The Past, Present and Future: Celebrating the Achievements, Looking at the Gaps

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Food Allergen Management Symposium
May 30, 2023

A Time of Many Challenges for Allergic Consumers

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

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

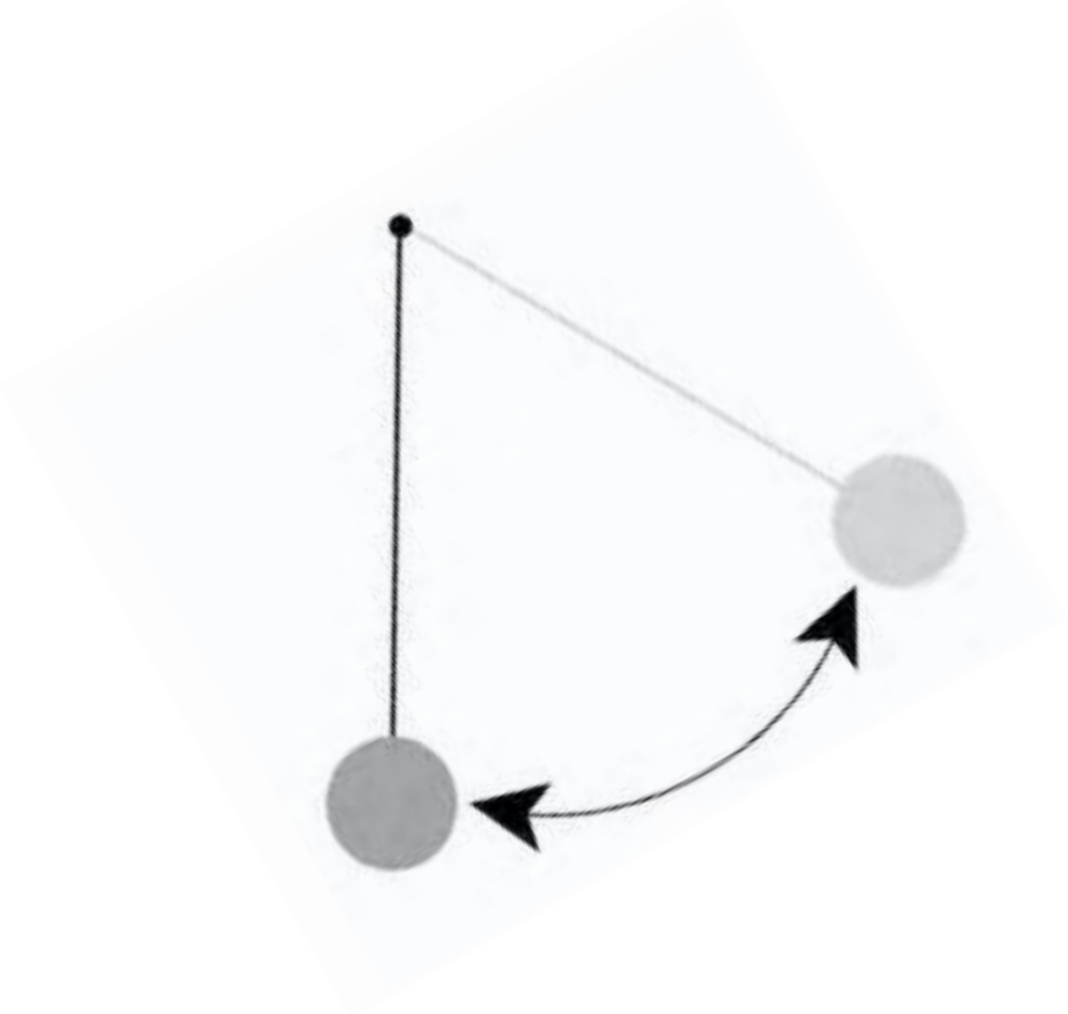
- Limitations in our Understanding:
  1. Clinical uncertainty on prevalence, potency and severity
  2. Allergen control practices in the food industry and foodservice
  3. Labelling transparency

Documented Risks Associated with Food Allergies

Health Risks

Regulatory Risks

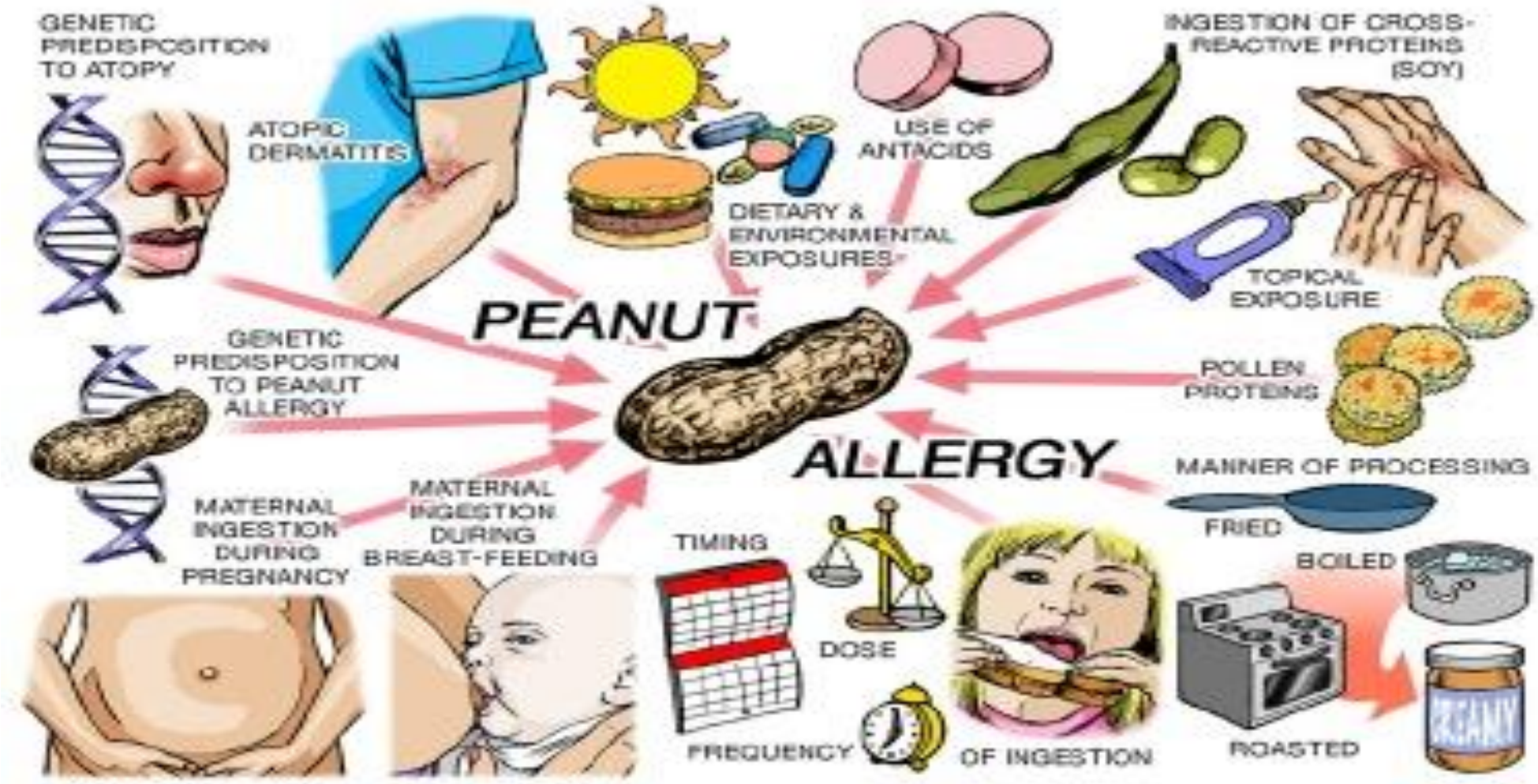
Business Risks



A Need for Research and Communication

Clinical Advancements

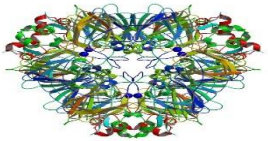
Potential Factors Involved with the Increasing Prevalence of Food Allergies



Sicherer and Sampson. J Allergy Clin Immunol. 2007; 120:491-503.

Common Causes of Food Allergies

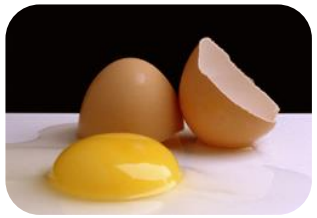
Ara h 2



Ara h 3

"The Big 8"

Milk



Egg

Crustacea

Fish

Peanut

Soybean

Tree nuts

Wheat

Causative Agents

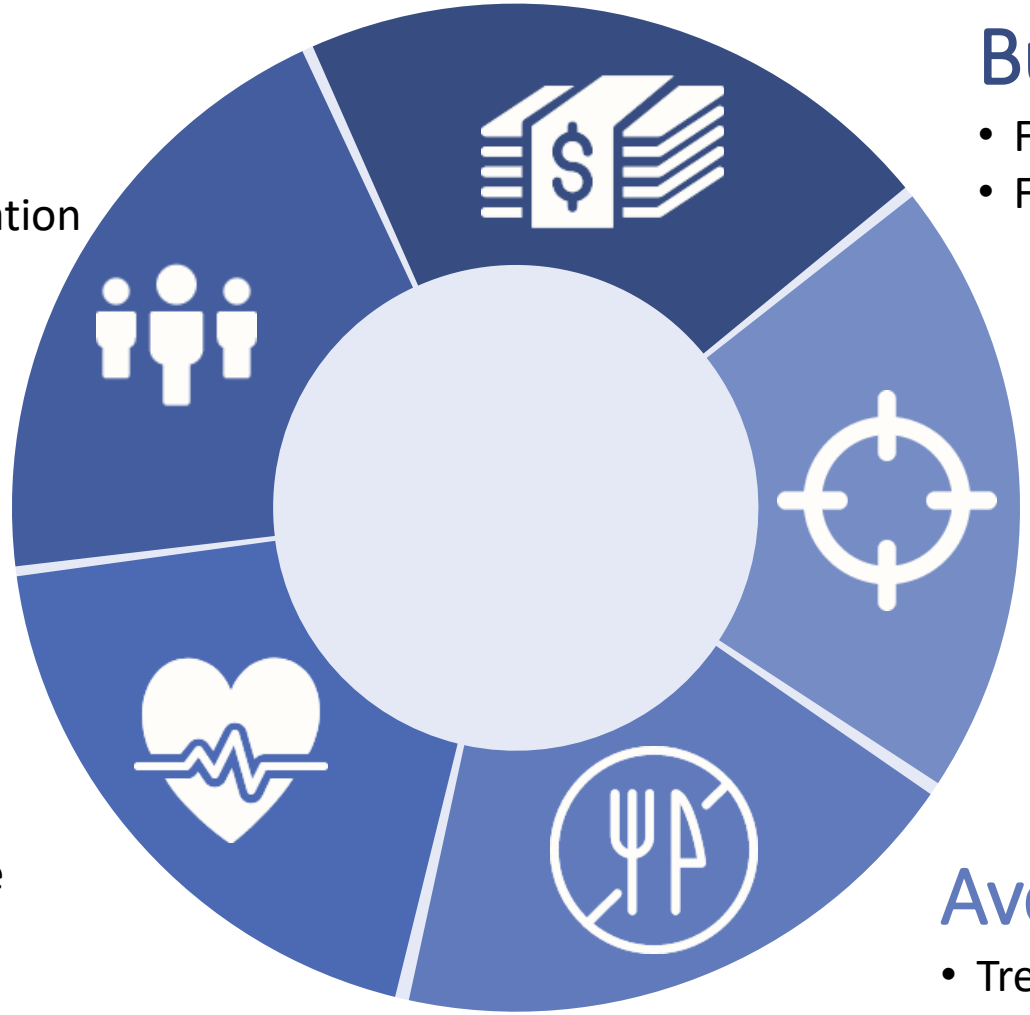
- Naturally-occurring **proteins**

- Heat-resistant
- Resistant to proteolysis
- Resistant to extremes in pH
- Usually the major proteins of the food
- Foods can have 1 or many allergens

Food Allergies

Prevalence

- Affects 3-4% of the population
  - 4-8% of children
  - 1-2% of adults



Burdens

- Financial, quality of life
- Fear, anxiety, social isolation

Sensitivity

- Small amounts can cause reactions
- Low mg or ppm total food protein

Severity

- Reactions potentially life-threatening
- Reactions are preventable

Avoidance Diets

- Treatments are scarce
- Strict avoidance diets

How Much Food Is Too Much? Threshold Doses for Allergenic Foods

Susan L. Hefle, PhD and Steve L. Taylor, PhD

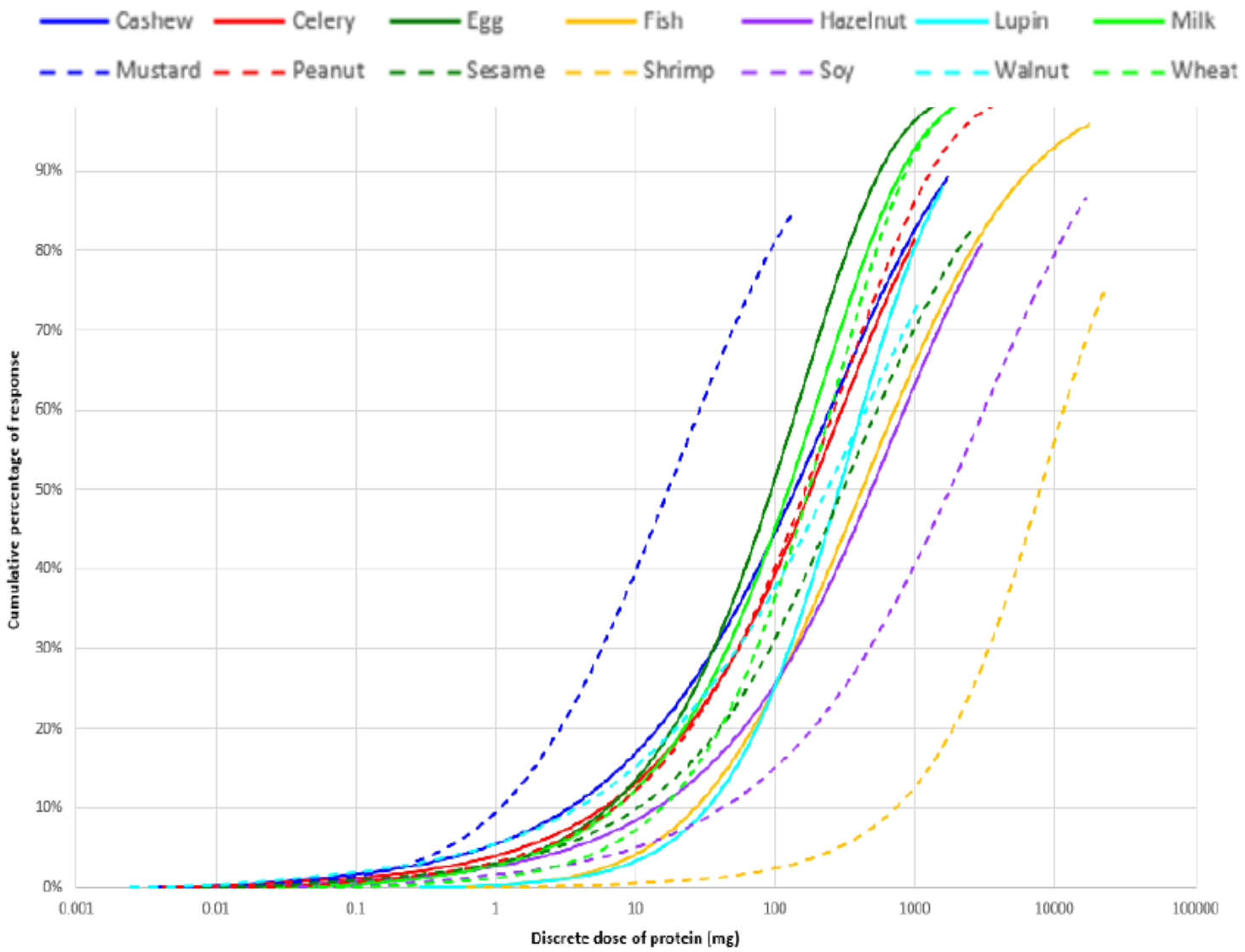
- Food allergies can cause several and even fatal response
  - But we lacked an understanding of what doses could cause mild to severe allergic response
    - ➢ Early DBPCFCs often started at 100s of mg of the allergenic food
      - Often observed 20-25% of the study population react, some with severe reactions
    - ➢ Dogma became “low doses cause severe and fatal reactions”
- Drove a zero risk, zero threshold approach with many approaches (regulatory, industry management, etc.)

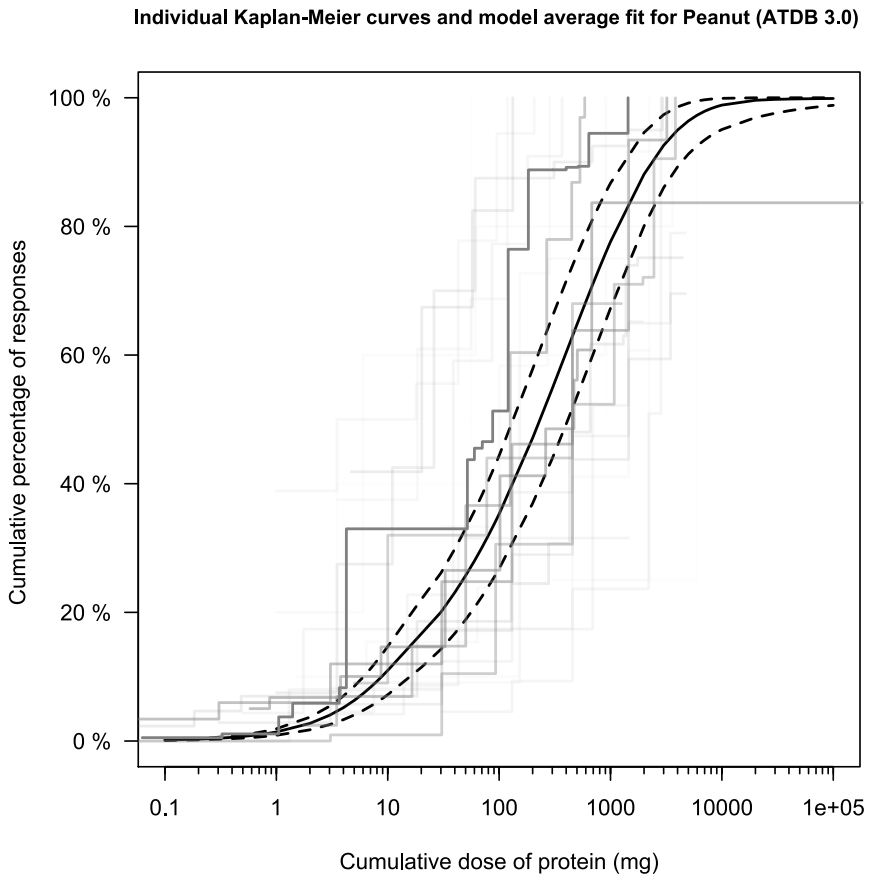
Current Allergy and Asthma Reports 2002, **2**:63–66
Current Science Inc. ISSN 1529–7322

Allergic Patients Present with Different Levels of Sensitivity

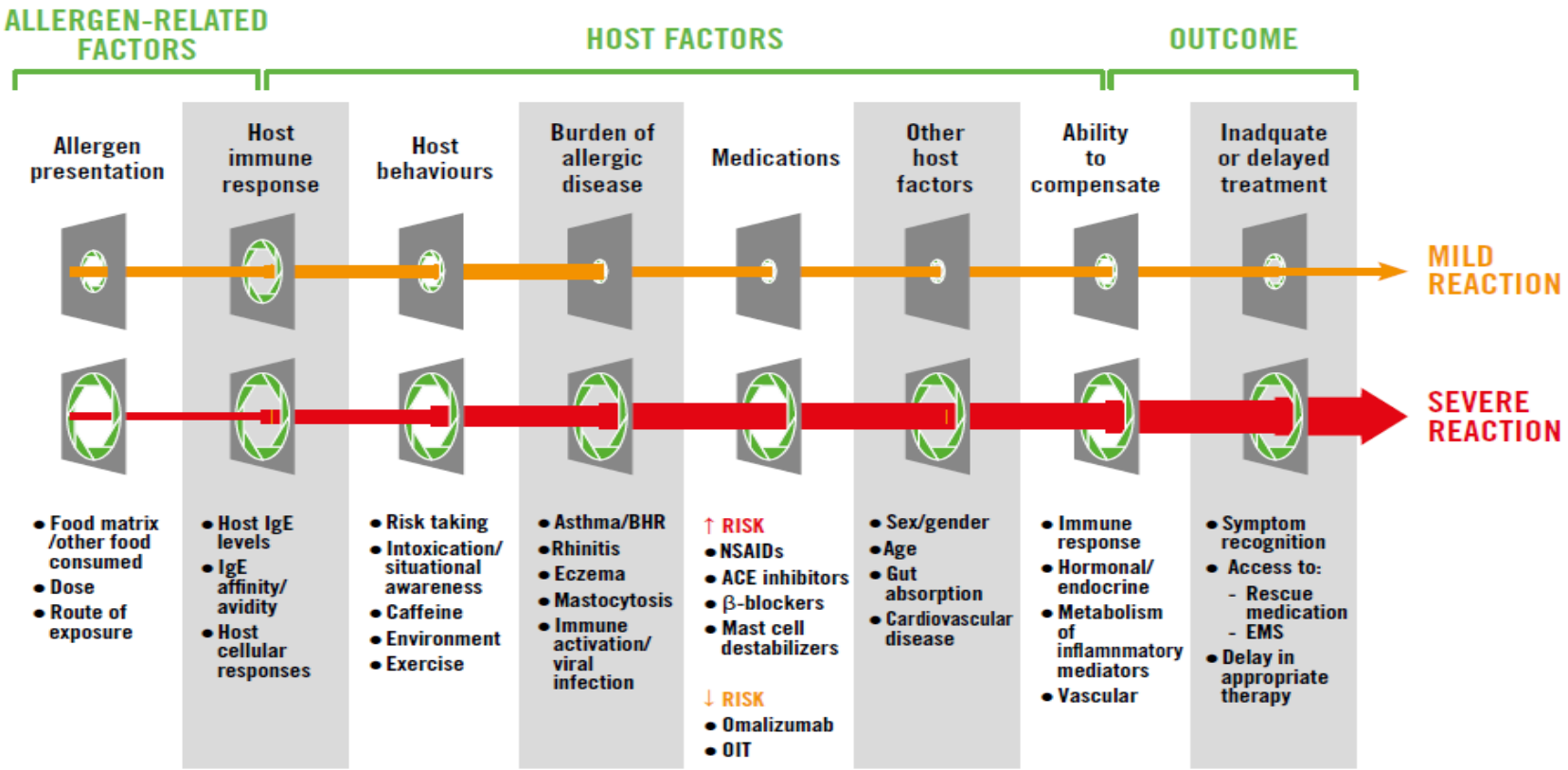
Ballmer-Weber and Hourihane; image used with permission

Dose Distributions for Various Food Allergens: Not all food allergens are created equal





Houben et al. FCT 2020

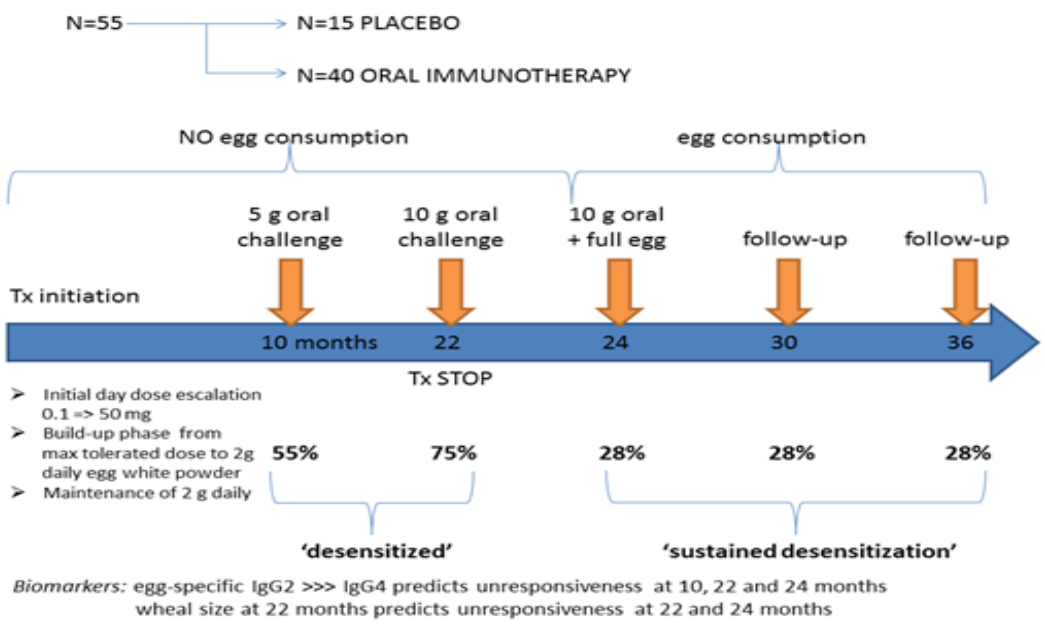


Source: Adapted with permission from Dubois *et al.* 2018.

Note: BHR, bronchial hyper responsiveness; NSAIDs, non-steroidal anti-inflammatory drugs; ACE, angiotensin-converting enzyme; EMS, emergency medical services.

Dubois, A.E.J., Turner, P.J., Hourihane, J., Ballmer-Weber, B., Beyer, K., Chan, C.-H., Gowland, M.H. ***et al.*** 2018. How does dose impact on the severity of food-induced allergic reactions, and can this improve risk assessment for allergenic foods?: Report from an ILSI Europe Food Allergy Task Force Expert Group and Workshop. *Allergy*, 73(7): 1383–1392. https://doi.org/10.1111/all.13405

Research in Food Allergy Treatment and Prevention



DBV Technologies VIASKIN® Peanut (https://dbv-technologies.com/)

Burks et al. (2012). Oral immunotherapy for treatment of egg allergy in children. *N Engl J Med.* 19:233-243.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 26, 2015 VOL. 372 NO. 9

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

George Du Toit, M.B., B.Ch., Graham Roberts, D.M., Peter H. Sayre, M.D., Ph.D., Henry T. Bahnson, M.P.H., Suzana Radulovic, M.D., Alexandra F. Santos, M.D., Helen A. Brough, M.B., B.S., Deborah Phippard, Ph.D., Monica Basting, M.A., Mary Feeney, M.Sc., R.D., Victor Turcanu, M.D., Ph.D., Michelle L. Sever, M.S.P.H., Ph.D., Margarita Gomez Lorenzo, M.D., Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team*

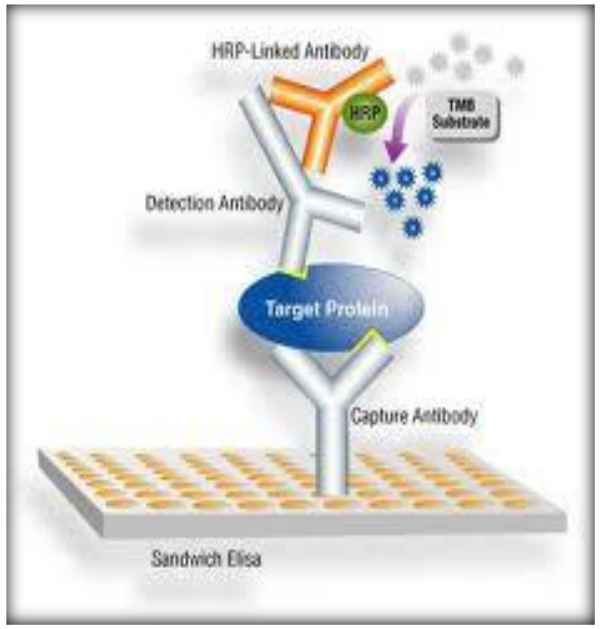
Allergen Management Advancements in the Food Industry

1980s and 1990s: Growing Awareness of Food Allergies in the Food Industry

- Allergen regulations emerged requiring source allergen labelling
- Allergen control programs were needed to minimize cross-contact
  - But how much was too much residue or how clean was clean enough?
  - How does industry validate removal of allergen residue?

Analytical Tools Added to the Toolbox

- Immunochemical methods (ELISA and LFD) were developed which aided in allergen residue detection
- Mass spectrometry also developed in more recent years
- There is a continued need to improve methods



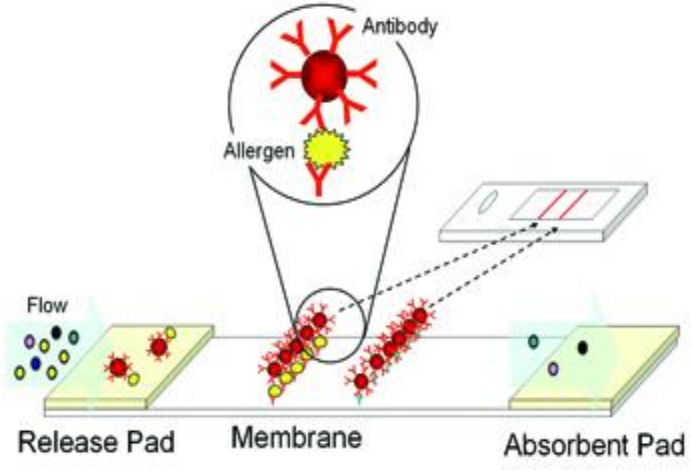
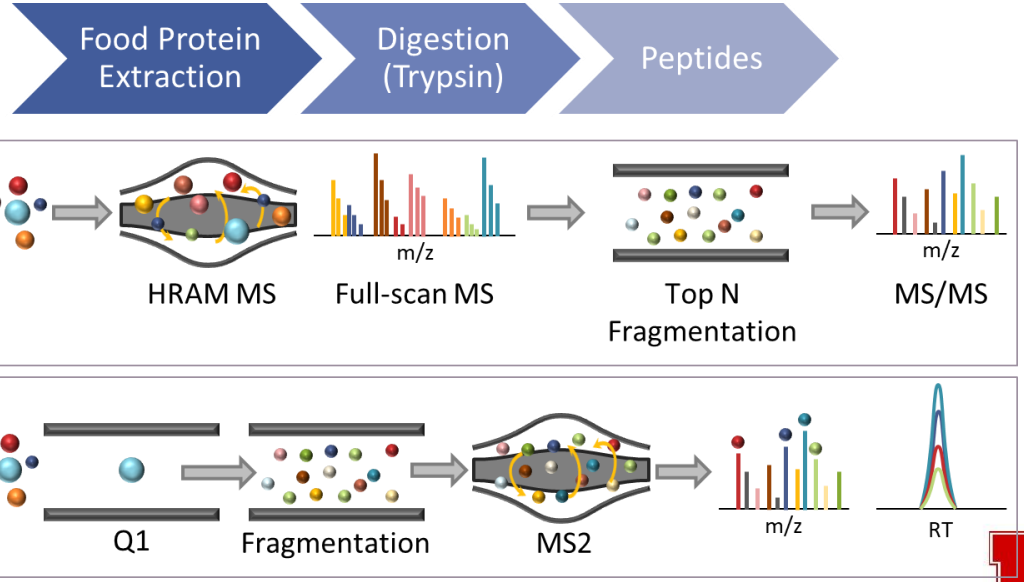
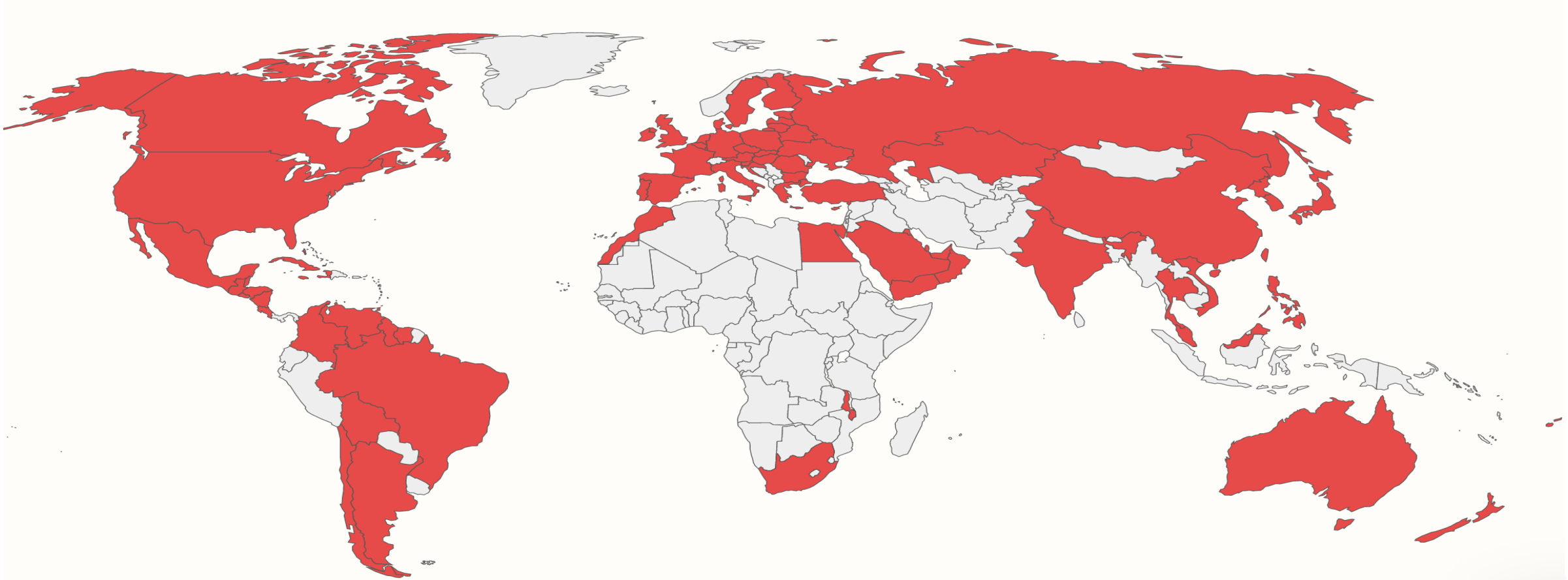


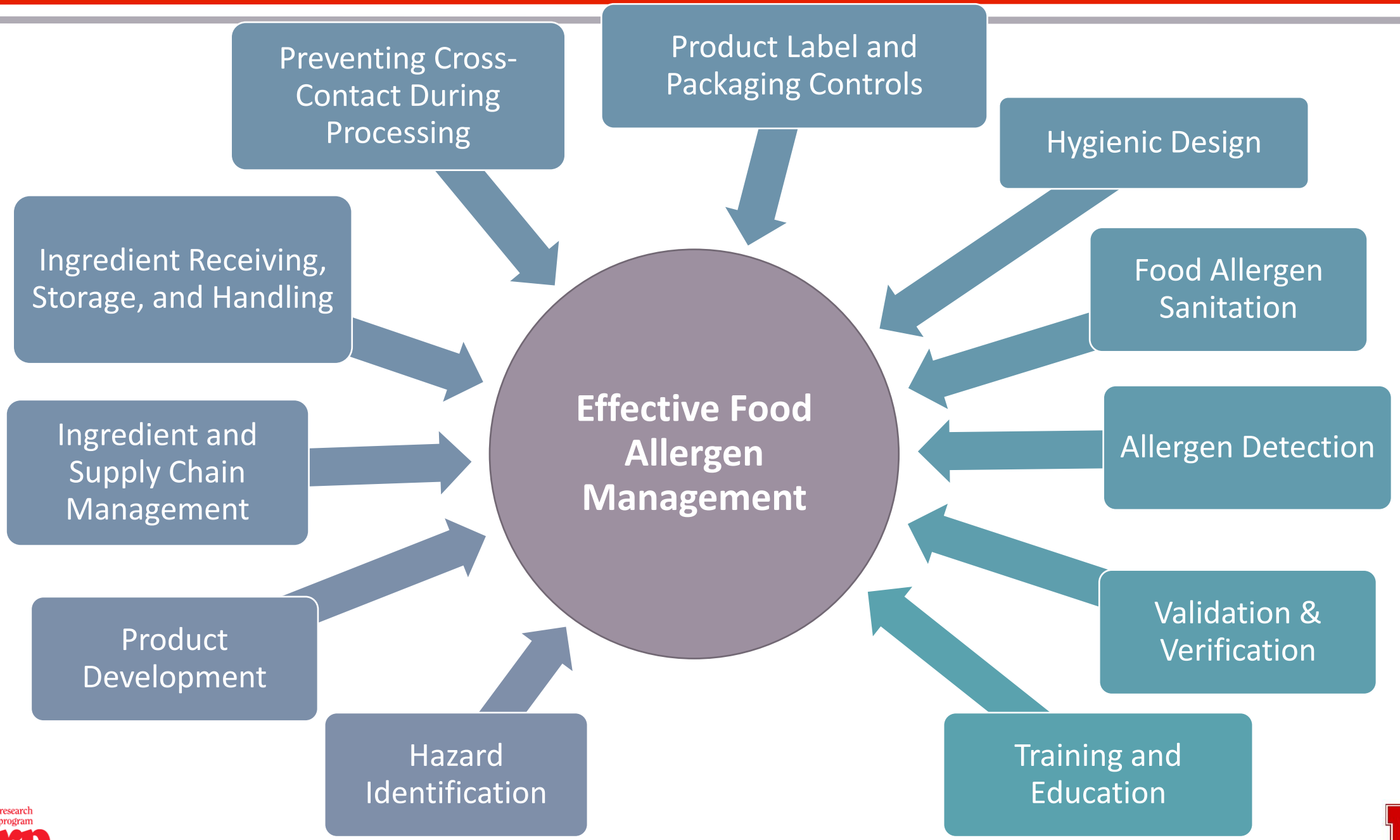
Figure 1: Principle of a strip test: Anti-allergen antibody-coated colored beads form a complex with allergens in the sample and anti-allergen antibodies on the strip. This leads to a colored test line indicating a positive (i.e., allergen-containing) sample. A colored control band indicates correct performance of the test.



International Allergen Labelling Regulations



https://farrp.unl.edu/IRChart


Preventing Cross-Contact During Processing
Product Label and Packaging Controls
Hygienic Design
Ingredient Receiving, Storage, and Handling
Food Allergen Sanitation
Ingredient and Supply Chain Management
Effective Food Allergen Management
Allergen Detection
Product Development
Validation & Verification
Hazard Identification
Training and Education

Food Safety Management at Home:

- Control source materials
- Consider use of shared equipment and utensils
- Preparation (sequence and schedule)
- Manage cleaning
- Training
- Buy-in of system by family members

Food Safety Management at Home: Deviations from Prerequisite Program

Management (mom) on vacation

+

Operations (me) in charge of dinner preparation

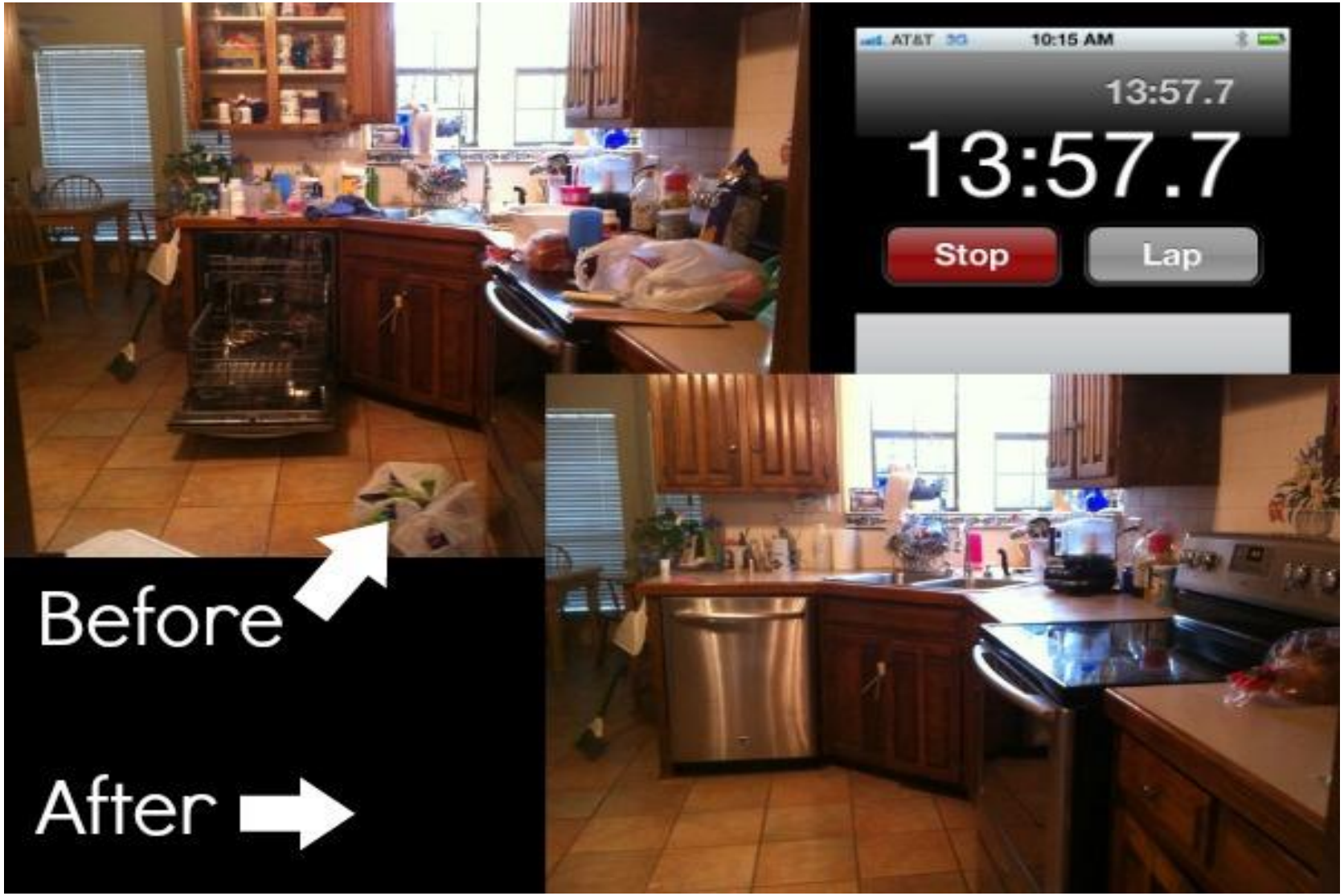
+

New (untrained) employee

= Compliance Issue (deviation from mom's set protocol)

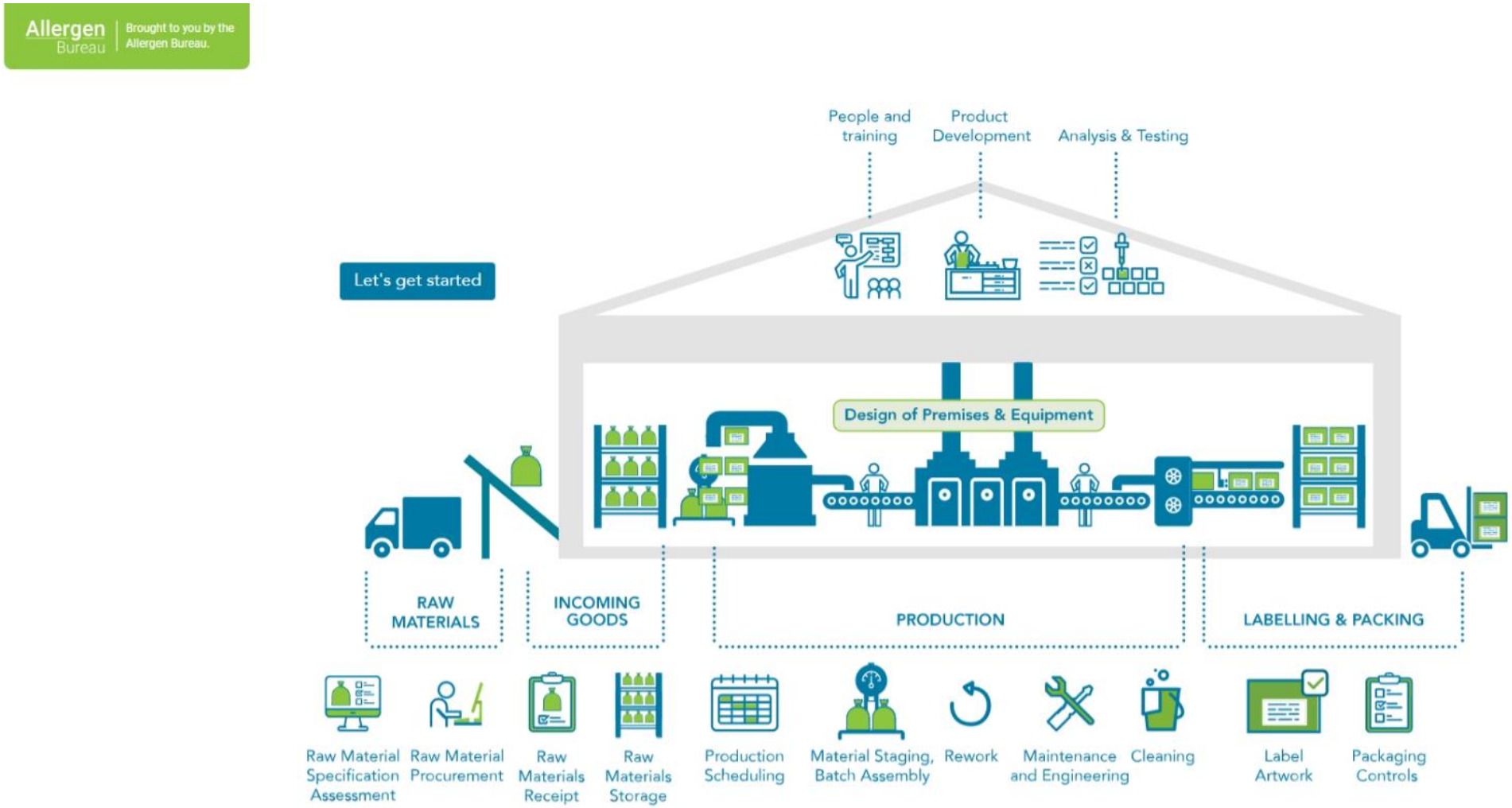
Food Safety Management at Home:

Food Safety Management at Home:



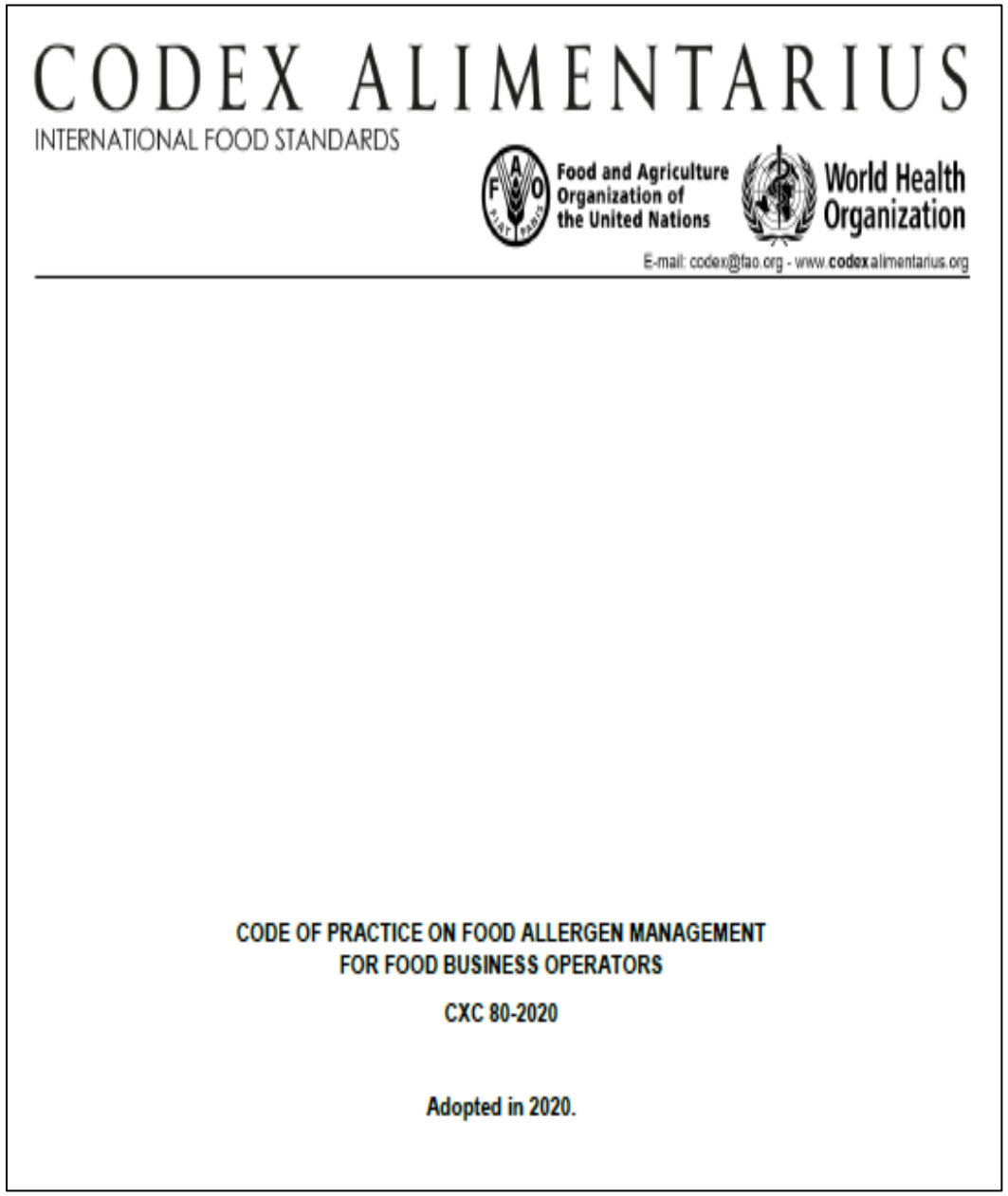
Food Industry Operations: Scale-Up

Hazard Identification- Tracking Allergens in a Facility



VITAL® Risk Review Tool

https://info.allergenbureau.net/infographic/



CODEX ALIMENTARIUS

INTERNATIONAL FOOD STANDARDS

Food and Agriculture Organization of the United Nations

World Health Organization

E-mail: codex@fao.org - www.codexalimentarius.org

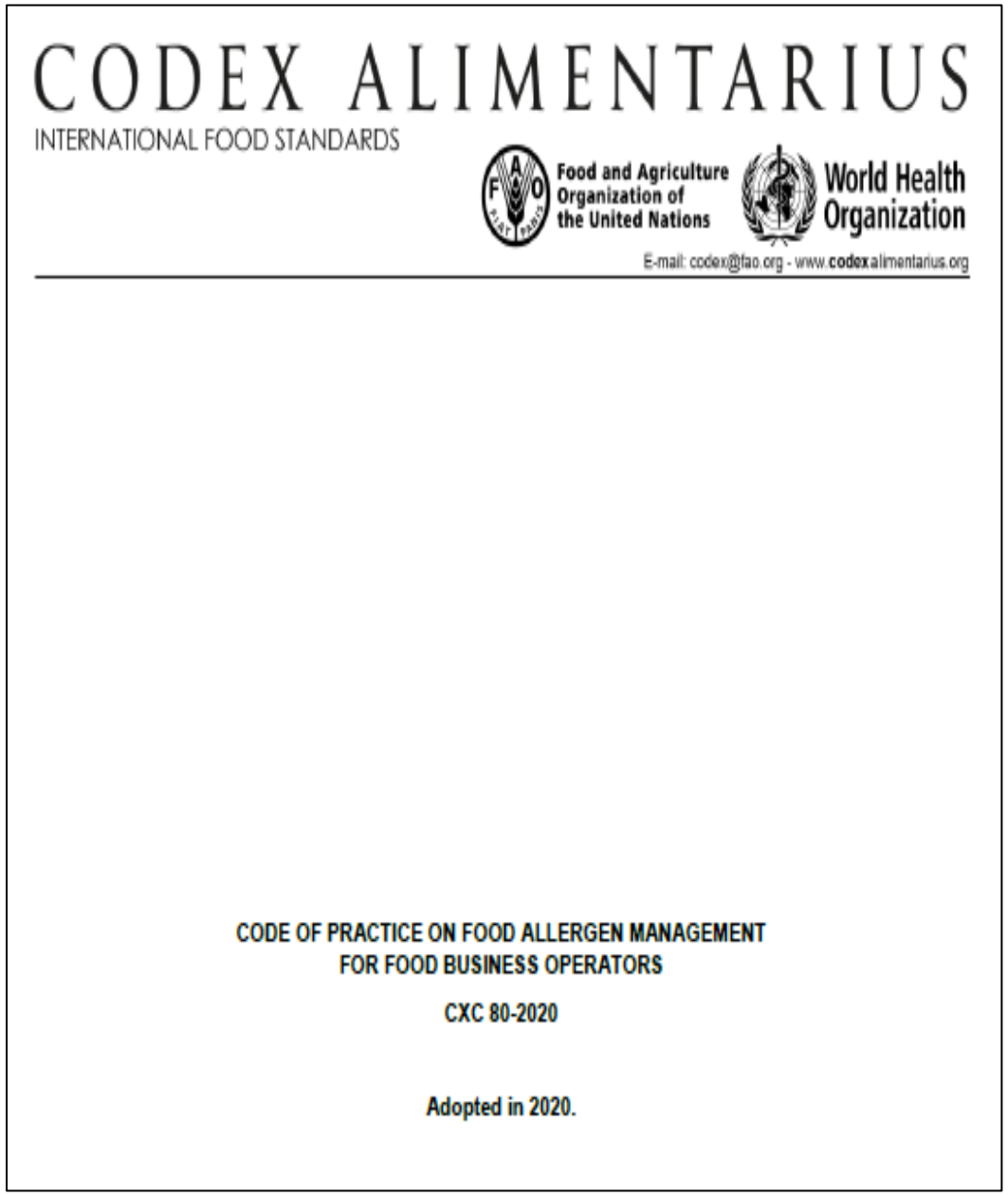
CODE OF PRACTICE ON FOOD ALLERGEN MANAGEMENT FOR FOOD BUSINESS OPERATORS

CXC 80-2020

Adopted in 2020.

- **Farm to fork guidance for allergen management**
  - prevent or minimize the potential for allergen cross-contact that is of risk to the consumer with a food allergy
  - prevent or minimize the potential for undeclared allergens being present in a food due to errors arising in the supply chain
  - ensure the correct allergen label is applied to prepackaged foods
  - ensure that accurate information can be provided to consumers at point of sale when the food is not prepackaged

http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXC%2B80-2020%252FCXC_080e.pdf



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CODE OF PRACTICE ON FOOD ALLERGEN MANAGEMENT FOR FOOD BUSINESS OPERATORS

CXC 80-2020

Adopted in 2020.

- **Updated in 2020 by the CCFH**
  - **Co-chaired by Australia, U.S. and the U.K.**

  - The Code follows the format of the *General Principles of Food Hygiene (CXC 1-196)*
    - Should be used in conjunction with other codes and standards
      - *General Standard for Labelling Foods (CXC 1-1985)*
      - *Code for Hygienic Practice for the Transport of Food in Bulk and Semi-packed Food (CXC 47-2001)*

http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXC%2B80-2020%252FCXC_080e.pdf

Food Allergen Recalls: Causes

- Review of FDA allergen recalls FY 2007- FY 2012 (Gendel and Zhu 2013)
  - Identified 732 allergen recalls

TABLE 6. *The number of recalls involving each of the most frequent food-allergen combinations FY 2007 through FY 2012*

	Bakery	Snack	Candy	Dressing	Dairy
Peanut	10	19	18	0	9
Egg	44	4	6	8	11
Milk	107	41	22	21	13
Soy	36	25	14	21	12
Wheat	58	11	7	17	10
Tree nuts	44	17	20	3	18

TABLE 7. *The number of allergen recalls and the distribution of recall classifications for each root cause FY 2007 to FY 2012*

Root cause[a]	No.	Recall class (1/2/3)
Computer error	21	15/4/2
Cross-contact	52	41/11/0
In process	19	15/4/0
Ingredient mislabeled	26	16/10/0
Knowledge	28	14/14/0
No carry-through	70	39/31/0
No declaration	12	1/10/1
Not updated	22	12/9/1
Omission	191	128/63/0
Other	14	12/2/0
Rework	9	9/0/0
Terminology	85	20/63/2
Unknown	15	15/0/0
Wrong ingredient	31	26/4/1
Wrong label	50	37/10/3
Wrong package	87	63/23/1

Gendel, S.M. and J. Zhu. Journal of Food Protection, 2013. **76**(11): p. 1933-8.

The Challenge:
Precautionary/Advisory Labeling (PAL)

Precautionary/Advisory Allergen Labeling

- Precautionary Allergen Labeling (PAL)
- Voluntary statements that can be used to communicate potential risk to allergic consumers
- Because these statements are voluntary, food companies use varying criteria to decide when and whether to use PAL
- Regulatory agencies in the U.S. (FDA, FSIS) and other countries provide limited guidance on PAL usage

PAL Should Follow the Food Allergy Issues Alliance Guidelines*

Whether the presence of a major food allergen is documented through visual examination or analytical testing of the processing line, equipment, ingredient or product, or other means;

Whether the risk of presence of a major food allergen is unavoidable even when current good manufacturing practices are followed;

Whether a major food allergen is present in some, but not all, of the product; and

Whether the presence of a major food allergen is potentially hazardous.

*All guidelines need to be met to utilize PAL

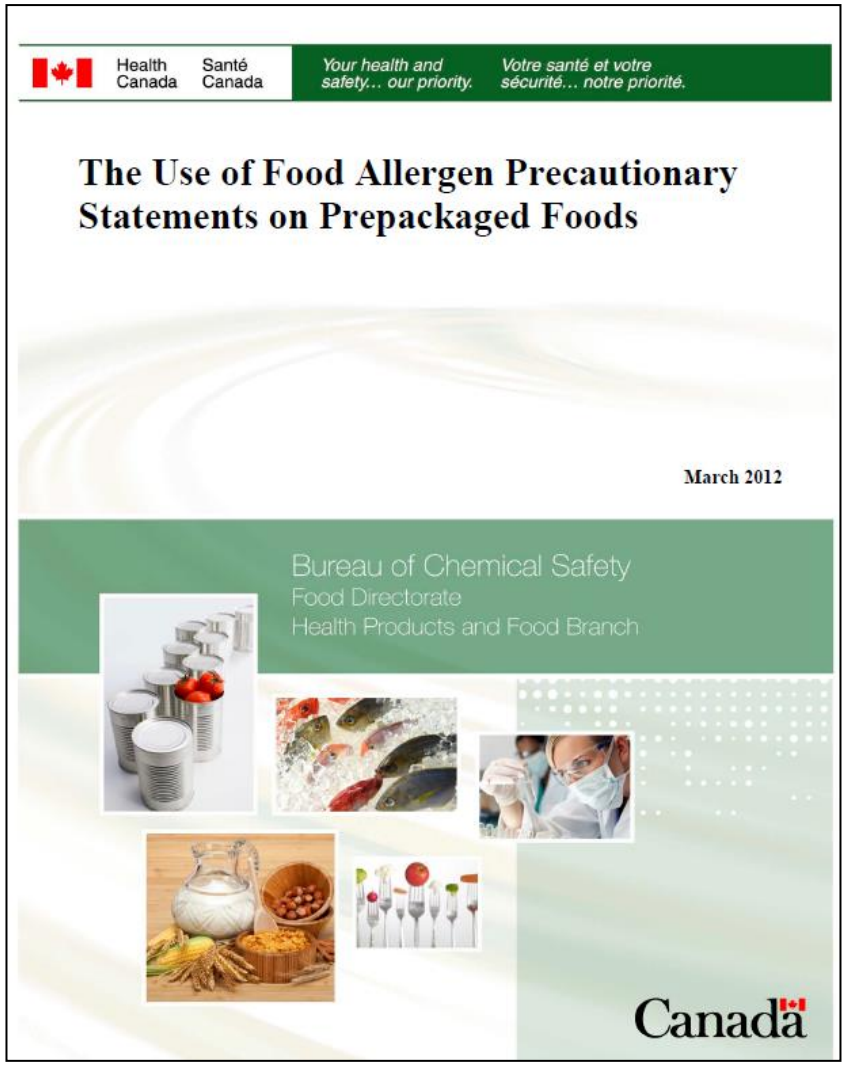
Food Allergy Issues Alliance, "Food Allergen Labeling Guidelines," May 2001.

Label Declaration of Allergenic Substances in Foods; Notice to Manufacturers

June 10, 1996
NOTICE TO MANUFACTURERS
Label Declaration of Allergenic Substances in Foods

- One of the first U.S. regulatory references to precautionary labeling came from the FDA in 1996.

"The agency is aware that some manufacturers are voluntarily labeling their products with statements such as "may contain (insert name of allergenic ingredient)." FDA advises that, because adhering to good manufacturing practice (GMP) is essential for effective reduction of adverse reactions, **such precautionary labeling should not be used in lieu of adherence to GMP.** The agency urges manufacturers to take all steps necessary to eliminate cross contamination and to ensure the absence of the identified food."



Health Canada

- Health Canada supports the appropriate use of voluntary food allergen precautionary statements as a risk management tool, where warranted
  - All statements are subject to section 5(1) of the *Food and Drugs Act*
  - *Policy first set in 1994*
- Statements must be truthful, clear and non-ambiguous and CANNOT be a substitute for Good Manufacturing Practices
- With increasing use of precautionary statements Health Canada recommended the use of only one precautionary statement:
  - "May Contain [X]"

Health Canada
http://www.hc-sc.gc.ca/fn-an/label-etiquet/allergen/precaution_label-etiquette-eng.php

U.K. Food Standards Agency

- “PAL should only be used when a genuine risk of allergen cross-contact within the supply chain is identified that cannot be removed through careful risk management actions. This should be identified by a thorough risk assessment.”

UK Food Standards Agency
https://www.food.gov.uk/business-guidance/precautionary-allergen-labelling

PAL Statements Commonly Used: "May Contain…"

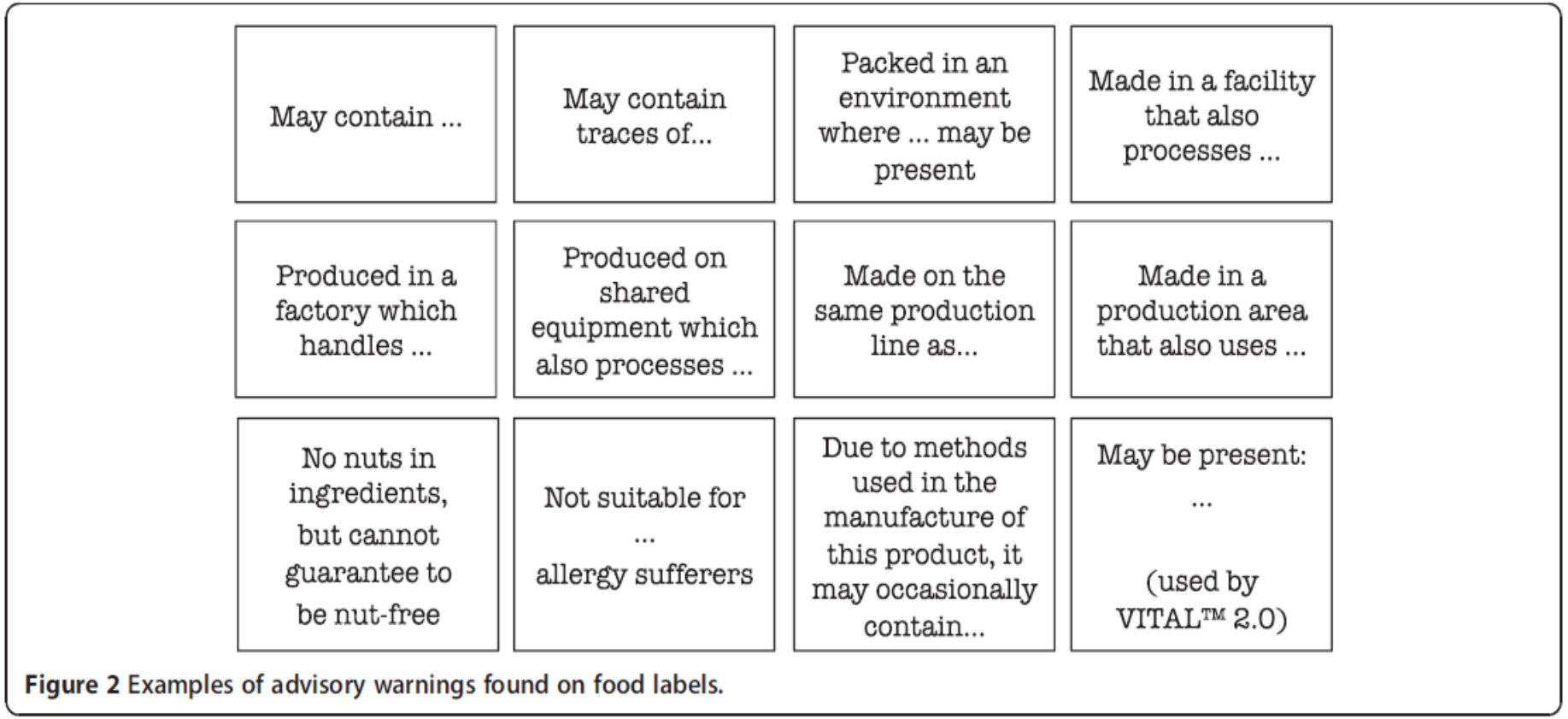
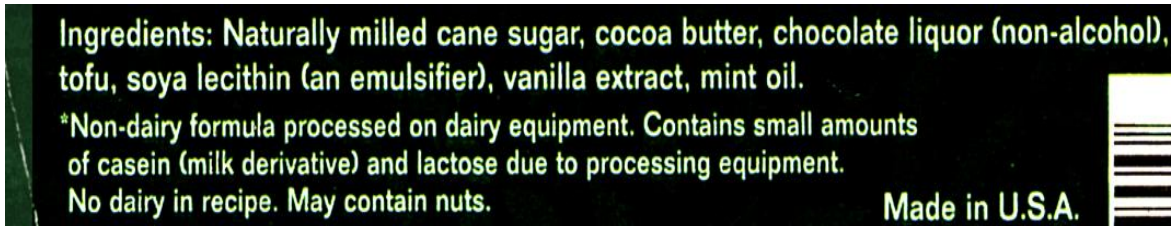
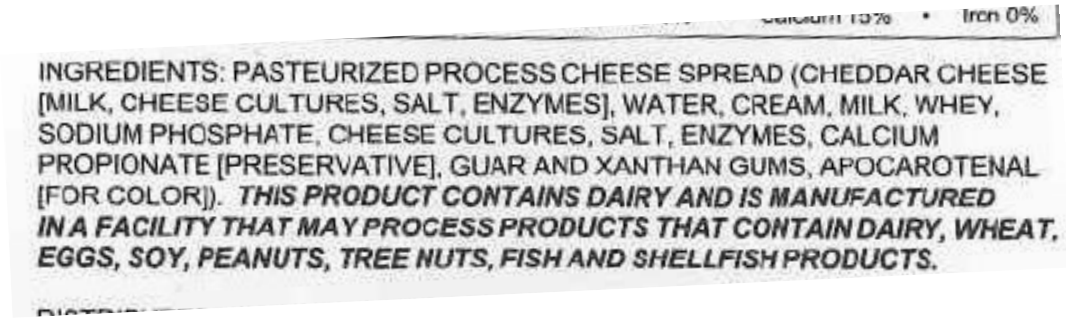


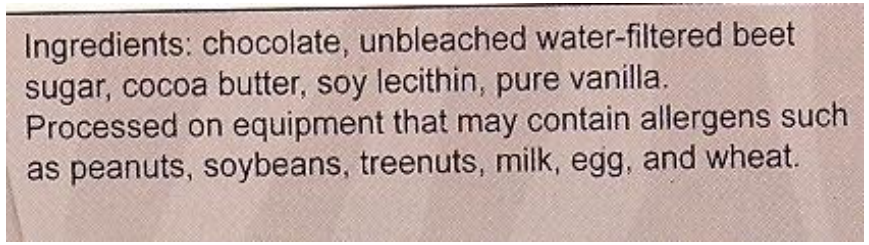
Figure 2 Examples of advisory warnings found on food labels.

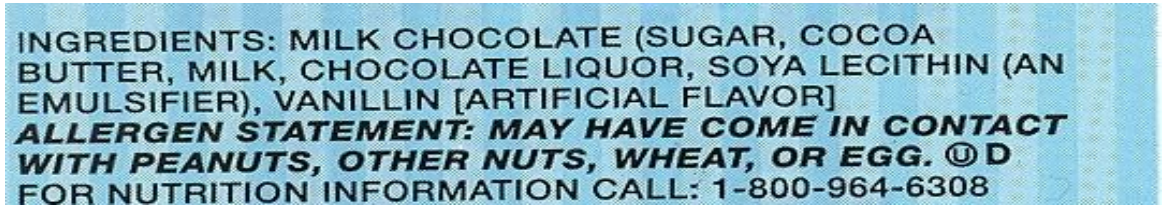
Allen, et. al., "Precautionary labelling of foods for allergen content: are we ready for a global framework?" *World Allergy Organization Journal*, 2014.

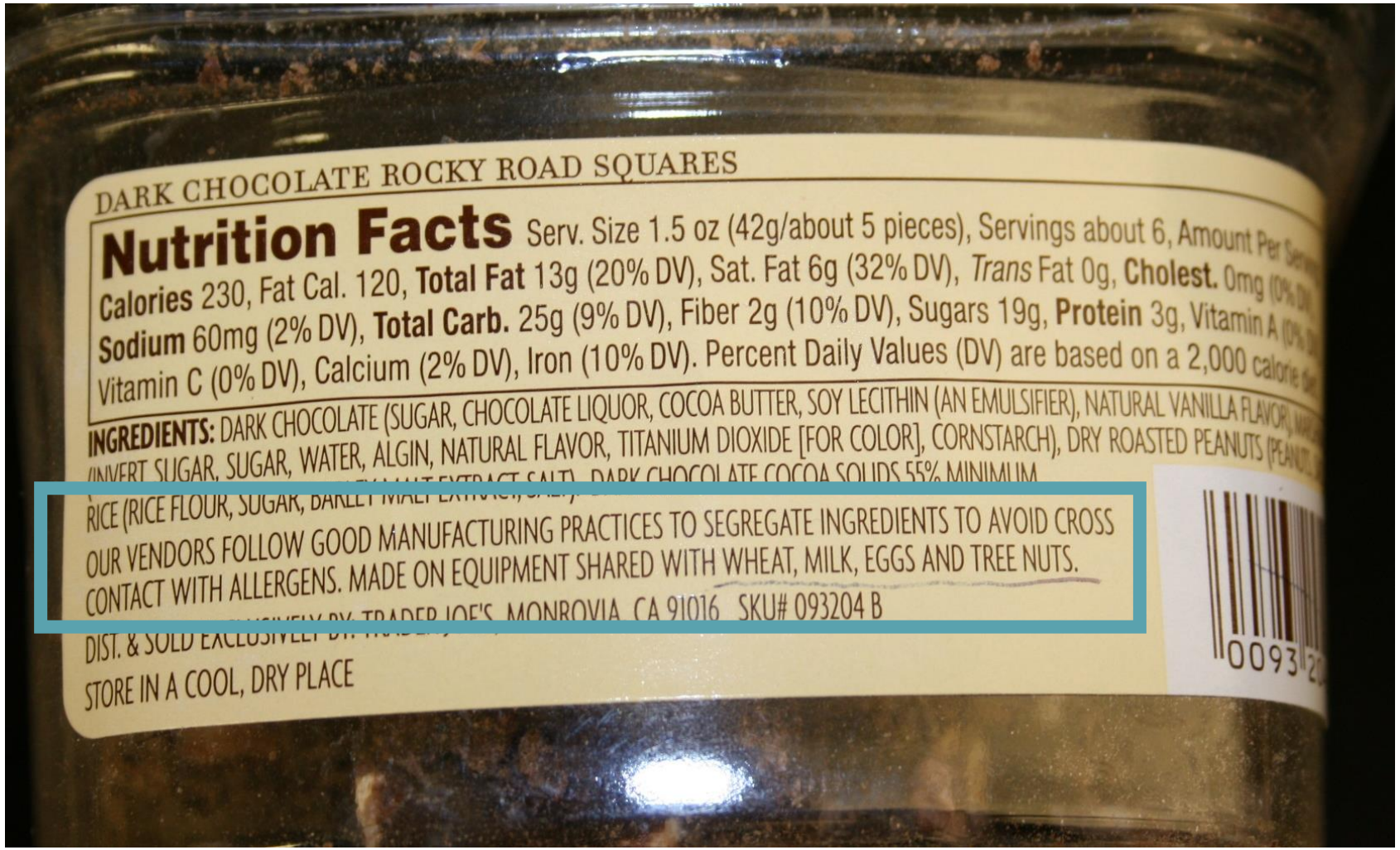
Precautionary Allergen Labeling



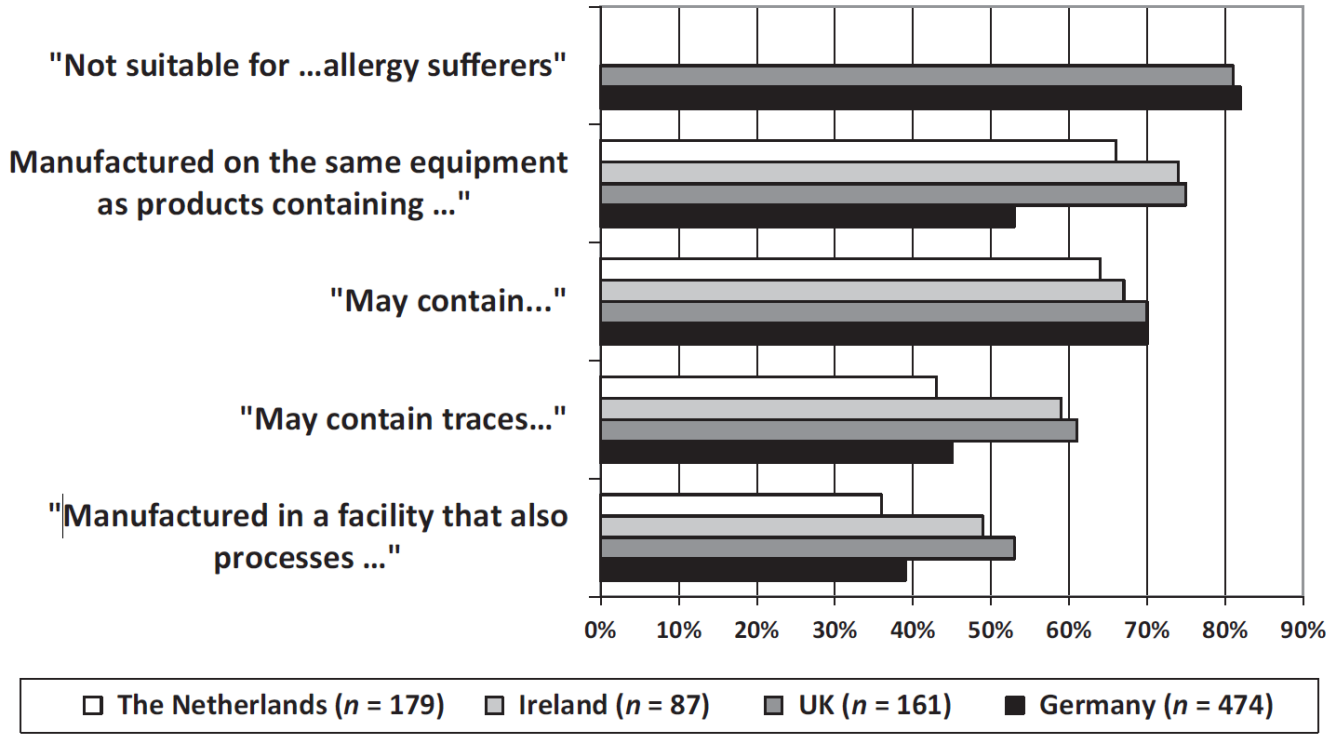







DARK CHOCOLATE ROCKY ROAD SQUARES
Nutrition Facts Serv. Size 1.5 oz (42g/about 5 pieces), Servings about 6, Amount Per
Calories 230, Fat Cal. 120, Total Fat 13g (20% DV), Sat. Fat 6g (32% DV), Trans Fat 0g, Cholest. 0mg
Sodium 60mg (2% DV), Total Carb. 25g (9% DV), Fiber 2g (10% DV), Sugars 19g, Protein 3g, Vitamin A
Vitamin C (0% DV), Calcium (2% DV), Iron (10% DV). Percent Daily Values (DV) are based on a 2,000 calorie
INGREDIENTS: DARK CHOCOLATE (SUGAR, CHOCOLATE LIQUOR, COCOA BUTTER, SOY LECITHIN (AN EMULSIFIER), NATURAL VANILLA FLAVOR,
(INVERT SUGAR, SUGAR, WATER, ALGIN, NATURAL FLAVOR, TITANIUM DIOXIDE [FOR COLOR], CORNSTARCH), DRY ROASTED PEANUTS (PEANUT
RICE (RICE FLOUR, SUGAR, BARLEY MALT EXTRACT, SALT). DARK CHOCOLATE COCOA SOLIDS 55% MINIMUM.
OUR VENDORS FOLLOW GOOD MANUFACTURING PRACTICES TO SEGREGATE INGREDIENTS TO AVOID CROSS
CONTACT WITH ALLERGENS. MADE ON EQUIPMENT SHARED WITH WHEAT, MILK, EGGS AND TREE NUTS.
DIST. & SOLD EXCLUSIVELY BY: TRADER JOE'S, MONROVIA, CA 91016 SKU# 093204 B
STORE IN A COOL, DRY PLACE
0093

Consumer Adherence to PAL



Percentage of food-allergic consumers that would "never" buy a product with precautionary allergen label according to the wording used

DunnGalvin et al. (2015). *Allergy.* 70:1039-1051

Moving Forward with PAL

Use of PAL should be based on scientifically sound reference doses to benchmark the risk

Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens

- Part 1: Review and validation of Codex priority allergen list through risk assessment
- Part 2: Review and establish threshold levels in foods of the priority allergens
- Part 3: Review and establish precautionary labelling in foods of the priority allergens
- Part 4: Review and establish exemptions for the food allergens

More info on Part 1 (full report), virtual meeting, 30 November – 11 December 2020, 28 January 2021, 8 February 2021
More info on Part 2 (summary and conclusions), virtual meeting, 15 March – 2 April 2021
More info on Part 3 (summary and conclusions)
More info on Part 4 – Recently completed (November 2022)

Can We Move Ahead?

- Communication is key!
- Stakeholders must agree upon Reference Doses
- Public health authorities must move first but consumers probably need to push them
  - Codex Alimentarius Commission and Codex Committee on Food Labelling could play important role
- Food industry must move beyond zero risk and towards risk-based approaches as outlined by VITAL, FAO/WHO, and others
- Analytical methods must continue to improve to support risk-based management practices

Thank You For Your Attention

Joe Baumert, Ph.D.

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