Fri från… – men inte noll.

Märkning utifrån kvantitativ riskvärdering.

Presentation 7 dec 2017

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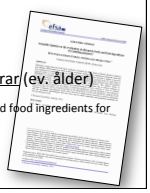
- Bakgrund
- Riskbedömning, referensdos, portionsstorlek och åtgärdsnivå (action level)
- Hur gör andra i vår omvärld?
  - VITAL i Australien
  - FARRP i USA
- Fri från… eller Kan innehålla spår av...?

Vad behövs för en bra risk-bedömning?

- Information om vilken mängd allergen allergiska individer reagerar på.
  - VITAL-referensdoser, InformAll databas, Phadia/Thermo Scientific databas, EFSAs "Scientific Opinion on the evaluation of allergenic foods and food ingredients for labelling purposes"
- Information om vilken mängd produkt (portionsstorlek) allergiska individer konsumerar.
  - Producentens kunskap
  - TNO-modeller
- Information om antal allergiska individer som reagerar (ev. ålder)
  - EFSAs "Scientific Opinion on the evaluation of allergenic foods and food ingredients for labelling purposes"



Hur vi kommer fram till en åtgärdsnivå

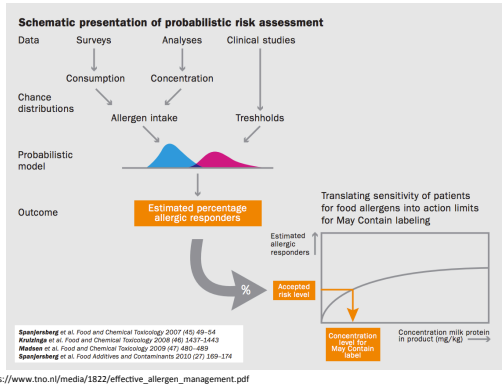
- Först gör man kliniska försök för att få reda på vid vilken mängd allergen 1 % (3%) av allergiker får en mild reaktion
- Då får man en tabell med referensdoser (där pågår forskning hela tiden, vi har nu osäkerhet kring t ex fisk, selleri och räkor)
- Sedan bestämmer man sig för en "portion", en sk referensmängd, alltså hur mycket ens kundgrupp kan tänkas äta vid varje måltid
- Och så använder man den berömda formeln:

$$\frac{\text{REFERENSDOS (mg allergent protein)}}{\text{REFERENSMÄNGD (kg produkt)}} = \text{ÅTGÄRDSNIVÅ (ppm)}$$

Table with Reference doses (Taylor et al 2014*)

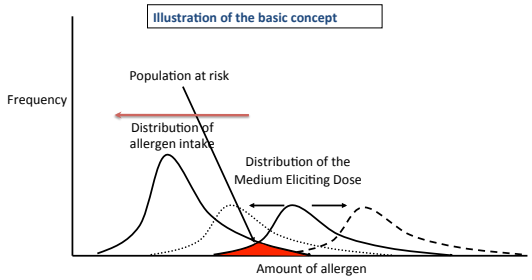
Allergen	Reference Dose (mg total protein of allergenic food)
Peanut	0.2
Milk	0.1
Egg	0.03
Hazelnut	0.1
Soya	1.0
Wheat	1.0
Mustard	0.05
Lupin	4.0
Sesame	0.2
Shrimp	10
Cashew	2 mg (provisional)
Celery	No sufficient data
Fish	No sufficient data (provisional in VITAL online))
Other treenuts	No sufficient data (provisional in VITAL online)

Taylor et al 2014 Establishment of Reference Doses for residues of allergenic foods: Report of the VITAL Expert Panel in Food and Chemical Toxicology 63 (2014) 9–17.



https://www.tno.nl/media/1822/effective_allergen_management.pdf

Vad händer då i slutändan…?

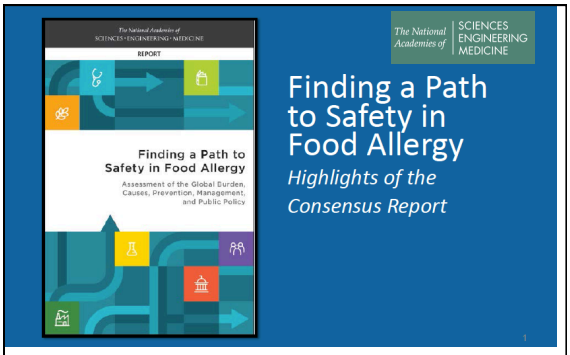


Att gå från ”Kan innehålla spår av” till ”Fri från”

- Vi har frågat efter tröskelvärden för allergener – Det får vi aldrig
- Men i stället får vi referensdoser (VITAL m fl) = 1-3 % risk för en mild reaktion
- Dessa kombinerar vi med portionsstorlekar (reference amounts) för att få en ’action level’ för varje produkt
- Detta är grunden för en ansvarsfull ”Kan innehålla spår av”-märkning
- Vi kan aldrig räkna med ”0”-nivå, alltså inte en enda molekyl

Forts. Att gå från ”Kan innehålla spår av” till ”Fri från”

- Mellan vår action level och nollnivå – finns det utrymme för en märkning som förenklar för allergiker, och samtidigt är pålitlig?
- En ”Fri från”-märkning (alternativt < x mg/kg) som kan accepteras av alla led i kedjan, utifrån gemensamma definitioner?
- Vad gör en person med risk för mycket allvarliga reaktioner vid små doser –
- När vi tänkte över detta – kom det brev från Amerika…



publ. maj 2017 https://www.nap.edu/read/23658/chapter/11#369

https://www.nap.edu/resource/23658/Slideset-highlights-food-allergy.pdf

Why a Study on Food Allergies?

Knowledge gaps in several areas:

- ***Prevalence*: what is the prevalence of food allergy and is it rising?**
- ***Diagnosis*: is there a best test for diagnosis?**
- ***Prevention*: what are the risk factors for food allergies?**
- ***Management*: what is the role of healthcare providers? Food industry? Individuals? Others?**

Statement of Task

The committee will examine critical issues related to food allergy…..and

- **bring together leading investigators from relevant fields, clinicians, and parents; and to develop a framework for future work; and**
- **recommend actions to be implemented by both government and non-government agencies**

EDUCATION AND TRAINING

FOR FOOD INDUSTRY PERSONNEL

The committee recommends that

- food industry leaders provide the necessary resources for integrating food allergy training into existing general food safety and customer service training for employees at all levels and stages in the food industry

IMPROVE POLICIES AND PREVENTION OF SEVERE REACTIONS

IMPROVE POLICIES AND PREVENTION OF SEVERE REACTIONS

POLICIES REGARDING LABELING OF PACKAGED FOODS

The committee recommends that

- the Codex Alimentarius Commission and public health authorities in individual countries decide on a periodic basis about which allergenic foods should be included in their priority lists based on scientific and clinical evidence of regional prevalence and severity of food allergies as well as allergen potency

IMPROVE POLICIES AND PREVENTION OF SEVERE REACTIONS

POLICIES REGARDING LABELING OF PACKAGED FOODS

The committee recommends that:

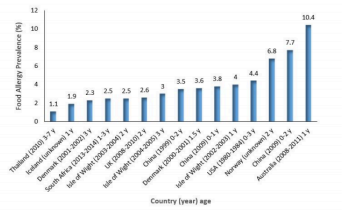
- the Food and Drug Administration makes its decisions about labeling exemptions for ingredients derived from priority allergenic sources based on a quantitative risk assessment framework

IMPROVE POLICIES AND PREVENTION OF SEVERE REACTIONS

POLICIES REGARDING LABELING OF PACKAGED FOODS

- …the food manufacturing industry, the Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA) work cooperatively to replace the Precautionary Allergen Labeling system for low-level allergen contaminants with a new risk-based labeling approach, such as the VITAL program used in Australia and New Zealand

Prevalence in Different Countries



New Knowledge on Allergen Thresholds

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Food Allergy Research & Resource Program
University of Nebraska

2017 ILSI Annual Meeting
San Diego CA
January 23, 2017

http://ilsina.org/wp-content/uploads/sites/6/2017/02/Steve-Taylor.pdf

Current Situation

- Clinical oral challenges have clearly documented that each food-allergic individual has a threshold dose below which they will not experience an adverse reaction – HUMAN DATA
- The distribution of individual threshold doses can be used to establish population thresholds that would estimate the percentage of allergic consumers who would be predicted to react to any specific dose of the allergenic food
- The science is solid

Exquisite Sensitivity of Some Food-Allergic Individuals

- Trace amounts of the offending food will trigger reactions
- BUT IT IS NOT ZERO!!
- SEVERE RXNS DO NOT OCCUR AT LOW DOSES!

Current Situation

- Public health authorities have not established regulatory action levels or thresholds for any of the allergenic foods
- Labeling laws/regulations in many countries impose a de facto zero threshold for labeling
- **The zero threshold approach is disadvantageous to all stakeholders!!**

Implications of Zero

- Food-allergic consumers:
  - have a diminished quality of life due to limited food choices
  - are faced with a proliferation of PAL
  - live with a constant fear of experiencing a severe, life-threatening reaction
  - attempt to make personal risk decisions based on interpretation of PAL statements
  - many choose to consumer some PAL products

Implications of Zero

- Public health authorities:
  - Spend time chasing zero and thus may miss situations that present biggest risk
  - Fail to recognize that many actions have no public health benefit
  - End up with a Reportable Food Registry where undeclared allergens are the #1 reason for recalls but questionable risks
  - Foster or even encourage use of PAL

Implications of Zero

- Physicians/Allergists:
  - must deal with scared and frustrated patients – if you treat all of them the same, then they all believe that they are the most sensitive
  - have no simple approach to identifying the most sensitive patients or way to give them differential advice even if they could
  - many advise at least some patients to ignore PAL

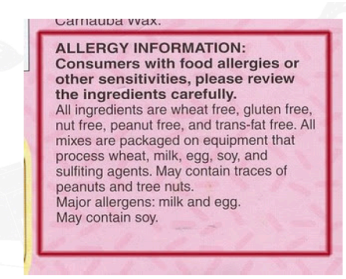
Implications of Zero

- Food industry:
  - cannot achieve nor prove zero
  - cannot trust that any detectable level of allergen by any method would not be considered as a regulatory violation
  - reluctant to set corporate threshold levels without regulatory guidance
  - makes heavy use of PAL statements
  - limited ability to select best analytical methods

Implications of Zero

- Analytical test methods industry:
  - incentive exists to continue to pursue ever more sensitive methods; "zero" keeps getting less
  - no need to reach agreement on harmonization of test methods so lack of standardization on reporting units, standards, validation criteria, etc.
  - test methods have unfortunately become a major obstacle to threshold adoption

Vad ser den allergiska konsumenten?



Precautionary Labeling for Allergenic Foods (PAL)

- PAL is quite candidly a mess
- PAL does not serve allergic consumers well
- Because PAL is not truly risk-based
- PAL is confusing to consumers
- PAL serves the food industry better than consumers because it allows them to identify potential risks without really having to assess the risk
- PAL serves public health authorities very well because they can avoid difficult risk management decisions

Finns det ett bättre alternativ?

POLICIES REGARDING LABELING OF PACKAGED FOODS

A Risk-Based Labeling Approach

- FDA and USDA should establish Reference Doses (thresholds) for allergenic foods, where possible
- Sufficient clinical data on thresholds exist for peanut, milk, egg, certain tree nuts (hazelnut, cashew), soybean, wheat, fish and crustacean shellfish (shrimp) to establish Reference Doses
- With Reference Doses, foods should have PAL only when exposure would result in doses above the Reference Dose level
- FDA should restrict allowable PAL statements to one phrase
- FDA and USDA should educate consumers and health care providers on the meaning of PAL statements

Food Allergen Thresholds

- Clinical data exist on individual threshold doses for various allergenic foods from oral challenges conducted for diagnosis, threshold trials, and immunotherapy trials – published and unpublished
- FARRP and TNO collaborate to develop a continuously updated dataset of individual thresholds
- Dose-distribution modeling can be performed to determine population thresholds which could be used as basis for Reference Doses

VITAL Dataset Progress

Assembled and evaluated clinical data on all possible priority allergenic foods

- Peanut
- Milk
- Egg
- Hazelnut

- Soybean
- Wheat
- Cashew
- Mustard
- Lupine
- Sesame seed
- Shrimp

- Celery
- Fish

VITAL Scientific Expert Panel Recommendations - 2012

Allergen	mg Protein Level
Peanut	0.2
Milk	0.1
Egg	0.03
Hazelnut	0.1
Soy	1.0
Wheat	1.0
Cashew	2.0
Mustard	0.05
Lupin	4.0
Sesame	0.2
Shrimp	10.0
Celery	n/a
Fish	n/a

Dose of Peanuts Causing Reactions in Peanut-Allergic Individuals

0.2mg (0.05 mg) | 0.4mg (0.1 mg) | 1.0mg (0.25 mg) | 5.0mg (1.25 mg) | 25mg (6.25 mg) | 100mg (25 mg) | 400mg (100 mg)

Lowest Eliciting Dose in mg whole peanut (mg peanut protein)

Percent of Peanut-Allergic Population That Would React To Dose

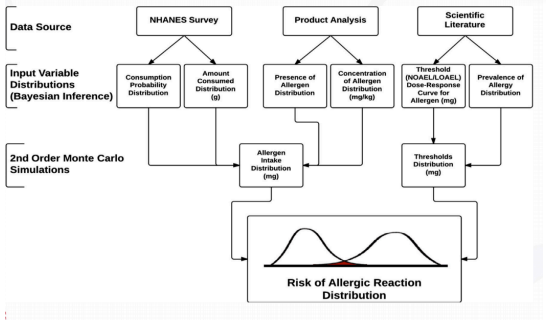
0.3% | 1% | 4.25% | 14% | 30% | 50%

Ballmer-Weber and Hourihane

Emerging Consensus on VITAL Reference Doses

- FDA (2006) indicated that probabilistic dose-distribution modeling was the best approach to use to establish thresholds
- EuroPrevall Workshop (2009) agreed with that approach
- VITAL (Australian Allergy Bureau) used that approach in 2011 to first establish Reference Doses
- ILSI-Europe endorsed use of VITAL Reference Doses in 2014
- U.S. National Academies of Science, Engineering & Medicine endorsed the VITAL approach in their report of November, 2016

Quantitative Risk Assessment



QRA – The Inputs

- Threshold dose-distributions: solid, validated especially for peanut, milk, egg, hazelnut
- Food consumption estimates (mean, 90%, 95%): excellent in U.S.; USDA NHANES database
- Analytical estimates of allergen residues: commercial ELISA methods available for many allergenic foods but not often validated with naturally incurred standards; have variable calibrators with questionable adjustment factors

Improved Allergen Risk Assessment Circa 2016

- Quantitative risk assessment is emerging as an approach to guide labeling, recalls, and ACPs
- Not yet widely adopted
- But we have human threshold data from allergic consumers
- Reliable analytical data can be obtained with caution
- Reliable consumption information exists in some countries
- These form the elements of QRA

Varför behöver vi en action level (åtgärdsnivå)?

- Vi vill märka med försiktighetsmärkning – men bara när det är nödvändigt
- Därför ska vi ta fram ett verktyg för att bedöma sannolikheten för en mild reaktion om vi släpper ut en kontaminerad produkt på marknaden
- Detta verktyg ger oss en åtgärdsnivå (action level)
- Om vi genom analys och beräkningar tror att våra produkter (genom kontaminering) innehåller ett visst allergen, men halten ligger under denna nivå, bör vi inte märka
- Om de ligger över kan vi använda ”Kan innehålla spår av”-märkning
- Ligger de högt över ska vi vidta andra åtgärder …!

Vågar vi skriva ”Fri från”?

- En consensus om en hållbar risk management
- Ett samförstånd genom hela kedjan – förankring av ny praxis bland berörda konsumenter
- Stöd från myndigheter
- Internationell consensus?
- Noll är alltså inte noll – men innebär en låg risk
- Vi har redan denna praxis för glutenfri < 20 ppm.
- Kan vi kombinera med information för att allergi kan variera från tillfälle till tillfälle? (Nej)