

Protecting the Consumer – Assessing Allergen Exposure Risks

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<http://www.cfsan.fda.gov/~dms/wh-alrgy.html>

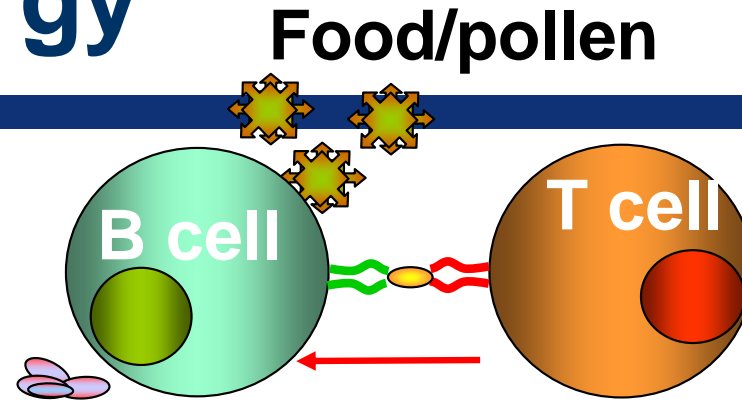
- FDA activities on food allergens

- Assessing allergenic risks
 - Food allergic reaction
 - Novel food allergens
 - Determination of safe doses (“thresholds”)

- Conclusions

- ❖ Food label enforcement and compliance
 - Implementation of US food allergen labeling law (FALCPA)
 - Inspections and enforcement of GMPs in food facilities
 - Recalls: 30-40% of all recalls due to undeclared allergens
- ❖ Review and validation of analytical methods for allergens
- ❖ Safety evaluations/ Risk assessments
 - Premarket – novel foods/ ingredients
 - Labeling exemptions – *thresholds
 - Postmarket surveillance – CAERS (CFSAN Adverse Event Reporting System) and other databases

Sensitization

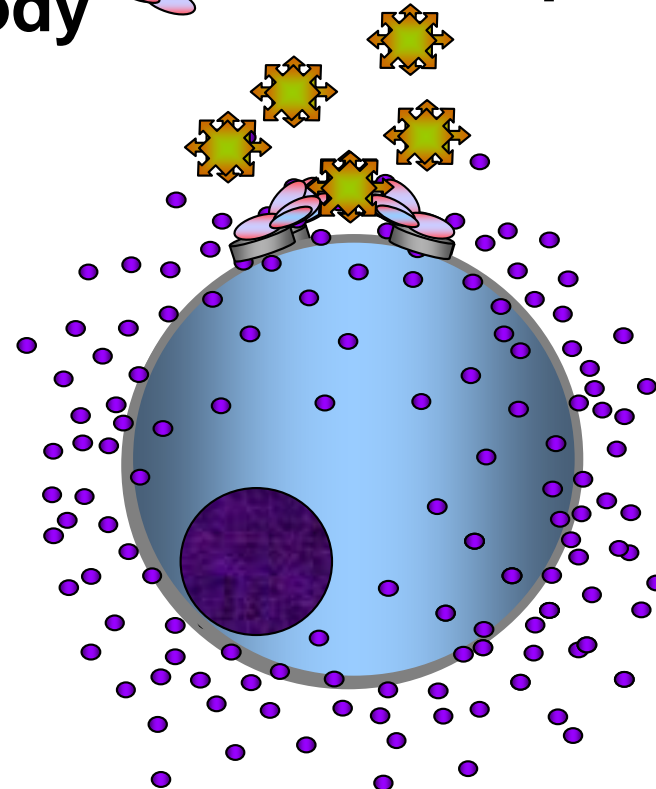


IgE
Antibody

Food protein

Anaphylaxis

Elicitation/ Reactivity



Mast cell/ Basophil

Skin- itchiness, flushing, hives, swelling, eczema
GI- nausea, vomiting, abdominal pain, diarrhea
Resp- tightness, runny nose, **wheezing**, **throat closing/swelling**
Vascular- dizziness, low blood pressure, heart irregularities, **shock**

- Complex immune reaction –sensitization and elicitation
 - Amplification mechanism

- Severity (i.e. anaphylaxis) is a moving target
 - Lack of predictive biological marker(s)

- One exposure \Rightarrow Potentially fatal
 - Consumer fears - \downarrow QOL

- One food \Rightarrow Multiple allergens
 - Heterogeneous population/ Potency varies

- Novel foods/ingredients – will they be or become allergens?
- Allergenic food ingredients – are there safe exposure levels, or thresholds?

➤ Weight of evidence approach:

- ✓ Source of protein
- ✓ Amino acid sequence homology
- ✓ Pepsin resistance
- ✓ Specific serum screening

Allergenicity safety assessment of foods derived from recombinant DNA plants (Codex Alimentarius, 2003)

➤ Types of allergen threshold:

- Individual
- Population
- Analytical
- **Regulatory**

US Allergen Labeling Law: Food Allergen Labeling & Consumer Protection Act (FALCPA)



- Tree nuts



- Milk



- Wheat



- Fish



- Peanut



- Soybean



- Egg



- Crustacea

❖ Ingredient exemptions from FALCPA requirement:

Contains no “allergenic protein”

Does not cause “allergic response that poses risk to human health”

➤ No thresholds currently established

❖ “Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food” (March, 2006)

(Journal of Food Protection, Vol. 71, No. 5, 2008, Pages 1043–1088)

- ✓ Analytical Methods - based
- ✓ Safety assessment - based
- ✓ Risk assessment - based
- ✓ Statutorily – derived (i.e. similar to levels in “highly refined oils”)

- Zero tolerance: Is it there or not?
- Used when validated tests are available
- Ex: Gluten-free (<20 ppm)

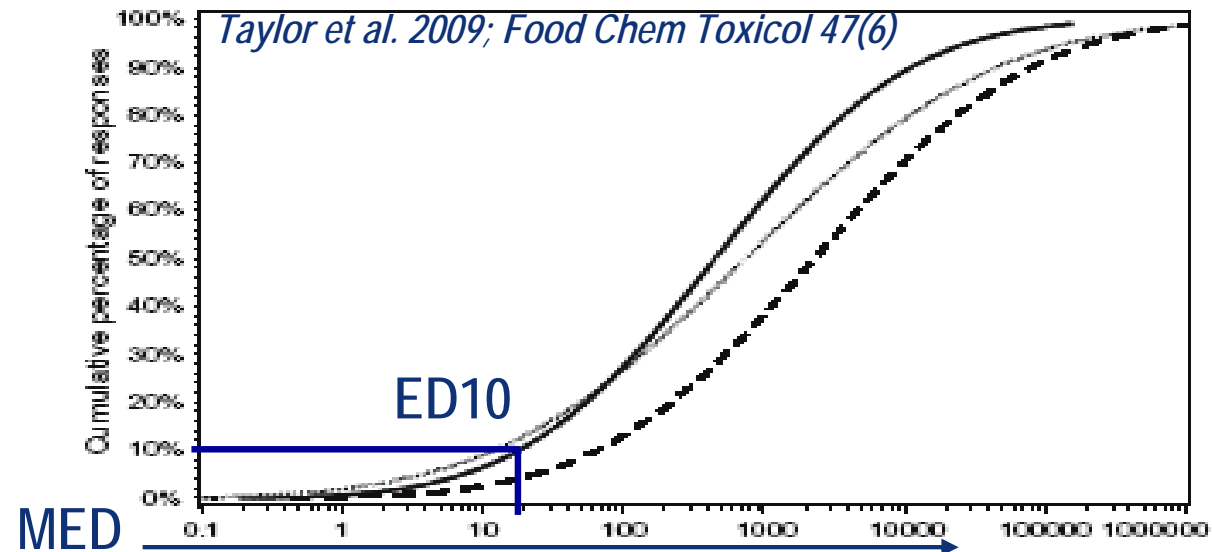
- Sensitive allergen food kits - $\mu\text{g/g}$ protein levels or lower

- Specificity concerns (e.g. food matrices)
- Kits not available for all allergens/ allergenic protein(s)
- End result not linked to biological response

- ❑ Traditional approach for establishing safe doses of food
- ❑ Safety ⇒ Acceptable risk
 - Determine LOAELs and NOAELs in study population and apply uncertainty factor(s)
- No validated food allergy models in animals
- ❖ Human food challenge data ⇒ minimal eliciting dose (MED) for individual or study population
- Gaps/ limitations of food challenge data:
 - Protocol bias – test materials, dosing regimen, etc.
 - Selection bias – exclusion of sensitive individuals?
 - Experimental MEDs = Real-life MEDs?

- ❑ Most scientifically rigorous approach
- ❑ Risk in relation to dose, exposure and severity

❖ Statistical modeling approaches
(Population MED dose-distributions)



- Size of population at risk (for severe outcome)?
 - Acceptable protective level: **ED10 vs ED5 vs ED1?**
- MED in relation to relevant severity endpoints
 - Dose-response distribution NOT severity curve

- Food allergens present unique challenges for safety/risk assessment
- Need for improved understanding of predictive biological endpoints for allergic sensitization, reaction and severity
- Better correlation needed between experimental MEDs and exposures to allergen levels in food products
- International discussions ongoing between various stakeholders for establishment of thresholds



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Elizabeth Harden
Rhonda Kane
John Kvenberg
Stefano Luccioli
Douglas Park
Richard Raybourne
Terry Troxell
Katherine Vierk

Other Acknowledgements

Curtis Barton
Hugh Dallas
Eric Garber

Michael Landa
Lori Pisciotta
Meredith Todd