Update on Food and Drug Administration (FDA) Compliance and Enforcement Activities

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Goals

- Background

- Labeling and other regulations

- Enforcement: Recalls (and warning letters)

- Testing

- Summary

Food allergy

FDA

- Immune response (IgE-mediated) to food, typically proteins

- Symptoms can range from mild lip swelling to severe anaphylaxis (with rare fatalities)

- Prevalence in the U.S. has increased: ≈ 4-5% of the population

- Over 90% of food allergies are due to certain foods/food groups
  - Milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, soybeans, sesame*

Food allergens

FDA

- No cures. So, strict avoidance is the key to allergen management

- Consumers rely on food labels to determine presence or absence of allergen hazards

- Regulations addressing food allergens:
  – **Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA)**
  – **Food Safety Modernization Act of 2011 (FSMA)**
  – **Food Allergy Safety, Treatment, Education, and Research Act (FASTER Act)**

- Undeclared food allergens are a leading cause of Class I food recalls

- FDA can carry out a number of regulatory actions for undeclared major food allergens

Regulatory activities- food allergens

FDA

CFSAN (Center for Food Safety and Applied Nutrition)

–*mission is to ensure safe, sanitary, wholesome, and honestly labeled food supply*

- Implementation of food allergen labeling laws
- Policy, guidance and consumer education
- Analytical methods to detect allergens in food
- Compliance and enforcement
  - Evaluate recalls and other actions for undeclared allergens
  - Import refusals and import alert
  - Work with **ORA** (Office of Regulatory Affairs) to conduct inspections and follow up
- Safety/risk assessments- novel food ingredients, health and other claims, labeling exemptions, health hazard evaluations (HHEs), thresholds
- Postmarket surveillance –CFSAN Adverse Event Reporting System (CAERS)
- ❑ Exceptions: meat/poultry (**USDA**); beer/spirits/wine (**TTB**); pesticides (**EPA**)

Food Allergen Labeling & Consumer Protection Act of 2004 (FALCPA)

❖ Defines "**major food allergens**":

- **Peanut**   - **Tree nuts (list of 17 nuts; incl. coconuts)**

- **Milk**   - **Wheat (any species in *Triticum* genus)**

- **Egg**   - **Fish (list species)**

-**Soybean**   - **Crustacean shellfish (list species)**

- Sesame (*FASTER Act,* *effective Jan 1, 2023*)

Must label <u>source</u> of protein-containing ingredient (including spices, flavors, colors processing aids)

- Defines "**gluten-free**" standard (2013)
    - *"Gluten-Free Labeling of Fermented or Hydrolyzed Foods"***(2020)**
- <u>Other</u> : Sulfites (>10ppm), yellow 5, yellow 6, carmine (cochineal)

Sesame as an allergen

- In Oct. 2018, FDA statement noted sesame allergies may be a growing concern in the U.S. and new effort to consider labeling for sesame to help sesame allergic consumers

- In Nov. 2020, FDA issued **Draft guidance for industry on voluntary disclosure of sesame as an allergen**
  - Recommended manufacturers to voluntarily declare sesame following spice or flavor
  - Recommended sesame to be voluntarily included in parentheses following the ingredient, such as tahini, when sesame is not in the common name of food

- In April 2021, the FASTER Act was signed into law, declaring sesame as the 9th major food allergen. Effective on Jan. 1, 2023.

- Beginning in Jan. 2023, sesame allergen labeling required under the FD&C Act for major food allergens and controls (cross-contact and label) required under the CGMP and PC rule

FALCPA

- Exemptions: Highly refined oils, ice structuring protein (ISP; fish), soy lecithin used as processing aid

- No current thresholds or regulatory limits established for allergen labeling

- No specific requirements for "**allergen (X)-free**" claims (except gluten-free)

- No label requirements for "unintentional introduction of allergens into products" by way of allergen cross-contact

  ➢ Has led to voluntary use of statements called **advisory allergen statements,** AKA "Precautionary allergen labeling (PAL)" :
    ❏ *"May contain X", "Produced in a facility that uses X",* etc
    ❏ No specific statement endorsed

  ➢ **If advisory statement used, must be:**
    ▪ **Truthful and not misleading**
    ▪ **Not used in lieu of good manufacturing practices**

CGMP and Preventive Controls Rule (21 CFR Part 117)

- Defines allergen cross-contact as "the unintentional incorporation of a food allergen into a food" (§117.3).

- Updated CGMPs (Subpart B) to explicitly address allergen cross-contact:
    - Personnel (§117.10)
    - Plant construction and design (§117.20)
    - Sanitary operations (§117.35)
    - Equipment and utensils (§117.40)
    - Process and controls (§117.80)
    - Warehousing and distribution (§117.93)

21 CFR Part 117

FDA

- Hazard Analysis and Risk-based Preventive Controls (Subpart C) requires written **food safety plan** (§117.126), including hazard analysis, preventive controls, etc.

- Preventive controls to assure allergen hazards are significantly minimized or prevented in food (§117.135).
  - Food allergen controls include cross-contact and label controls.
  - Sanitation controls to prevent allergen cross-contact.
  - Supply-chain controls.

- Facilities don't need to validate allergen control and sanitation control(§117.160(c))

- No risk-based thresholds established (but this is an area of global interest)

- Guidance document on Food Allergen Controls coming soon

Reportable Food Registry (RFR)

- RFR - an electronic portal to submit instances of reportable food

- Reportable food – food/feed with reasonable probability to cause serious adverse health consequences or death to humans or animals (Class I)

- One-third of foods reported through RFR involve undeclared allergen

- Undeclared allergens increased from 30% in Year 1 to 47% in Year 5

Distribution of Primary RFR Entries by Food Safety Hazard
Sept. 8, 2009 - Sept. 7, 2014

Year 5 — 9%, 25%
Year 4 — 10%, 29%
Year 3 — 13%, 28%
Year 2 — 11%, 38%
Year 1 — 18%, 38%

Legend:
- Salmonella
- Listeria monocytogenes
- Undeclared Allergens
- Others

33%, 38%, 44%, 47%
30%
14%, 18%, 21%, 17%, 19%
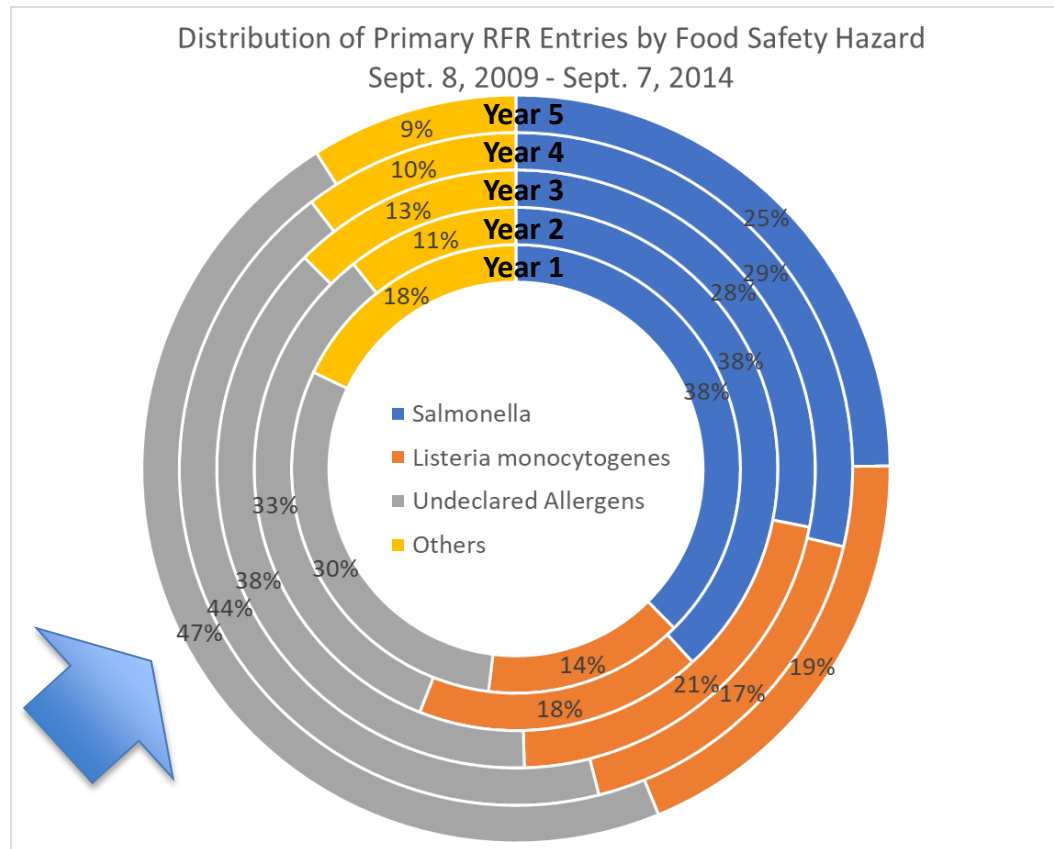
- Class I : reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death. (21 CFR 7.3(m)(1))
- Class II : may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote. (21 CFR 7.3(m)(2))
- Class III : not likely to cause adverse health consequences. (21 CFR 7.3 (m)(3))

Recalls – Undeclared allergens

- Bakery (31.5%) is the most frequently recalled food category for undeclared allergens, followed by snack (12.1%), candy (10%), dressing (8%) and dairy (7.9%).

- These 5 food categories represented 69.5% of total allergen recalls.

- Milk in bakery is the most frequently recalled allergen-food category combination.

Distribution of frequently recalled allergens

Gendel and Zhu, 2013, J. Food Prot., 76: 1933-1938
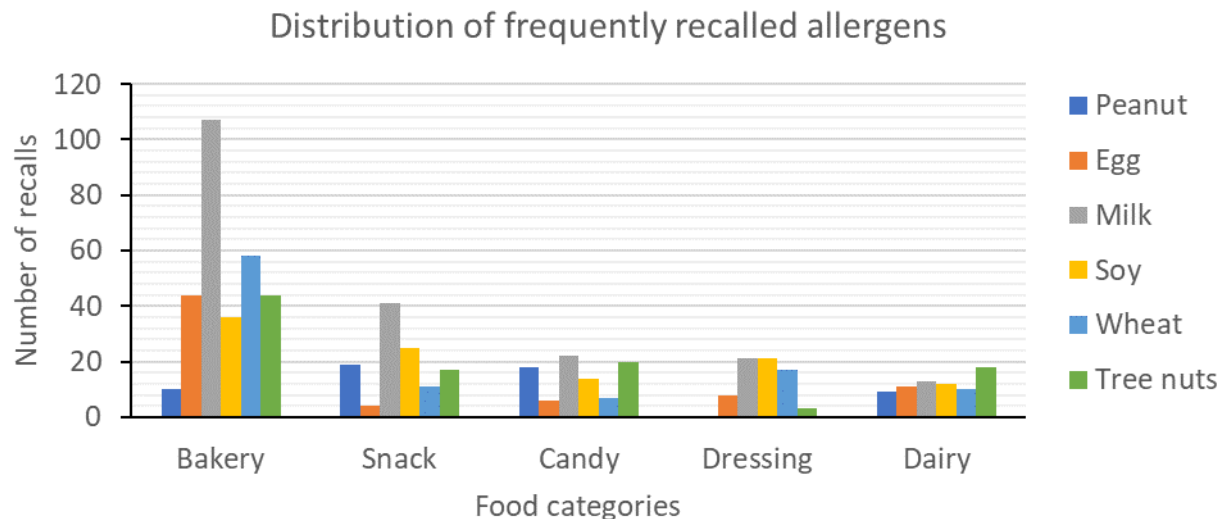
Reason for allergen recalls

FDA

- About 5-15% of allergen recalls involved reaction to an allergic consumer

- Of the 732 allergen recalls in FY 07-12, 526 had known root cause (excluding omission and unknown)

- Failure in label controls is responsible for 71.3% of recalls with known root cause
  - computer error, knowledge, no carry-through, no declaration, not updated, terminology, wrong label, wrong package

- Failure in CGMPs and cross-contact controls responsible for 21.1% of recalls with known root cause
  - cross-contact, in process, rework, wrong ingredient

- Failure in supplier controls responsible for 4.9% of recalls with known root cause

Top 10 root cause	Number of recalls (% of total)
Omission	191 (26.1%)
Wrong package or label	137 (18.7%)
Terminology	85 (11.6%)
No carry-through	70 (9.6%)
Cross-contact (cleaning)	52 (7.1%)
Wrong ingredient	31 (4.2%)
Knowledge	28 (3.8%)
Ingredient mislabeled	26 (3.6%)
Not updated	22 (3.0%)
Computer error	21 (2.9%)

Peanut in Cumin recalls

FDA

- In 2014-2015, more than 675 food products – from spice mixes to taco kits to burgers and meat products – were recalled due to cumin found to contain undeclared peanut
  - ***FDA Consumer Advice***, Feb 2015

- Cumin (high levels) traced to source in Turkey

- Concentrations of peanut in cumin detected by ELISA varied greatly

- Root cause not known- could be economic adulteration or cross- contact

Warning letters

FDA

In 2020, FDA sent warning letters to eight registered food facilities and one retailer that have manufactured and distributed foods with undeclared major food allergens that resulted in Class I recalls

- Whole Foods Market (**Retail food chain**) in December 2020 for a pattern of receiving and offering for sale misbranded food products. For the time period of October 2019 to November 2020, the firm recalled 32 food products due to undeclared allergen(s).

- Frito Lay in December 2020 for due to misbranding of the brand's "Original Potato Chips" due to misbranding for milk. (The chips inside were actually "Ruffles Cheddar and Sour Cream"). The FDA says Frito Lay has had five Class 1 recalls for potato chips and allergens in five years.

- Etai Food in November 2020 for both unsanitary conditions and lack of allergen cross-contact controls, such as storing nuts above onions and cheese cubes above oranges. The Colorado firm makes ready-to-eat (RTE) products such as salads, sandwiches, burritos and wraps.

- Ventura Foods in October 2020 for "garlic sauce" that contained undeclared milk and wheat.

- Dole Fresh Vegetables in September 2020 for a HEB brand Tuscan Herb Chopped Salad Kit, due to wheat noodles and a dressing that contained peanut butter and almond, cashew, and chow mein noodle (wheat) toppings.

- La Sonorense in September 2020 for bulk packaged wheat flour tortillas that did not contain a label with ingredients and failing to declare wheat as a top allergen.

- Bake'N Joy Foods in September 2020 for a recall that followed the discovery of walnut pieces in the firm's Sienna brand Cranberry Orange Flavored Muffin Batter. The batter's ingredients do not mention nuts.

- Winter Garden Quality Foods in August 2020 for failing to label that milk was an ingredient of Whole Foods brand Vodka Sauce.

- Pero Family Farms Food Company in August 2020 for failing to declare the presence of milk and egg in their company's Zucchini Spiral Pesto Side Dish Kits.

Allergen testing

FDA

- Tests used to support compliance and enforcement activities - ensure cross-contact prevention and label compliance

- Testing raw materials, finished product or food contact surface

- Methods are protein-based (immunochemical and mass spectrometry) or DNA-based

- Currently, FDA uses 2 ELISA kits for each allergen detection to overcome method-matrix limitation and confirm results

- Continued research on technologies for allergen detection

xMAP FADA

- A multiplex antibody-based food allergen detection assay (FADA) developed in collaboration with Radix® BioSolutions using the Luminex xMAP® technology.

- Advantage of analyzing 16 allergens in 1 well. Use of complimentary and secondary analytical end-points provide a built-in confirmation for an allergen.

Food Group	Bead ID	Extraction
Egg	25, 26 65*	Buffer SDS/β-mer
Milk	35, 36 66, 67	Buffer SDS/β-mer
Gluten	27, 28 73	Buffer SDS/β-mer
Crustacean Shellfish	22*	Buffer
Soy	45, 46	Buffer
Peanut	37, 38 72	Buffer SDS/β-mer

Food Group	Bead ID	Extraction
Almond	12, 13	Buffer
Brazil nut	14, 15	Buffer
Cashew	18, 19	Buffer
Coconut	20, 21	Buffer
Hazelnut	29, 30	Buffer
Macadamia nut	33, 34	Buffer
Pine nut	39, 42	Buffer
Pistachio	43, 44	Buffer
Walnut	47, 48	Buffer
Sesame	66, 72, 73	Buffer

xMAP FADA

- ## Some applications:

  – Used to verify peanut presence in cumin along with other methods - 2015 recalls

  Garber et al, 2016, J. Agric. Food Chem. 64: 1202-1211

  – Detect **sesame** incurred or spiked in baked muffins, spice mix, canola oil, and in both raw and toasted sesame oils

  Cho et al, 2020, J. Food Prot., 83: 129-135

TABLE 3. *Percent recovery*[a]

Sample	Sesame (ppm)	Recovery by sesame bead set		
		-66	-72	-73
PBS[b]	1	67 ± 3	94 ± 5	215 ± 27
	10	41 ± 1	87 ± 7	206 ± 7
	100	46 ± 8	121 ± 1	>[c]
Baked muffin[d]	1	23 ± 2	42 ± 4	83 ± 14
	10	37 ± 4	62 ± 8	92 ± 13
	100	78 ± 1	88 ± 2	>
Spice mix[d]	1	65 ± 9	49 ± 21	119 ± 9
	10	84 ± 7	82 ± 7	132 ± 9
	100	89 ± 1	86 ± 2	>
Hummus[d]	1	89 ± 2	72 ± 4	31 ± 1
	10	97 ± 1	78 ± 5	49 ± 6
	100	96 ± 3	83 ± 1	75 ± 2

[a] Percent recovery of spiked ground sesame in PBS relative to sesame calibration standards calculated on the basis of interpolated ppm. Samples extracted ($n = 3$) according to UD buffer, buffered-detergent protocol. Extracts analyzed without subsequent dilution. Values are average % recovery of true triplicates ± 1× SD of the % recovery.

[b] Percent recovery of ground raw sesame in PBS relative to sesame calibration standards.

[c] >, MFI exceeded dynamic range (>S7, 750 ng of protein per mL).

[d] Apparent percent recovery of ground raw sesame in specified food relative to ground sesame spiked into PBS on a per MFI basis.

Summary

- Food allergens remain a major health concern

- Food allergen-related recalls have increased

- Implementation of appropriate controls for allergen cross-contact and labels can significantly reduce food recalls

- Testing methods continue to be developed to improve detection of allergen hazards

- Continue to explore risk-based strategies for thresholds and improving communication of allergen hazard/risks

- Sesame is the 9th major food allergen, effective January 1, 2023

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