow diagram (allergen map)
- Develop an allergen control plan specific to each processing facility
- Review the ACP on some regular basis and especially for new products, introduction of new processing capabilities, new ingredients

Allergen Control Team

- Manufacturing
- Quality
- Labeling/Regulatory Compliance
- Product Development
- Engineering/Equipment Selection & Design
- Sanitation
- Packaging
- Purchasing
- Consumer Affairs, Marketing, Human Resources

Strategies to Effectively Manage Food Allergens in Food Processing Facilities

Operations Strategies: Keys to Effective Allergen Control

- Dedicate – facility, system, line, etc.
- Segregate/Separate
- Schedule
- Sanitize

Product Development Strategies

- Develop an Allergen Gating Process
- Key questions to ask:
  - Do you really want to use this allergenic ingredient?
  - Will increased sales defray increased costs of manufacturing?

Allergen Gating Process

- Develop an approach to review potential new products at the concept stage to identify potential allergenic components
- Use the allergenic components if they are truly necessary
  - Only use allergenic ingredients if they make a discernable difference to taste or functionality
- Create a process to assure that the processing facility is notified before start-up

Supplier Qualification

- Documented allergen control plan
- Letters guaranteeing the absence of undeclared allergens; do they check their suppliers?
- Require notification of changes that affect allergen status of ingredients sold to your company
- Don't believe them – Audit
- Validated sanitation procedure
- Ingredient shipments in clearly marked, sealed containers

Receiving

- Review and inspect incoming shipments of raw materials for allergen information
- Develop a company-wide system for tagging all raw materials for easy identification in your facilities k-color coding, symbols/icons, etc.
- Assure that each incoming container is appropriately tagged
- Have a plan to handle any damaged containers to avoid allergen cross-contact and use it

Storage – Raw Material

- Segregate allergenic raw materials/products separately to avoid cross contact
- Use clean and closed containers
- Designate storage areas to one particular allergen type – all milk, all soy, etc.
- Avoid storing allergenic ingredients above non-allergens or different allergens.
- Develop, use and document plan for control of any spills of allergenic ingredients

Storage – Raw Material

- Mark or tag allergenic ingredients to allow their easy identification in storage and to help assure their segregation from non-allergens or different allergens
- Use clearly designated staging areas for allergenic ingredients/products
- When storing ingredients from same source together (e.g. all milk) consider the allergen load (butter oil – low; lactose – low to moderate; casein –high)

Operations Strategies

- Schedule long runs of allergenic products wherever possible (minimize changeovers)
- Schedule manufacturing of allergenic products just prior to end of shifts with major clean-up
- Introduce allergenic components into the products as late in the process as possible
- In-process totes/containers containing allergen should be clearly tagged for easy identification
- Develop an exact-into-exact rework policy or forbid the use of rework

Key Factors to Sanitation Success with Food Allergens

- Knowledge of system and product
- Sanitation design
  - cleanability and access; no static or hidden areas
- Personnel that are trained, dedicated, alert, and thorough

Key Factors to Sanitation Success with Food Allergens (cont'd)

- Efficient, dependable cleaning equipment
- Effective and sufficient cleaning supplies
- Good lighting

Key Factors to Sanitation Success with Food Allergens (cont'd)

- Sufficient time scheduled and allowed for sanitation
  - lack of performance during allergen cleanouts results in corrective action
  - production delays or shutdowns due to sanitation concerns have management support
  - allergen awareness training for personnel is done

Key Factors to Sanitation Success with Food Allergens (cont'd)

- Develop and implement clear SSOPs
- Validate your cleaning procedures using analytical methods where feasible to assure that they are effective
- Avoid having to do sanitation whenever and wherever possible
  - scheduling
  - dedicated lines

Key Factors to Sanitation Success with Food Allergens (cont'd)

- Establish target allergen residue levels for effective allergen cleaning; recommend non-detectable (<2.5 ppm) or 5 ppm
- Verify that allergen cleaning is done consistently each time; document it – keep compliance records
- Periodically audit and confirm that allergen cleaning is done in accord with established procedures

Allergen Control Program: Key Allergen Sanitation Issues

- Wet cleaning vs. Dry cleaning
  - Dry cleaning – brushes, vacuums and not air hoses
- Allergen content/potency of ingredient
- Uniform formulation vs. particulate
- Allergen composition – stickiness
- Push-through: an effective practice, but careful with particulates

Allergen Composition

- Peanut Pieces?
- Peanut Flour?
- Peanut Butter?

❖ Consider:
Difficulty to clean and potential risk factors.
How much equipment will be exposed?

Prevent Re-Contamination

- Protect clean equipment and areas
- Follow procedures, in sequence
- Control people and activities
- Remove allergen ingredients
- Label and seal clean systems
- Communicate during and after cleaning
- Re-inspect prior to start-up
- Flush and examine first product

Validation of Allergen Control Programs

Validation of Allergen Control Programs

- Regulatory action levels (thresholds) do not exist in any country. Thus, need to establish a corporate target level that protects consumers
- In my expert opinion, BLQ (below limit of quantitation) by allergen-specific test does protect consumers (<2.5 or <5 ppm)

Using ELISAs for Sanitation Validation/Assessment

- Visually clean is the standard in the food industry
  - If residue is present on the equipment surface, a positive ELISA is likely
  - No need to test – clean again
- Visual inspection can be quite effective
  - Analytical validation and verification of allergen removal is needed
  - Swabbing equipment surfaces (contact surfaces and hard to reach areas) or testing CIP final rinse water (when possible) is commonly done for allergen assessment

Possible Detection Methods

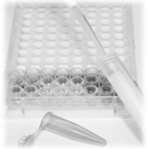
- Enzyme Linked Immunosorbent Assay (ELISA)
- General Protein Tests
- ATP/Bioluminescence Tests
- Polymerase Chain Reaction (PCR)

How To Decide What Test to Use in a Specific Situation?

- The specificity of the test method is one concern – protein, allergenic source protein, DNA, or ATP
- The sensitivity of the test method is a second concern; will the method support the corporate target level?; or can you correlate the method results to the corporate target level?

ELISA and ELISA-Based Technologies

- Include ELISA kits, lateral flow devices (dipsticks), swabs
- Have become the standard of care of allergen validation
- Specific and sensitive
- Rapid analytical assessment
  - 5 min-1 hr analytical process
- Suitable for food-processing settings



ELISA and ELISA-Based Technologies

- Specific – detects protein(s) from source; not always specific for allergenic protein
- Sensitive (low ppm and could be less)
  - Limit of Quantitation (LOQ) of 1-2.5 ppm
  - No clinical reason to "chase molecules"
- Quantitative (96 well) and Qualitative formats (lateral flow and swab) formats

Commercial ELISAs

- Peanut
- Milk
- Egg
- Gluten
- Almond
- Hazelnut
- Walnut
- Soybean
- Crustacea
- Mustard
- Lupine
- Sesame seed
- Buckwheat



Lateral Flow ELISAs for Sanitation Validation

- Results in 10 min or less
- Only one step after extraction
- Used for environmental swabs or CIP rinse

Picking the Best Test Method General Comments

- Recommended to validate removal of allergenic residue using specific ELISAs
  - ATP and general protein tests do not detect proteins from allergenic sources specifically so the effectiveness of these tests ALONE as the sole approach must be carefully examined
- Surrogate testing (protein, ATP) can be helpful in some cases
  - ATP or general protein swabs can provide a good quick check on sanitation effectiveness during routine cleaning

ELISA Test Method Choice

- What do you want to measure?
  - Select appropriate detection system according to major components in the product
    - Example: Milk
      - Neogen: Total Milk
      - r-Biopharm: β-lactoglobulin
      - ELISA Systems: Casein
- What is used as the standards in the method?
  - For milk, recommend NFDM (non-fat dry milk)

Validation and Verification

- No fixed acceptable frequency of testing, experience is the best teacher
- More frequently in early stages of product manufacturing
- Depends on level of confidence in product, process, SSOP, test methods, etc.

Change Management

- When ***anything*** changes, then you must re-evaluate the entire allergen control plan
  - Re-Validate by doing a new Quantitative Risk Analysis
  - Does the existing Allergen Control Plan still work with the new conditions?

Thank You for Your Attention

Joe L. Baumert, Ph.D.
University of Nebraska
Food Allergy Research & Resource Program
jbaumert2@unl.edu