Quantitative Food Allergen Risk Assessment

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Current Status of Regulatory Thresholds

- Public health authorities have not established regulatory action levels for any of the allergenic foods
  - ➢With the exception of Japan (10 µg/g protein limit for labeling)
- Labeling laws/regulations in many countries impose a zero threshold for source labeling of ingredients
- Food industry and regulators are acutely aware of allergens
  - ➢How much allergenic residue is too much OR how clean is clean enough??
    (Remember it is impossible to assure zero risk with anything in life)
    - With little or no guidance on action levels/thresholds, extensive use of precautionary labeling ("may contain") currently exists

The Zero Risk/Zero Threshold Paradigm

Exposure Dose is always greater than 0

- Zero risk/zero threshold approach is unsustainable operationally and statistically
- A transparent, science-based risk assessment and management process is needed moving forward

Development of Risk Assessment Approaches for Food Allergens

- 2007 workshop on risk assessment approaches – EuroPrevall, ILSI-EU and UK FSA
  1. Safety Assessment Approach
  2. Benchmark Dose (BMD) and Margin of Exposure (MoE) Approach
  3. Probabilistic Approach
- Workshop concluded that the BMD/MoE and probabilistic approaches had the most merit
  - Rely upon low-dose extrapolation from dose-distributions of clinical thresholds rather than a single point estimate
- 2006 FDA Threshold Working Group also concluded that a quantitative risk assessment approach to establishment of thresholds/actions levels provided the most robust information on population-based health hazard assessment

Emerging Consensus on Thresholds/Reference Doses

- VITAL 2.0 (Allergy Bureau of Australia and New Zealand) Reference Doses were underpinned by use of quantitative (probabilistic) risk assessment
- ILSI-Europe endorsed use of VITAL Reference Doses in 2014
- iFAAM utilized the same threshold data for development of Tier 1 and Tier 2 risk assessment models
- U.S. National Academies of Science, Engineering & Medicine endorsed the VITAL approach in their report of November, 2016
- Several countries have proposed the use of reference doses/action levels to evaluate the risk of unintended allergen presence

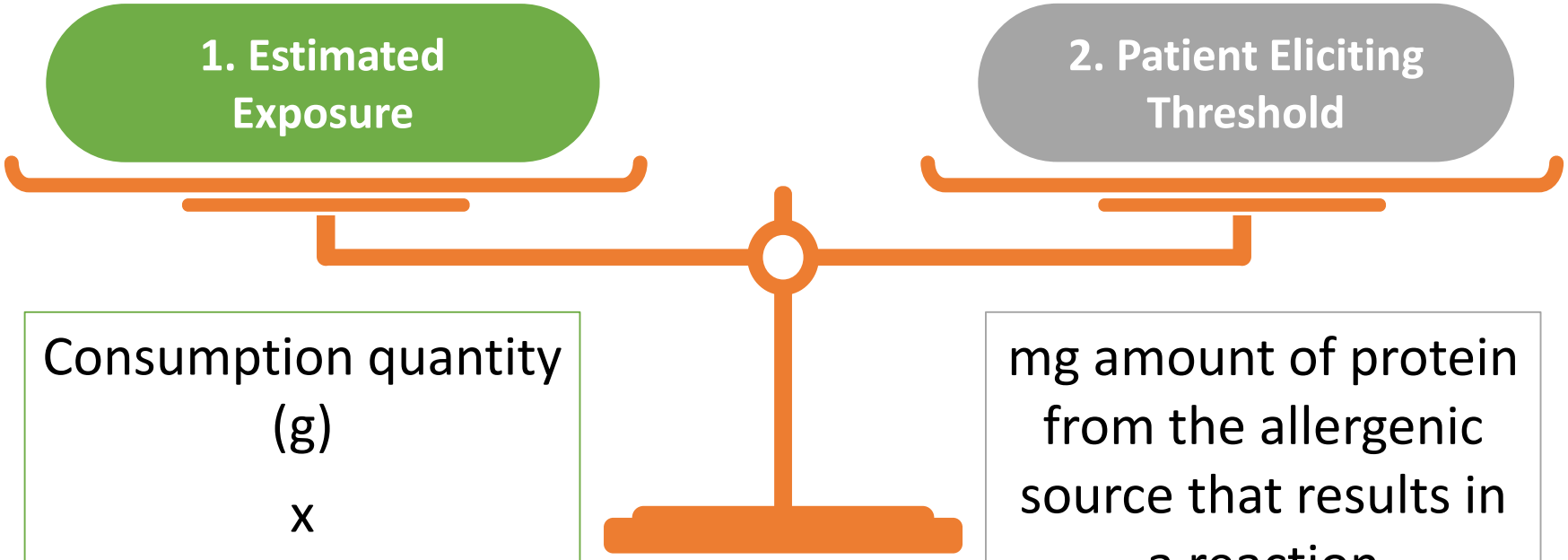
Risk Assessment

- A function of the exposure dose (mg of protein from the allergenic source) compared to the threshold dose (mg of protein from the allergenic source)

Exposure Dose < Threshold Dose = no predicted reaction
Exposure Dose ≥ Threshold Dose = a predicted reaction

- Risk assessments can evaluate the risk on an individual or population basis

Comparing Exposure Doses Versus Patient Eliciting Doses (Thresholds) to Estimate the Potential for a Reaction to Occur



Which Product Provides the Greater Exposure Risk?

- Product 1:

  10 ppm
  Peanut Protein
  (µg/g)

- Product 2:

  4.17 ppm
  Peanut Protein
  (µg/g)

- Product 3:

  0.84 ppm
  Peanut Protein
  (µg/g)

Which Product Provides the Greater Exposure Risk?

- Product 1:

10 ppm
Peanut Protein
(µg/g)

75th Percentile Consumption of Spices:
20g per eating occasion

- Product 2:

4.17 ppm
Peanut Protein
(µg/g)

75th Percentile Consumption of Biscuits:
48g per eating occasion

- Product 3:

0.84 ppm
Peanut Protein
(µg/g)

75th Percentile Consumption of a Composite Dish:
237g per eating occasion

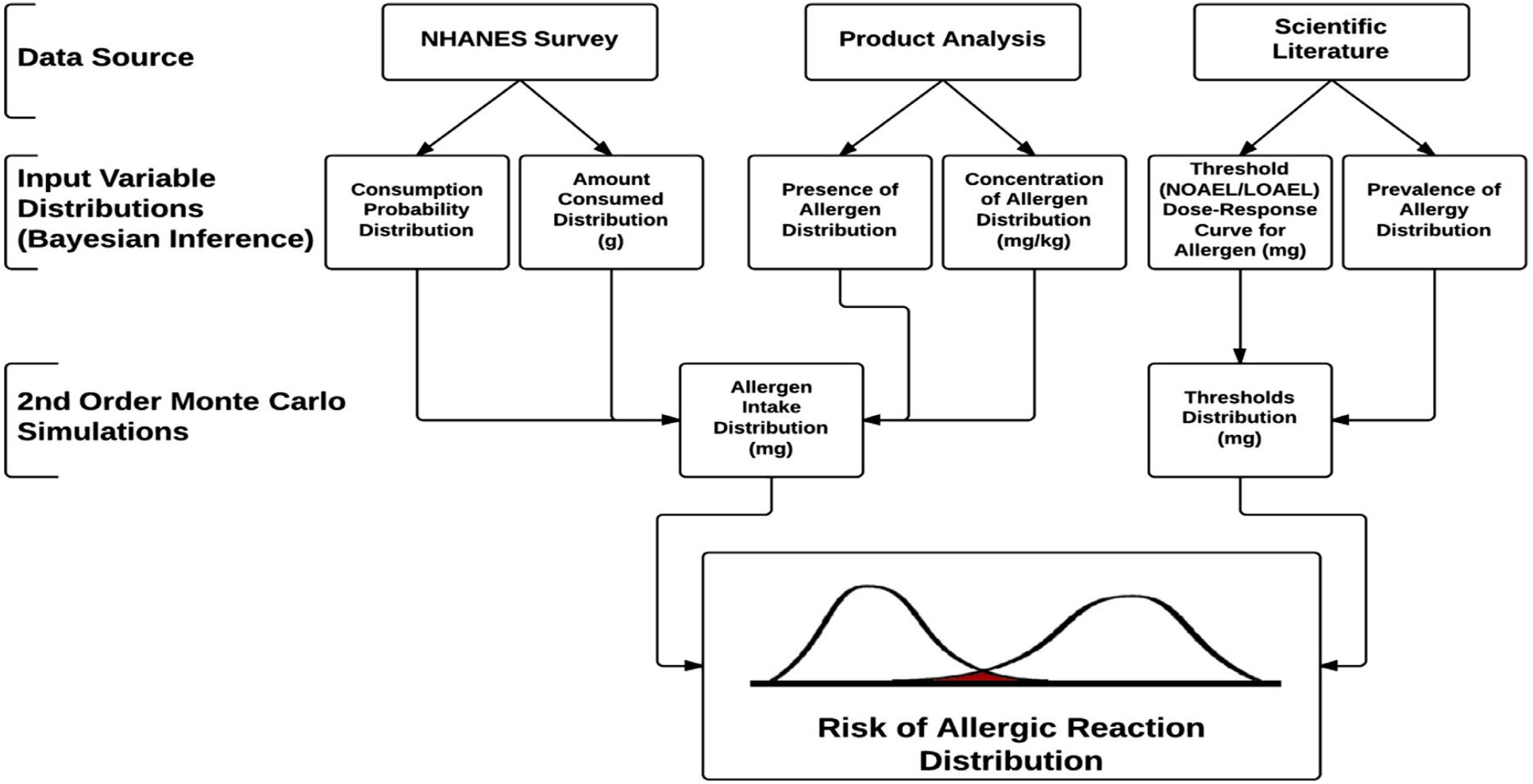
Birot et al. (2017). J. Food Composition & Analysis. 59:111-113

Which Product Provides the Greater Exposure Risk?

- Product 1: 20g pepper x 10 µg/g = 200 µg peanut protein (0.2 mg)
- Product 2: 48g biscuit x 4.17 µg/g = 200 µg peanut protein (0.2 mg)
- Product 3: 237g lasagna x 0.84 µg/g = 200 µg peanut protein (0.2 mg)

VITAL 2.0 Reference Dose = 0.2 mg peanut protein

Population-Based Quantitative (Probabilistic) Risk Assessment (QRA)



Key Components of a Risk Assessment: Primary Input Parameters:

- Understanding where UAP may occur
  - Understand your vulnerabilities
  - Tracking allergens
- Clinical threshold data from low-dose food challenges
  *Note: data from food-allergic individuals rather than extrapolation from animal models as in classical toxicological approaches
- Exposure Assessment
  - Food intake/consumption (g; quantity & frequency)
  - Level of allergen cross-contact (µg/g or ppm; & frequency)

Exposure Assessment

- Exposure assessment has 2 main components:
  - Food consumption (g)
  - Level of allergen cross-contact in the food
    (µg/g or ppm protein from the allergenic source)

- Accurate exposure assessment is an important component of the overall risk assessment
  - Must ensure that the consumption data is reflective of the entire population of consumers
  - Cross-contact data must be carefully calculated or analytically assessed

Exposure Assessment: Food Consumption Data

- Consumption data can be gleaned from dietary surveys or recommended portion sizes
  - 7 days dietary record, 2 days dietary record, or 24 hour recall
    - The primary goal is to gather nutritional data and data on consumption patterns – reflects the organisation of data

- Different levels of detail in dietary surveys
  - Intake per day or intake per meal/eating occasion
  - Food groups (e.g. Bread)
    - Wheat bread
      - Whole grain wheat bread, white bread
        - Brand name

Exposure Assessment: Food Consumption Data

- Must ensure that the consumption estimates are reflective of the entire population of consumers
  - portion size
  - mean (average) consumption amount
  - P75 of food consumption distribution
  - maximum consumption amount (very conservative)

Exposure Assessment: Contamination Data

- The concentration of allergenic food residue (or protein from the allergenic source) can be determined either by calculation or by quantitative analysis

- Quantitative analysis commonly conducted on ingredients or finished food products that may contain an unintended allergenic residue

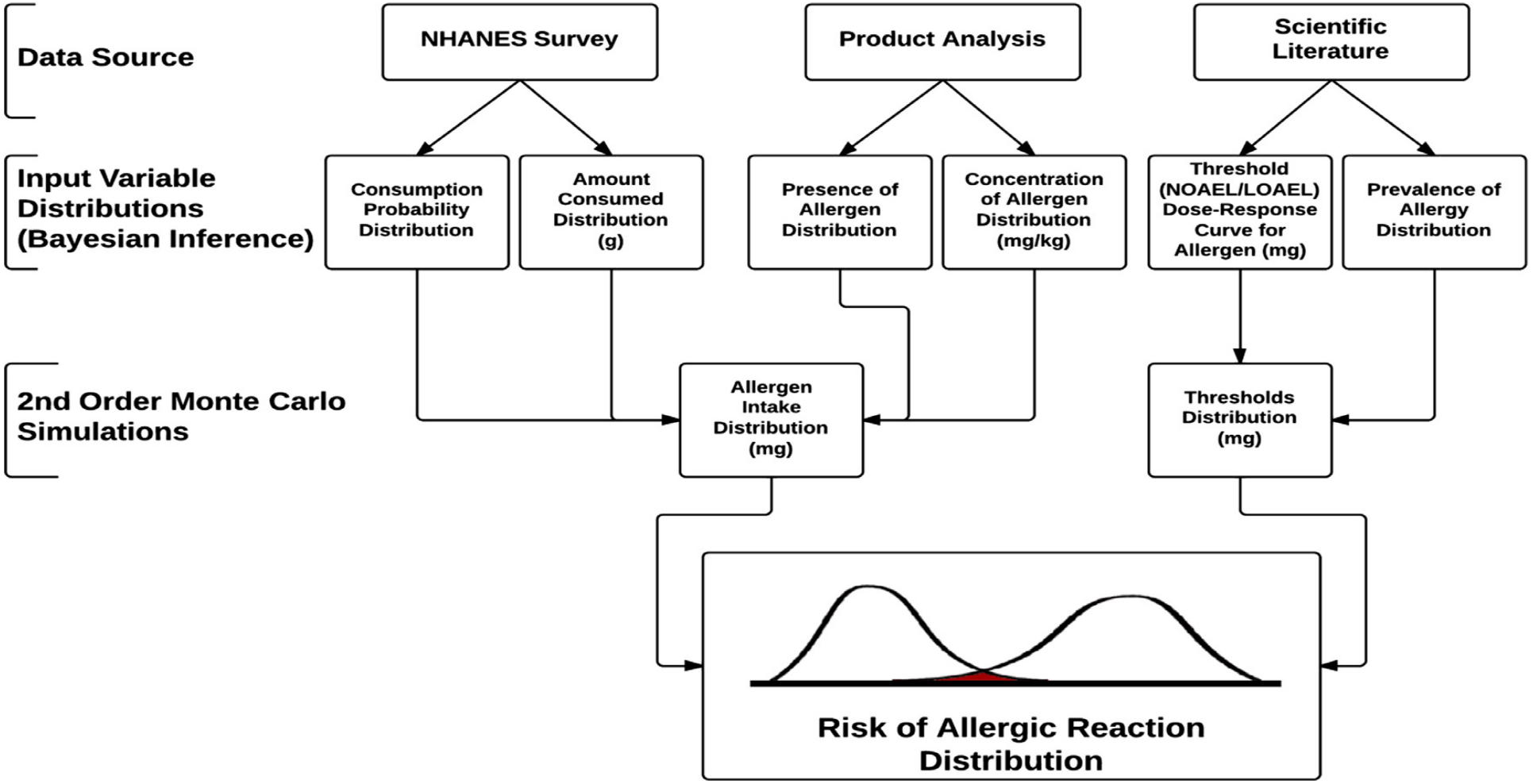
  - Ideally the analytical method used to determine the concentration of the unintended allergic residue would detect proteins from the allergenic source (rather than DNA or ATP)

  - There are important difference in target proteins that are detected and report units
  - (ppm WHAT???)
    - Commodity (e.g. NFDM)
    - Total protein from the allergenic source (e.g. total milk protein)
    - A certain protein fraction from the allergenic source (e.g. casein or whey)
    - A specific allergen (e.g. α-casein or β-lactoglobulin)

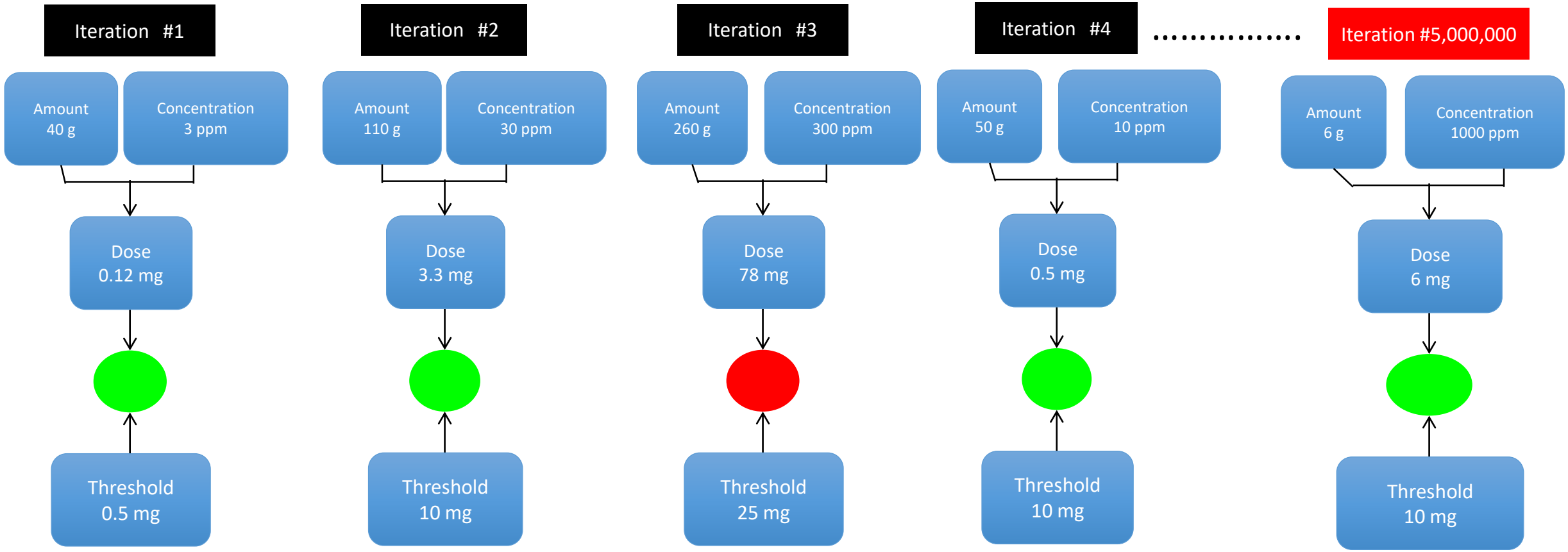
Expressions of Risk

- **User Risk**
  - Assumes everyone is allergic and consumes the product
- **Allergic Population Risk**
  - Assumes everyone is allergic but a specific percent (%) consume the product
- **Overall Population Risk**
  - Assumes a percent (%) of people are allergic and a specific percent (%) consume the product

Population-Based Quantitative (Probabilistic) Risk Assessment (QRA)



QRA Approach (Risk in the Population)



- Calculate risk of predicted allergic reaction during a single eating occasion (%)

Quantitative Risk Assessment Examples

Risk Assessment Example 1
RTE Popcorn

Calculation of Milk Protein in Ready-To-Eat Popcorn

Ingredient	% Milk protein in flavor	% Flavor in slurry	% Milk protein in slurry	Milk protein in slurry (ppm)	% Slurry on popcorn	% Protein in formula	ppm allergen in formula
Butter Flavor	0.000250%	5.0%	0.000012500%	0.13	16.00%	0.000002%	0.020000

Serving Size (g)	Allergen protein per serving (g)	Allergen protein per serving (mg)	VITAL 2.0 Reference Dose for milk (mg)	Amount of product achieving VITAL 2.0 Reference Dose (g)
31	0.000001	0.00062	0.1	5,000.00
76	0.000002	0.001526		

Cases	Bags per Case	Bags affected	Servings per bag	Servings affected
3,500	12	42,000	2.5	105,000

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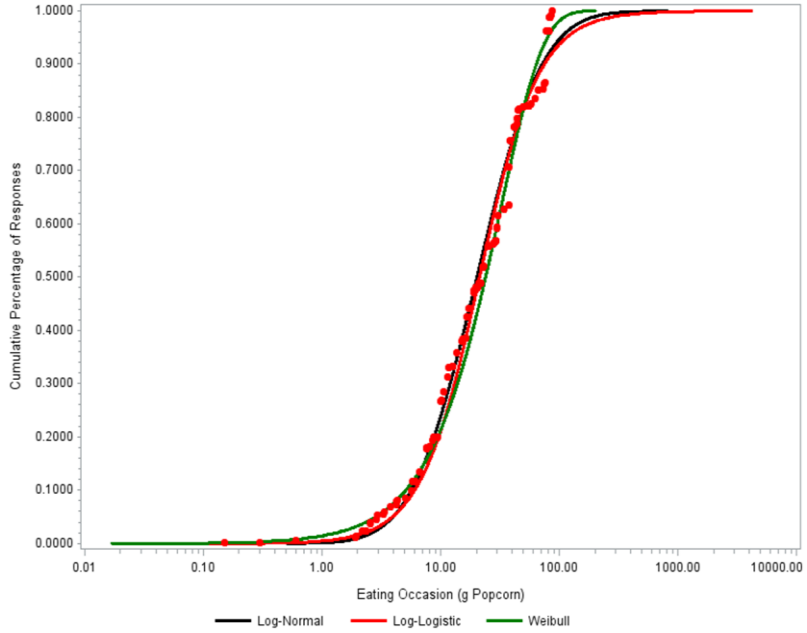
Quantitative Risk Assessment Consumption Analysis

Popcorn Consumption Estimates Using the 2003-2010 NHANES Dietary Surveys

Food Product Category	*# of Individuals Who Reported Consuming the Product Category*	*Estimated % of U.S. Population that Consume the Product Category*	*Consumption Estimates Per Eating Occasion (g)*			
			Average	90th Percentile	95th Percentile	99th Percentile
Ready-To-Eat Popcorn	500	1.5%	30	77	83	85



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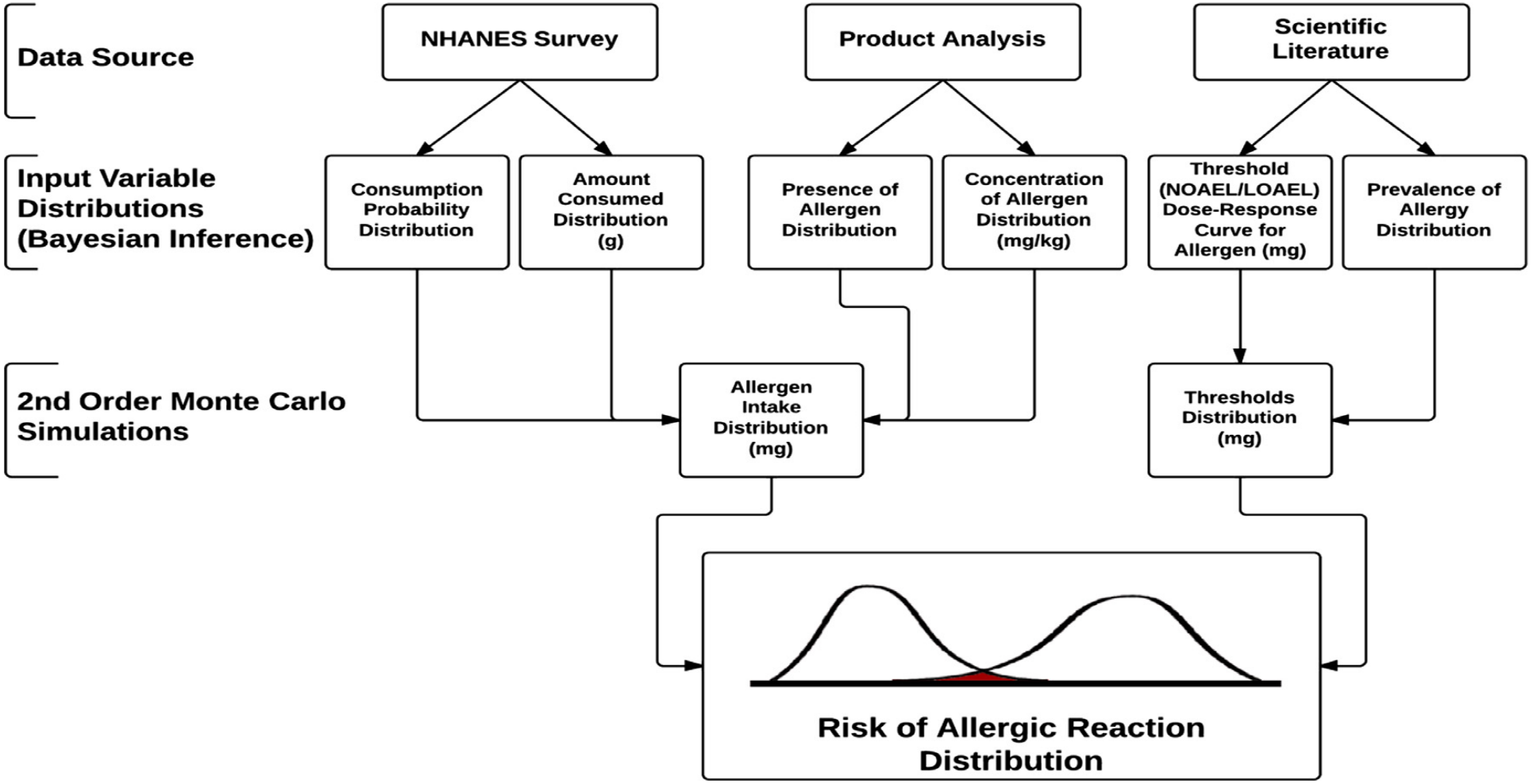
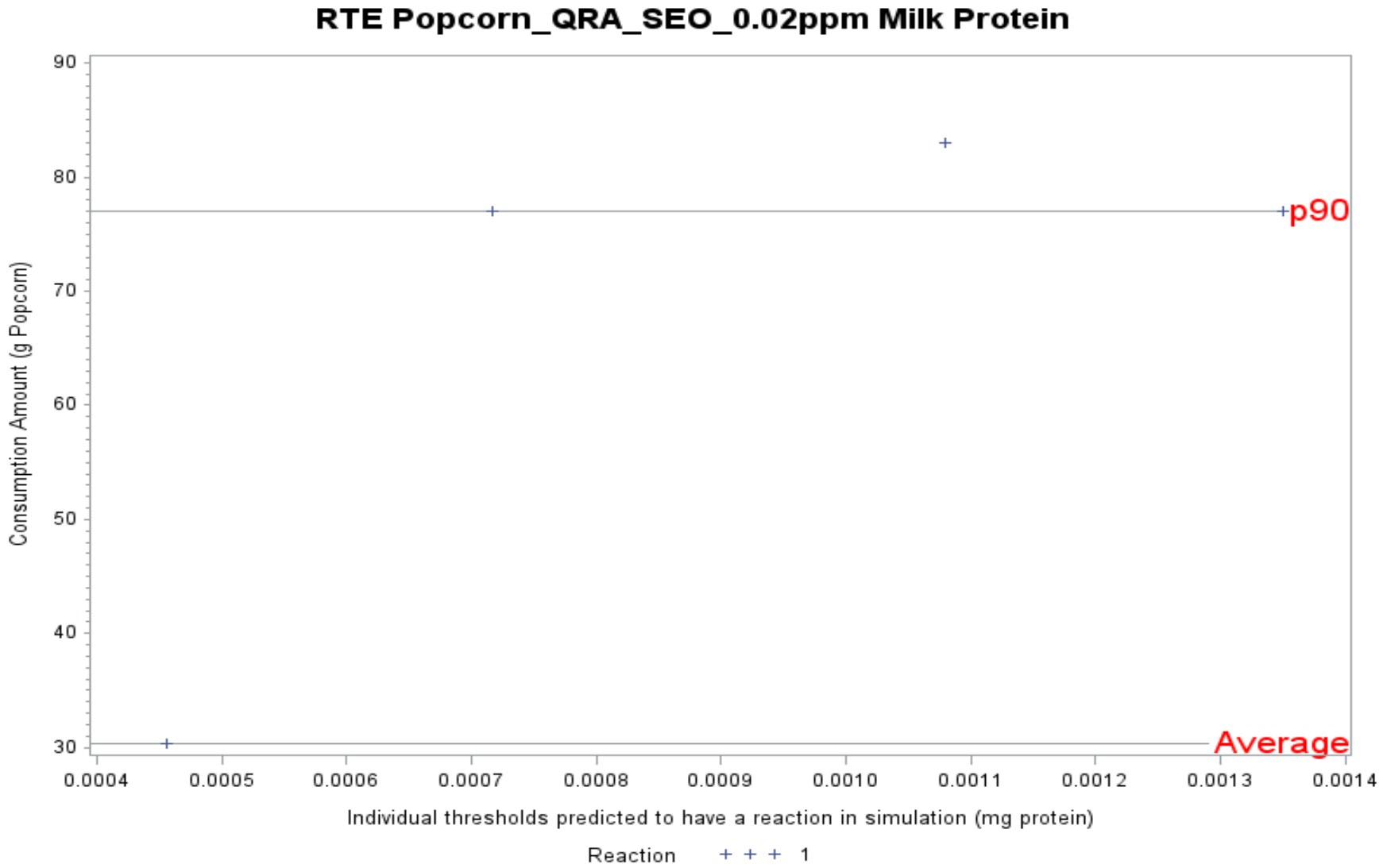


Quantitative Risk Assessment Results



Quantitative Risk Assessment of the RTE Popcorn that Contains 0.02 ppm Milk Protein Residue.

Product	Allergen Analyzed in Risk Assessment	ppm in Protein in Finished Product	User Risk	Milk Allergic Population	Overall Population
RTE Popcorn	Milk	ppm Milk Protein	# of Reactions per # of Milk Allergic Users (%)	# of Reactions per # of Milk Allergic Consumers (%)	# of Reactions per # of Individuals in the U.S. (%)
		0.02 ppm	8.0 per 10 million (0.00008%)	1.3 per 100 million (0.0000013%)	1.3 per 10 billion (0.000000013%)

***User Risk: assumes that all individuals consuming RTE popcorn are milk-allergic which is a very conservative assumption and likely overestimates the true risk of allergic reaction occurring upon consumption of these products.**

****Milk Allergic Population: assumes that 1.5% of the milk-allergic individuals consume RTE popcorn on any given eating occasion.**

*****Overall Population: assumes that 1.0% of the population is milk-allergic and 1.5% consume RTE popcorn on any given eating occasion.**

The most sensitive 1% of the milk allergic population would need to consume 5 kg of popcorn during a single eating occasion to reach their threshold dose. This is 58x the consumption of the 99% reported consumption of the 99 percentile consumers

Risk Assessment Example 2
Cheese Cracker

Risk Assessment Example 2
Cheese Cracker

Calculation of Peanut Protein in Cheese Cracker

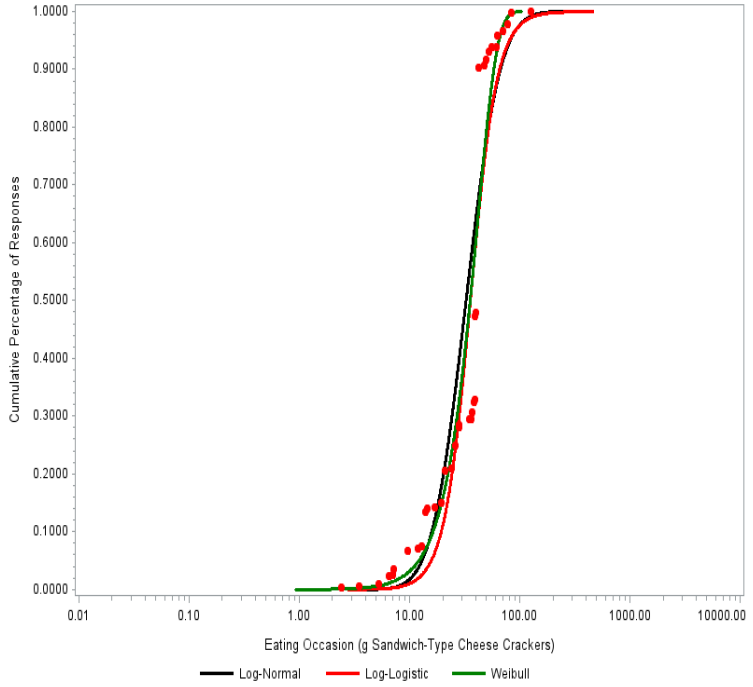
ppm Peanut Protein in Cracker: 5 ppm peanut protein

Serving Size (g)	Allergen protein per serving (g)	Allergen protein per serving (mg)	VITAL Reference Dose for protein (mg)	Amount of product achieving VITAL 2.0 Reference Dose (g)
40	0.0002	0.2	0.2	40
80	0.0004	0.4		

Quantitative Risk Assessment Consumption Analysis

Cheese Cracker Consumption Estimates Using the 2003-2010 NHANES Dietary Surveys

Food Product Category	*# of Individuals Who Reported Consuming the Product Category*	*Estimated % of U.S. Population that Consume the Product Category*	*Consumption Estimates Per Eating Occasion (g)*			
			Average	90th Percentile	95th Percentile	99th Percentile
Cheese Cracker	189	0.57%	37	42	63	84



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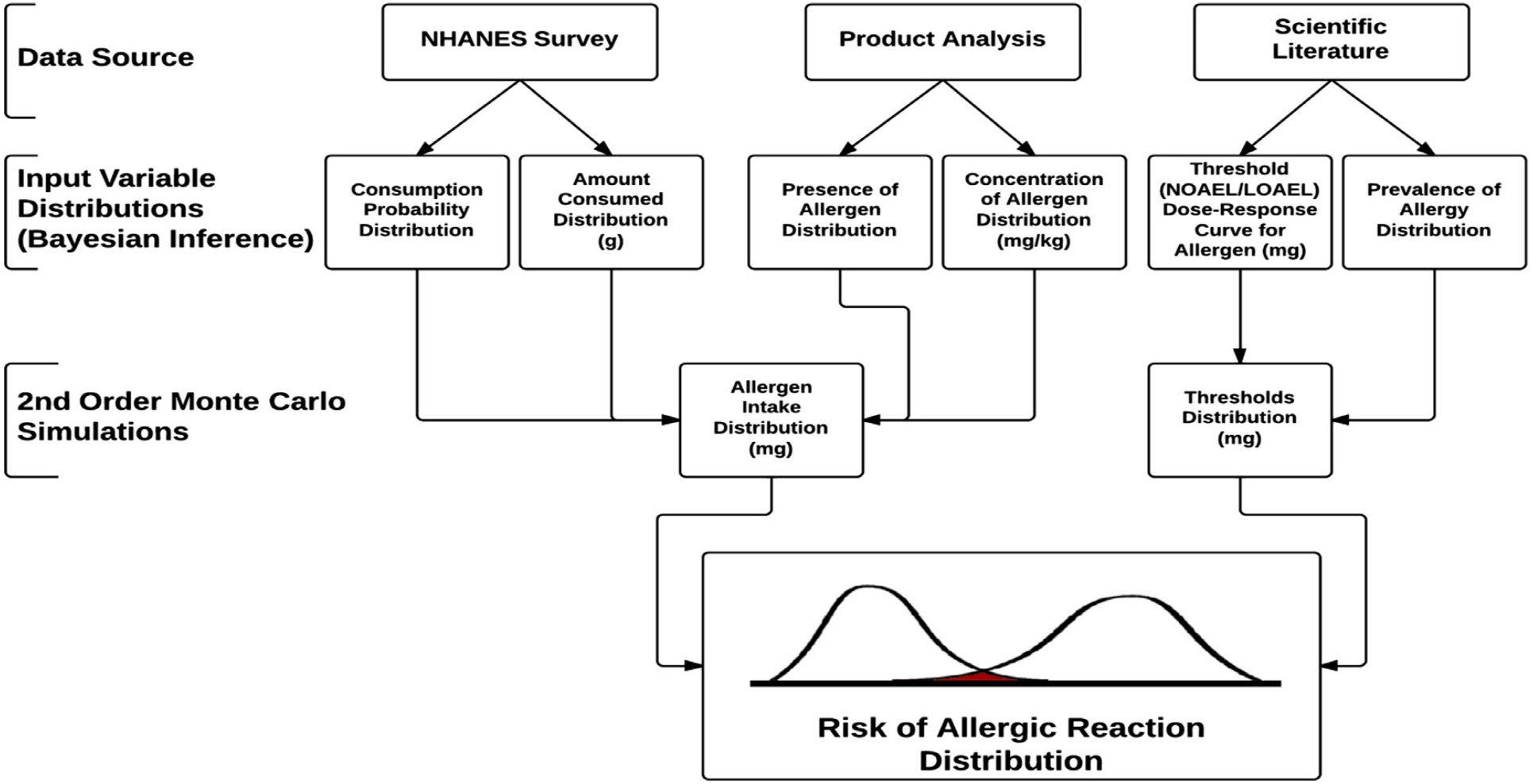
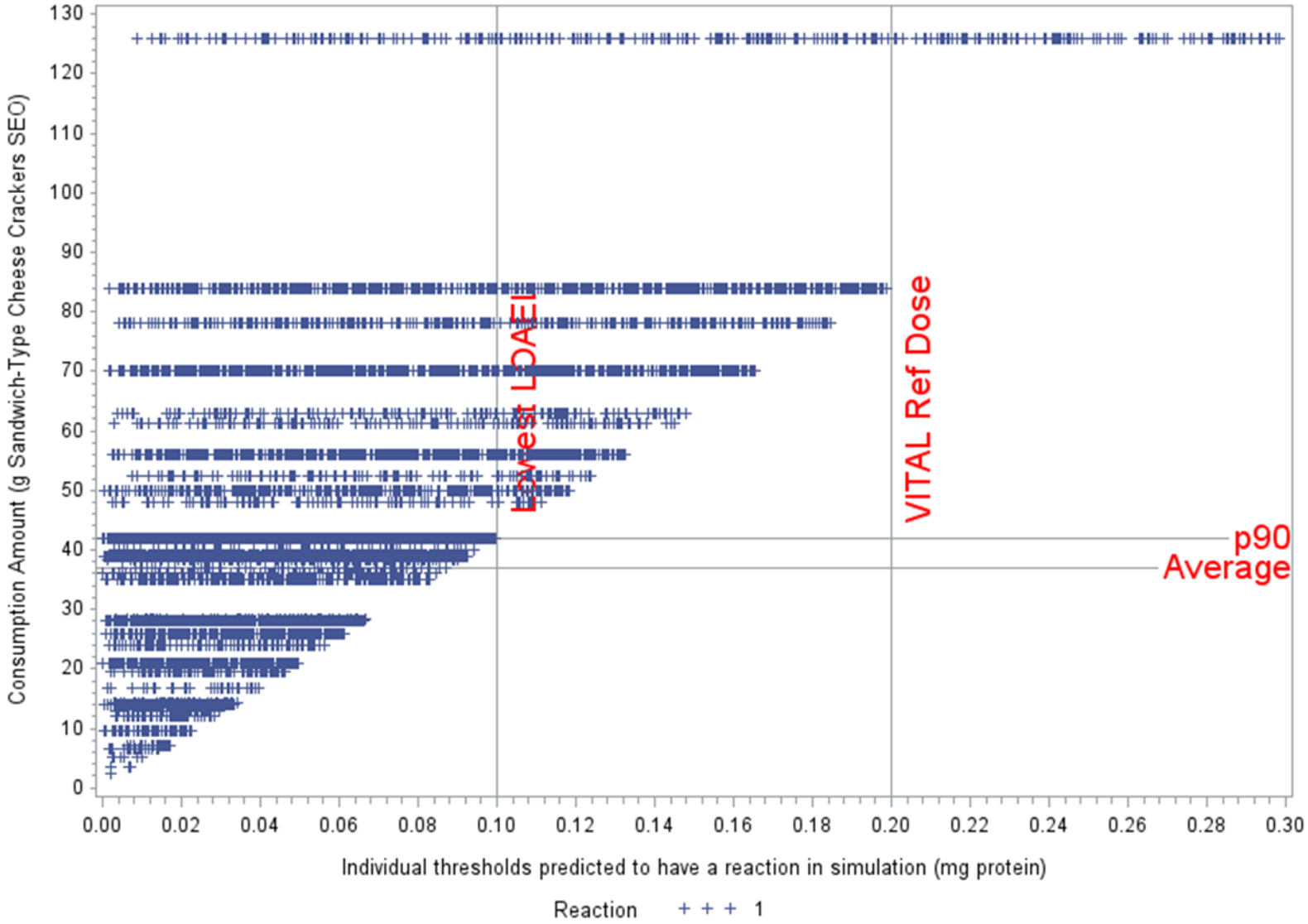


Quantitative Risk Assessment Results



Quantitative Risk Assessment of the Cheese Cracker that Contains 5 ppm Peanut Protein Residue.

Product	Allergen Analyzed in Risk Assessment	ppm in Protein in Finished Product	User Risk	Peanut Allergic Population	Overall Population
Cheese Cracker	Peanut	ppm Peanut Protein	# of Reactions per # of Peanut Allergic Users (%)	# of Reactions per # of Peanut Allergic Consumers (%)	# of Reactions per # of Individuals in the U.S. (%)
		5 ppm	4 per 1000 (0.4%)	3.2 per 100,000 (0.0032%)	3.2 per 10 million (0.000032%)

***User Risk: assumes that all individuals consuming cheese crackers are peanut-allergic which is a very conservative assumption and likely overestimates the true risk of allergic reaction occurring upon consumption of these products.**

****Peanut Allergic Population: assumes that 1% of the peanut-allergic individuals consume cheese crackers on any given eating occasion.**

*****Overall Population: assumes that 1.0% of the population is peanut-allergic and 0.57% consume cheese crackers on any given eating occasion.**

Conclusions

- QRA provides an in-depth analysis not available with previous methods
  - Integrates variability and uncertainty of inputs into the risk assessment model for a more realistic estimate of potential risk
- QRA is flexible and applicable to a wide range of scenarios
  - Can also be used to inform deterministic/safety assessment (Tier 1) approaches
- QRA enables risk assessors to make an informed decision based on the true risk of a product

Thank You For Your Attention

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