

Allergens: Lessons learnt

Dr Harris Steinman

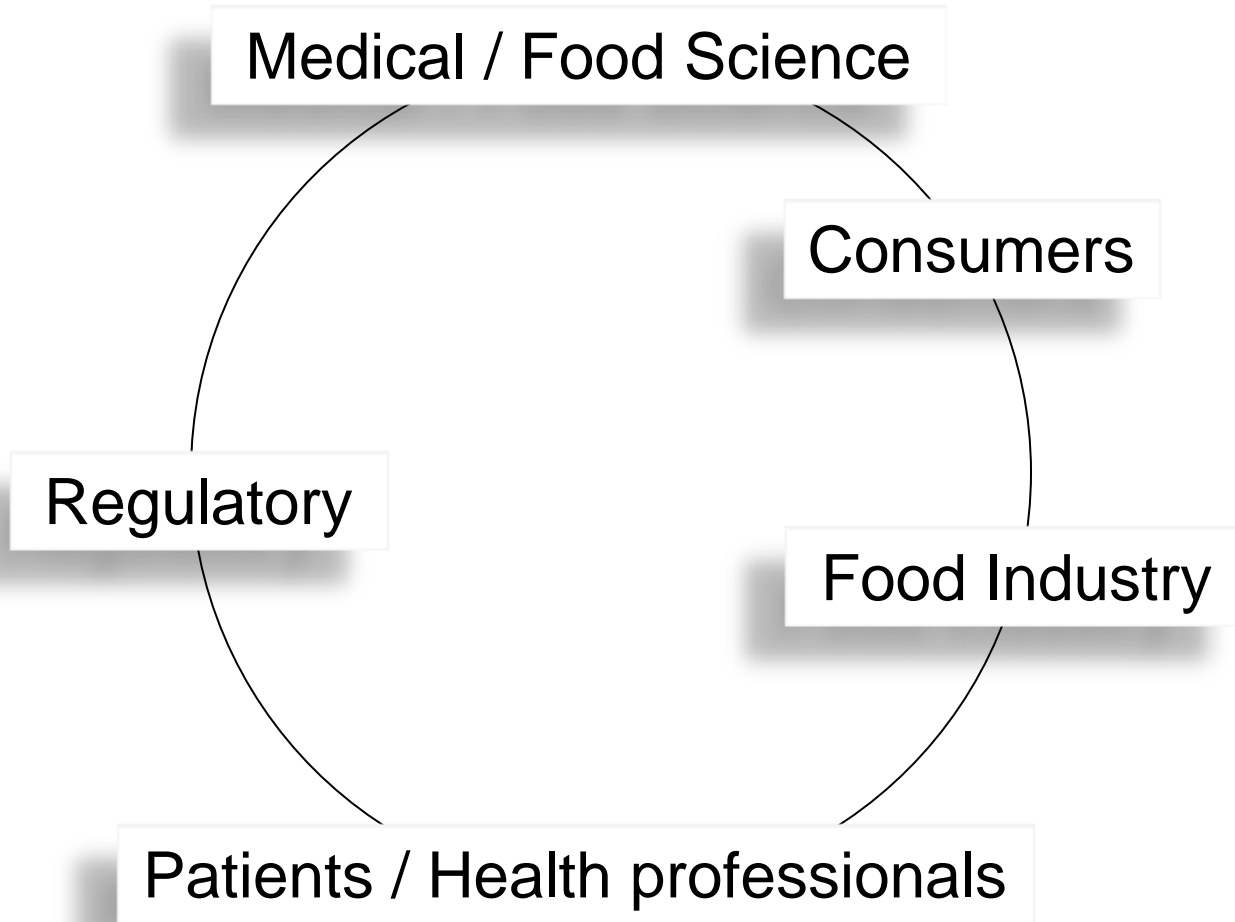
FACTS



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Setting



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Science

- ❖ First addressed
- ❖ Prevalence – then and now
- ❖ Allergen characteristics
- ❖ New allergens
- ❖ Tests and LODs
- ❖ Thresholds

Prevalence

- Childhood food allergy in the USA
- Data for 38,480 children
- Food allergy prevalence 8.0%
- Children with food allergy:
 - 38.7% history of severe reactions
 - 30.4% had multiple food allergies.
- Peanut (25.2%), milk (21.1%), shellfish (17.2%)

Gupta RS, Springston EE, Warrier MR, Smith B, Kumar R, Pongracic J, Holl JL. The prevalence, severity, and distribution of childhood food allergy in the United States. *Pediatrics* 2011 Jul;128(1):e9-17



CDC Home



Centers for Disease Control and Prevention
Your Online Source for Credible Health Information

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CDC Online Newsroom

For Immediate Release: October 22, 2008

CDC Study Finds 3 Million U.S. Children have Food or Digestive Allergies

The number of young people who had a food or digestive allergy **increased 18 percent** between 1997 and 2007, according to a new report by the Centers for Disease Control and Prevention.

From 2004 to 2006, there were approximately 9,537 hospital discharges per year



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<http://www.cdc.gov/media/pressrel/2008/r081022.htm>

Prevalence of Coeliac disease

- 1 in 100 diagnosed with Celiac Disease in UK
- Celiac disease is linked to multiple affections including osteoporosis and cancer

Table 1: Prevalence of CD in Europe compared to Middle East population based on serological screenings.⁹⁻¹⁷

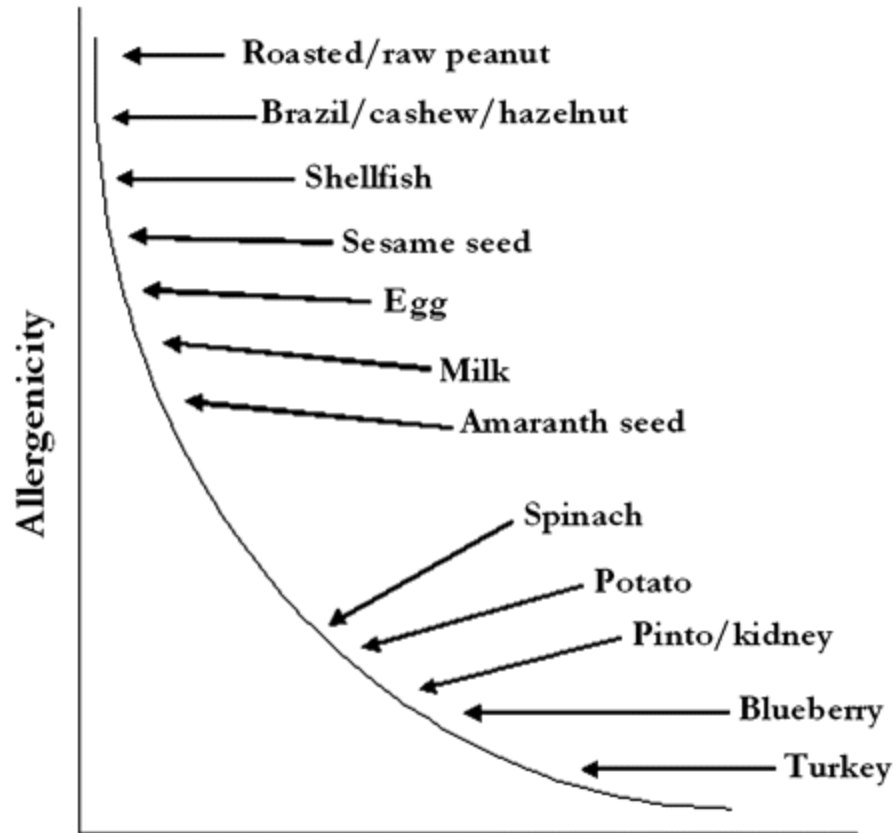
| Europe | Prevalence | Asia | Prevalence |
|----------------|------------|--------------------------------|----------------|
| Italy | 1:106 | Iran | 1:166 |
| Czech | 1:218 | Israel | 1:157 |
| Norway | 1:262 | Syria | 1.5:100 |
| Portugal | 1:134 | Turkey | 1:87 |
| Sweden | 1:190 | Anatolian adults | 1:100 |
| Netherlands | 1:198 | Kuwait (Chronic diarrhea) | 1:18 |
| United Kingdom | 1:100 | Saudi Arabia (Type 1 diabetes) | 12:100 |
| Switzerland | 1:132 | Japan | 1:20,000 |
| Spain | 1:118 | India | 1:500-1:20,000 |

Coeliac disease vs NCGS

- Avoidance of wheat- and gluten-containing products a worldwide phenomenon.
- Coeliac disease is a well-established entity
- 'Non-celiac gluten sensitivity' (NCGS)
- Complexity of wheat and the ability of its carbohydrate as well as protein components to trigger gastrointestinal symptoms

Biesiekierski JR, Muir JG, Gibson PR. Is gluten a cause of gastrointestinal symptoms in people without celiac disease? *Curr Allergy Asthma Rep* 2013 Sep 12;

Allergen Characteristics

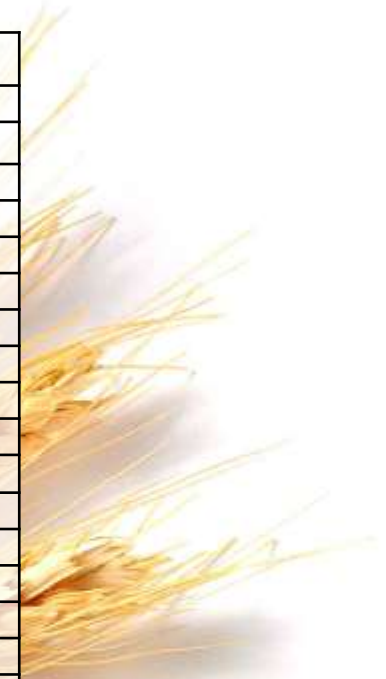


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Wheat

| Allergen Name | Common Names |
|----------------------|---|
| Tri a 12 | Profilin |
| Tri a Bd 17K | |
| Tri a 18 | Hevein-like protein |
| Tri a Gliadin | Gluten, Gliadin, Gamma-gliadin, Omega-gliadin |
| Tri a Chitinase | Class 1 Chitinase |
| Tri a 25 | Thioredoxin |
| Tri a 26 | Glutenin subunit / HMW-glutenin |
| Tri a 30 | alpha-Amylase Inhibitor, Trypsin Inhibitor, CM3 |
| Tri a Bd36K | Peroxidase |
| Tri a Germin | Germin, Germin-like protein |
| Tri a Peroxidase | |
| Tri a TPIS | TPIS |
| Tri a 14 | LTP |
| Tri a 19 | Omega5-gliadin, Gliadin, Gluten, Omega-gliadin |
| Tri a 21 | alpha/beta Gliadin, Gliadin, Gluten |
| Tri a alpha Gliadin | alpha-Gliadin, Gliadin, Gluten |
| Tri a beta Gliadin | beta-Gliadin, Gliadin, Gluten |
| Tri a gamma Gliadin | Gamma-gliadin, Gliadin |
| Tri a omega2 Gliadin | Gliadin, Gluten, Omega-gliadin, Omega2-gliadin |
| Tri a 35 | Dehydrin |
| Tri a GST | GST, Glutathione-S-transferase, #38 |
| Tri a 32 | Peroxiredoxine, PER, #112 |
| Tri a 27 | Thiol reductase |
| Tri a 29 | alpha-amylase inhibitor, CM2 |
| Tri a 28 | alpha-amylase inhibitor, 0.19, 0.53 |
| Tri a 10kD | |
| Tri a 23kd | Leucine-rich repeat protein |



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Wheat

| Allergen Name | Common Names |
|---------------------|--|
| Tri a LMW-GS B16 | Glutenin subunit |
| Tri a LMW-GS P42 | Glutenin subunit |
| Tri a LMW-GS P73 | Glutenin subunit |
| Tri a 34 | Glyceraldehyde-3-phosphate dehydrogenase / GAPDH |
| Tri a Bd 27K | |
| Tri a TLP | Thaumatococcus, Thaumatococcus-like Protein, TLP |
| Tri a 36 | Glutenin, Glutenin subunit, LMW Glutenin |
| Tri a 15 | alpha-amylase inhibitor, wmai-0.28, 0.28 |
| Tri a 20 | Gliadin, Prolamin |
| Tri a 33 | Serpin |
| Tri a 37 | alpha-Purothionin, Pur-B1, Purothionin |
| Tri a 39 | Serine protease inhibitor, #10 |
| Tri a aA_Sl | alpha-Amylase/Subtilisin Inhibitor, aA/Sl |
| Tri a bA | beta-Amylase |
| Tri a CM16 | alpha-Amylase, CM16, Trypsin Inhibitor |
| Tri a CMX | alpha-Amylase Inhibitor, C-C, CMX1, CMX2, CMX3 |
| Tri a DH | Dehydrin, DH, #126, |
| Tri a Endochitinase | Chitinase |
| Tri a GBSS_I | Starch synthase |
| Tri a LTP2 | Lipid Transfer Protein 2, LTP |
| Tri a PAP | Purple acid phosphatase |
| Tri a Peroxidase 1 | Peroxidase |
| Tri a Tritin | Tritin, Ribosomal inactivating protein / RIP |
| Tri a Trx | Thioredoxin, Trx, #37 |
| Tri a XI | Xylanase inhibitor |



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New allergens?



Tests

- ELISA
- PCR
- Liquid chromatography and triple-quadrupole tandem mass spectrometry

Heick J, Fischer M, Pöpping B. First screening method for the simultaneous detection of seven allergens by liquid chromatography mass spectrometry. J Chromatogr A. 2011 Feb 18;1218(7):938-43.

Thresholds

- The eliciting dose (ED) for a peanut allergic reaction in 5% of the peanut allergic population, the ED05, is 1.5 mg of peanut protein.
- Therefore:
if average peanut = 1 gram, then $1.5/1000 = 0.15\%$ of a peanut

Zurzolo GA, Allen KJ, Taylor SL, Shreffler WG, Baumert JL, Tang ML, Gurrin LC, Mathai ML, Nordlee JA, Dunngalvin A, Hourihane JO. Peanut Allergen Threshold Study (PATS): validation of eliciting doses using a novel single-dose challenge protocol. *Allergy Asthma Clin Immunol* 2013 Sep 12;9(1):35



Thresholds

Lowest doses resulting in reactions in DBPCFC

- 0.0002 g of roasted peanut
- 0.0064 g of raw hazelnut
- 0.7 g of raw celery

- Thus target food in a processed food product: 0.01% - 0.001%

Vieths S. Avoidance of hidden allergens in processed foods: a challenge for food chemists and manufacturers. *Nahrung* 2003;47(2):73

Eller E, Hansen TK, Bindslev-Jensen C. Clinical thresholds to egg, hazelnut, milk and peanut: results from a single-center study using standardized challenges. *Ann Allergy Asthma Immunol* 2012 May;108(5):332-336

Gluten

10 mg in 500 g of food = 20 ppm

10 mg gluten ingested in 1/250th of slice of bread
(containing 2.5 g gluten)

Forbes GM. Modifying the gluten-free threshold for foods: first do no harm Med J Aust 2013; 199 (6): 393.

B. Patients and health professionals

- Education
- Awareness
- Interpretation
- Compliance

C. Consumers

- Perceptions
- Complaints

Precautionary label: UK

- Online survey - buying behaviour of food-allergic consumers in Great Britain.
- 2/3 always read product labels first time, however only 1/3 on every occasion.
- 1/3 always avoid products with 'may contain' labels

Cochrane SA, Gowland MH, Sheffield D, Crevel RW. Characteristics and purchasing behaviours of food-allergic consumers and those who buy food for them in Great Britain. Clin Transl Allergy 2013 Sep 23;3(1):31

Precautionary label: UK

- Substantial proportion regularly take risks purchasing food including those reporting severe reactions: current application of precautionary labelling to mitigate and communicate risk is of limited effectiveness
- Failure to read labels on every occasion highlights the importance of thinking beyond legal compliance when designing labels, for example when adding an allergen to a product that previously did not contain it

Cochrane SA, Gowland MH, Sheffield D, Crevel RW. Characteristics and purchasing behaviours of food-allergic consumers and those who buy food for them in Great Britain. Clin Transl Allergy 2013 Sep 23;3(1):31



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Precautionary label: Australia

- Avoidance of foods - depends on the wording
- 65% ignore “made in the same factory” vs 22% “may be present”
- No difference whether a history of anaphylaxis

Zurzolo GA, Koplin JJ, Mathai ML, Tang MKL, Allen KJ. Perceptions of precautionary labelling among parents of children with food allergy and anaphylaxis. *Med J Aust* 2013;198(11):621-623.



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Precautionary label: Australia

- Consumers choose a gradient level of risk based on the wording of the precautionary statements
- Appear to be complacent about precautionary labelling
- Many statements now disregarded by a sizeable proportion of parents of food-allergic children, including those caring for children with a past history of anaphylaxis

Zurzolo GA, Koplin JJ, Mathai ML, Tang MKL, Allen KJ. Perceptions of precautionary labelling among parents of children with food allergy and anaphylaxis. *Med J Aust* 2013;198(11):621-623.

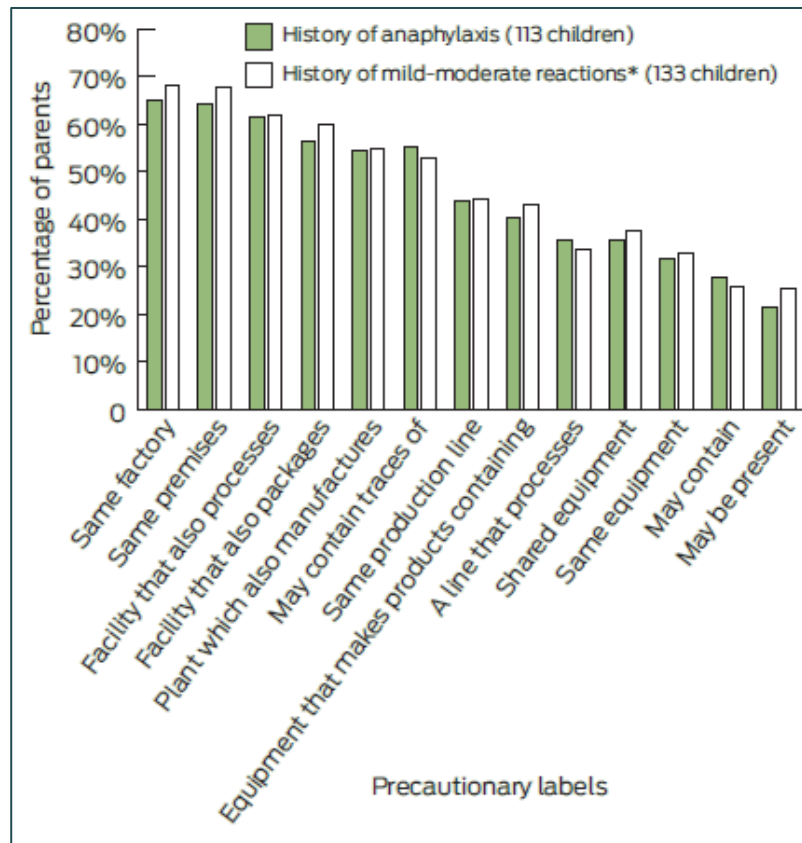


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Precautionary label: Australia

Percentage of parents of food-allergic children who reported that they **would ignore** a particular precautionary label, stratified by risk



Zurzolo GA, Koplin JJ, Mathai ML, Tang MKL, Allen KJ. Perceptions of precautionary labelling among parents of children with food allergy and anaphylaxis. *Med J Aust* 2013;198(11):621-623.



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Foods with precautionary allergen labelling rarely contain detectable allergen

Giovanni A. Zurzolo, Jennifer J. Koplin, Michael L. Mathai, Steve L. Taylor, et al. Foods with precautionary allergen labeling in Australia rarely contain detectable allergen. *J Allergy Clin Immunol: In Practise* 2013;1(4):401-403.



D. Food Industry

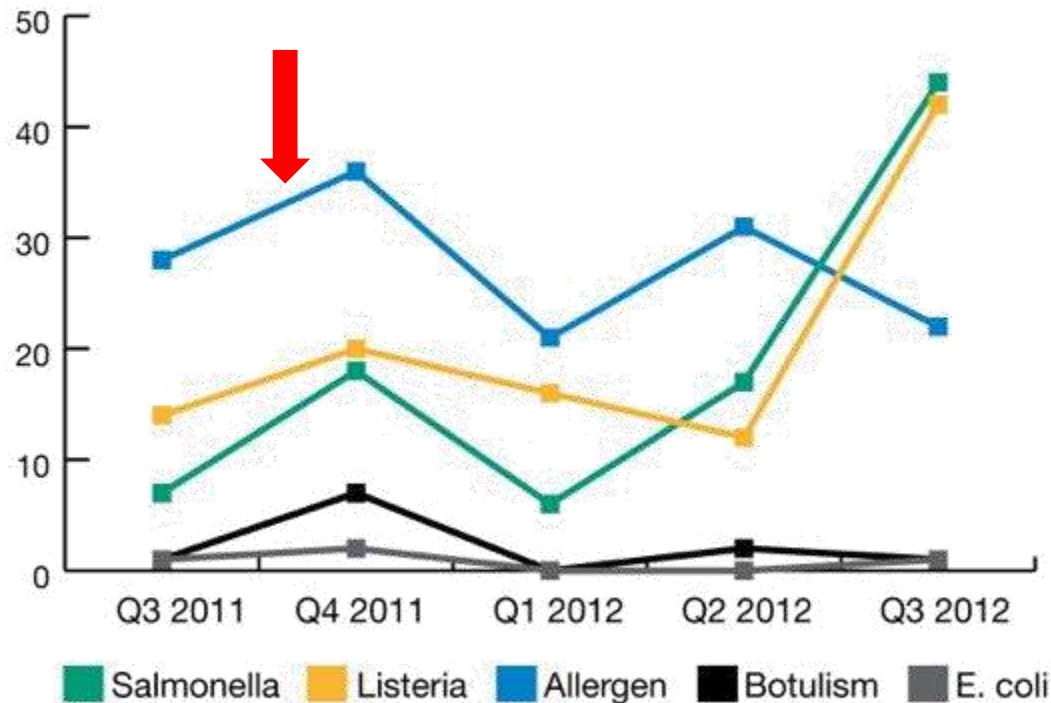
- Compliance
- Cost of business
- ACP - HACCP – Audits
- Suppliers
- Labelling practises
- Risks

D. Food Industry

- Food processing changes
- New Ingredients
- Suppliers

Undeclared allergens – not pathogens involving bacteria, viruses or parasites – are driving the overwhelming majority of recalls

**Leading Causes of Food Recalls
According to Recall Announcements on FDA Website**

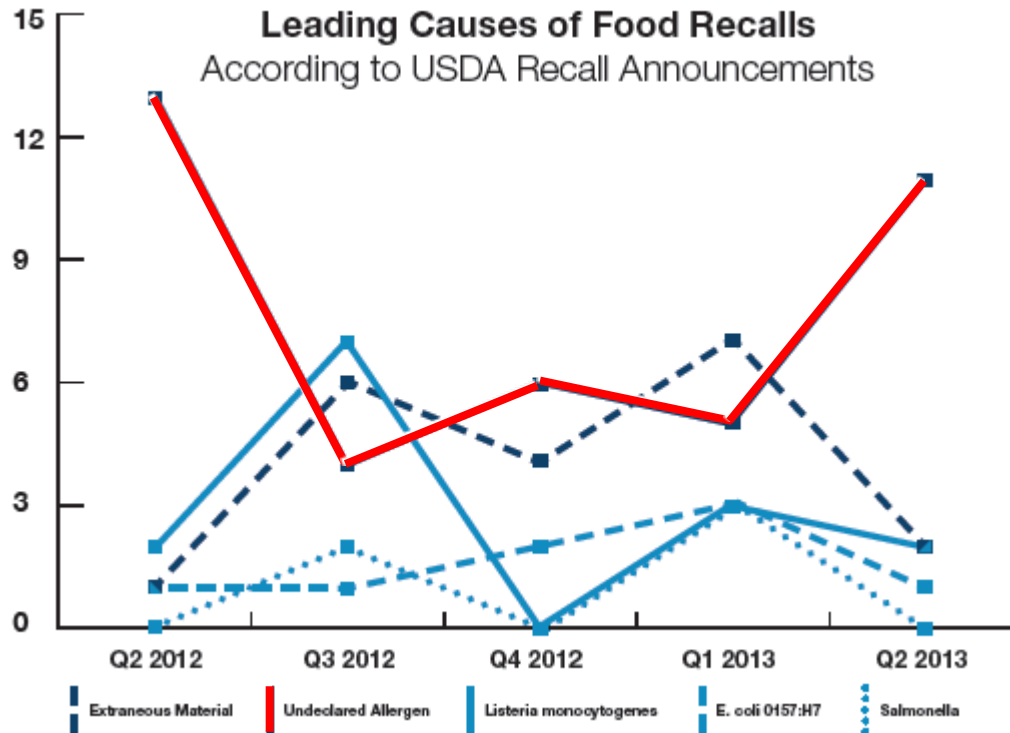


<http://www.foodsafetynews.com/2013/08/undeclared-allergens-top-reason-for-second-quarter-recalls/#.UhW09tI3CeF>



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<http://www.foodsafetynews.com/2013/08/undeclared-allergens-top-reason-for-second-quarter-recalls/#.UHW09tI3CeF>



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Table 1. Total number of yearly food product recalls, recalls due to undeclared allergens per year and recalls associated with allergic reactions

| | 2005 | 2006 | 2007 | 2008 | 2009 | 2010* | Total |
|---|---------------|---------------|---------------|---------------|---------------|----------------|----------------|
| Total number of food product recalls | 276 | 213 | 254 | 242 | 259 | 393 | 1637 |
| Undeclared allergen recalls (% of total) | 64 (23.2%) | 69 (32.4%) | 82 (32.3%) | 87 (36%) | 71 (27.4%) | 147 (37.4%) | 520 (31.8%) |
| Recalls associated with allergic reactions (% of total allergen recalls) | 10 (15.6%) | 11 (15.9%) | 17 (20.7%) | 11 (12.6%) | 7 (9.9%) | 8 (5.4%) | 64 (12.3%) |

* A significant increase in number of recalls is noted compared to prior years. We currently do not have an explanation for this increase.

I. Malyukova; S. M. Gendel; S. Luccioli. Milk is the predominant undeclared allergen in US food product recall
Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, Food and Drug Administration MD, USA



Food Standards Agency Annual Report of Incidents 2013

1,604 food and environmental contamination incidents

Three largest contributors:

- microbiological contamination (20%)
- environmental contamination (15%)
- natural chemical contamination (13%)

<http://www.food.gov.uk/news-updates/news/2013/jun/fsa-incidents#.UIE4W0BuLVw>



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Food Standards Agency Annual Report of Incidents

<http://www.food.gov.uk/news-updates>

Tesco recalls its Finest Sweet and Zesty Side Salad
Withdrawal of Walkers Sensations Chutney Poppadoms
Tesco Frozen Classic Turkey Dinner recalled
True Foods recalls its Steak Diane Sauce
Freemans Confectionery Supplies recalls Many Thanks Pralines with Hazelnut Filling
Asda withdraws its Cocktail Sausage and Tomato Dip
Asda withdraws Beastie Bites
Coco Cafe Mocha recalled
Organica-branded chocolate bars withdrawn
Tesco Finest Restaurant Collection 2 Triple Belgian Chocolate Crowns recalled
Vegan Organica Marzipan and Dark Chocolate Bar recalled
Harrods Chocolatier Dark Chocolate withdrawn
Tesco recalls Simply Ginger Beer
Botham's of Whitby withdraws its Finest Quality Plum Bread
Iceland recalls its 4 Chinese Pork Quarter Pounders
Crunch Craving Chocolate Coated Raisins recalled
Blue Dragon Wasabi Plum Shot withdrawn
Asda withdraws Little Eat Beef, Cheese & Tomato Burgers
EH Booths withdraws roasted monkey nuts
Asda withdraws own-brand noodle pouch
Asda withdraws own-brand Tomato and Onion Dip
Bodrum dried fruit products withdrawn
Booths withdraws Edamame Bean Stir Fry
Wholebake Limited recalls 9 Bar brand original mixed seed bar
Undeclared sulphites in Montezuma's Chocolates products
Asda withdraws potato salad
SuperValu tuna and sweetcorn sandwiches recalled
Raw Ecstasy Wasabi Miso flavoured Activated Walnuts and Activated Almonds recalled
Greencity Wholefoods withdraws yogurt-coated products
Asda withdraws own-brand almonds
Tesco Mini Chocolate Crispies withdrawn
Waitrose Channel Island Hazelnut Yogurt recalled
Sainsbury's recalls Honey Roasted Jumbo Cashews due to undeclared peanuts
Asda withdraws beef hotpot

SA Recalls

- Chocolate
- Mayonnaise
- Pillsbury muffins

Pillsbury Lemon Poppyseed Muffin Mix (Extra 20 percent Free) because it might contain nuts, an allergen not listed on the ingredient label.

Bottles of Crosse and Blackwell light mayonnaise have been pulled off the shelves of supermarkets, after Nestle realised its error in not listing eggs as part of the ingredients.



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Key Food Industry Lessons

Major company recalls

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

E. Regulatory framework

- International
- Local
- Precautionary labelling
- CPA

Case report 27

Food Control 32 (2013) 440–449

Contents lists available at SciVerse ScienceDirect

Food Control

139 Processed meat samples

25% Undeclared Soy

32% Undeclared gluten

Soy > 1,000 ppm



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Case report 5

Product tested: Rice milks

Dairy-free creamer



Tested for: Milk (ELISA)

Claims: Dairy free

Results: >25 ppm milk



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Case report 8

Product tested: xxxx Frozen chicken

Tested for: Milk

Method of Testing: Milk ELISA

Results: 13 ppm milk protein

Details: Likely to be incorporated in brine,
but not labelled



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Case report 6

Product tested: xxxx Yoghurt culture and probiotic

Tested for: Milk

Method of Testing: Milk ELISA

Results: >1200 ppm milk protein

Details: Milk proteins may be incorporated from culture medium.



Conclusions



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Registered Dietician

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