

Risk assessment and regulations for mycotoxins



Hans van Egmond, MycoRed session 14 October 2011



50 years ago: "Turkey-X disease"

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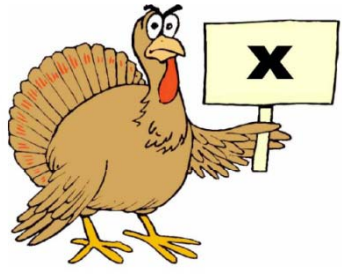
Telephone: BYELET 4091
 MEDIUM ADDLESTONE
 NEW HAW
 WEYBRIDGE
 SURREY

May 24th 1961

Dear Dr van der Swift,

Further to my letter of yesterday, this is to ask as suggested that a good reserve (say, about 5 tons) should be kept of the Brazilian groundnut meal of which you gave me a sample. It is one of the most highly toxic samples we have had (in fact the most toxic) and it is highly probable that you and me will require supplies of it for experimental purposes. In any case, steps should be taken as soon as possible to ensure that it

is not used for in any rations for live stock
 We now have a large outbreak of
 toxicity in store cattle (18-20 months old)
 which have been on rations containing B.S.M.
 for only 4 months so effects are not
 confined only to calves.
 There are so many aspects of this
 problem that I do think it would
 be best if you could come over and
 discuss them with all the people concerned
 as soon as you can after your holiday in
 Switzerland. Bring his van der Swift
 I too will stay with us - we would
 love to have you both.
 Please forgive haste - I just cannot get
 time to get that unsolicited B.M.A. congress
 paper written and the Brazilian groundnut problem
 is so very much more interesting than this
 dull paper.
 Kind regards - Yours sincerely
 Ruth Allcroft



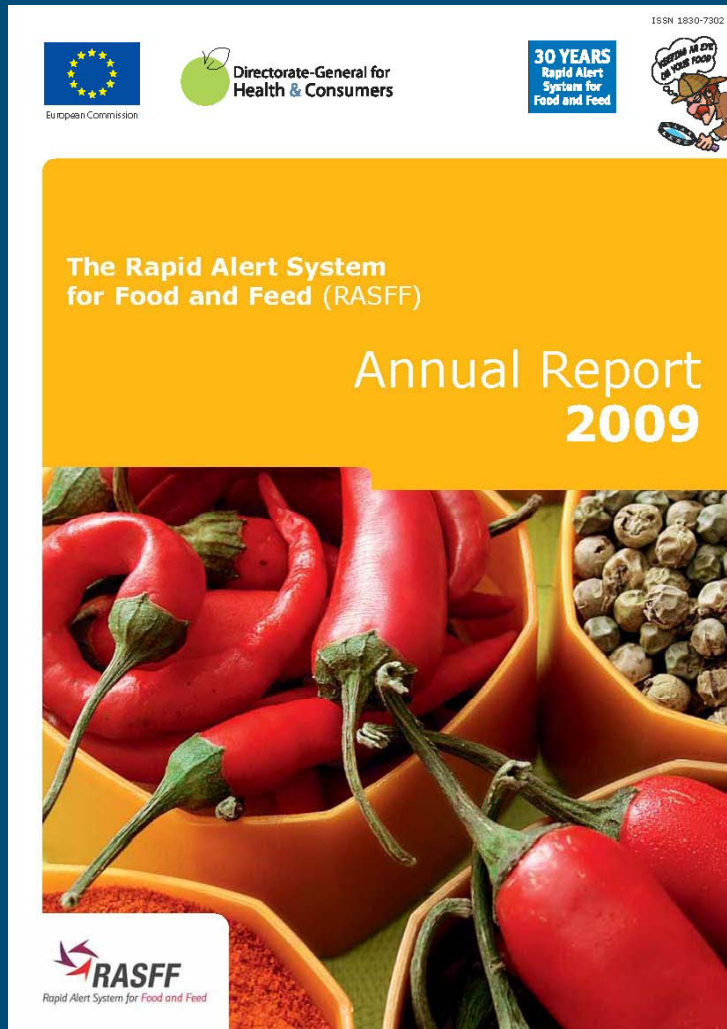
Turkey-X:

Citations from the correspondence



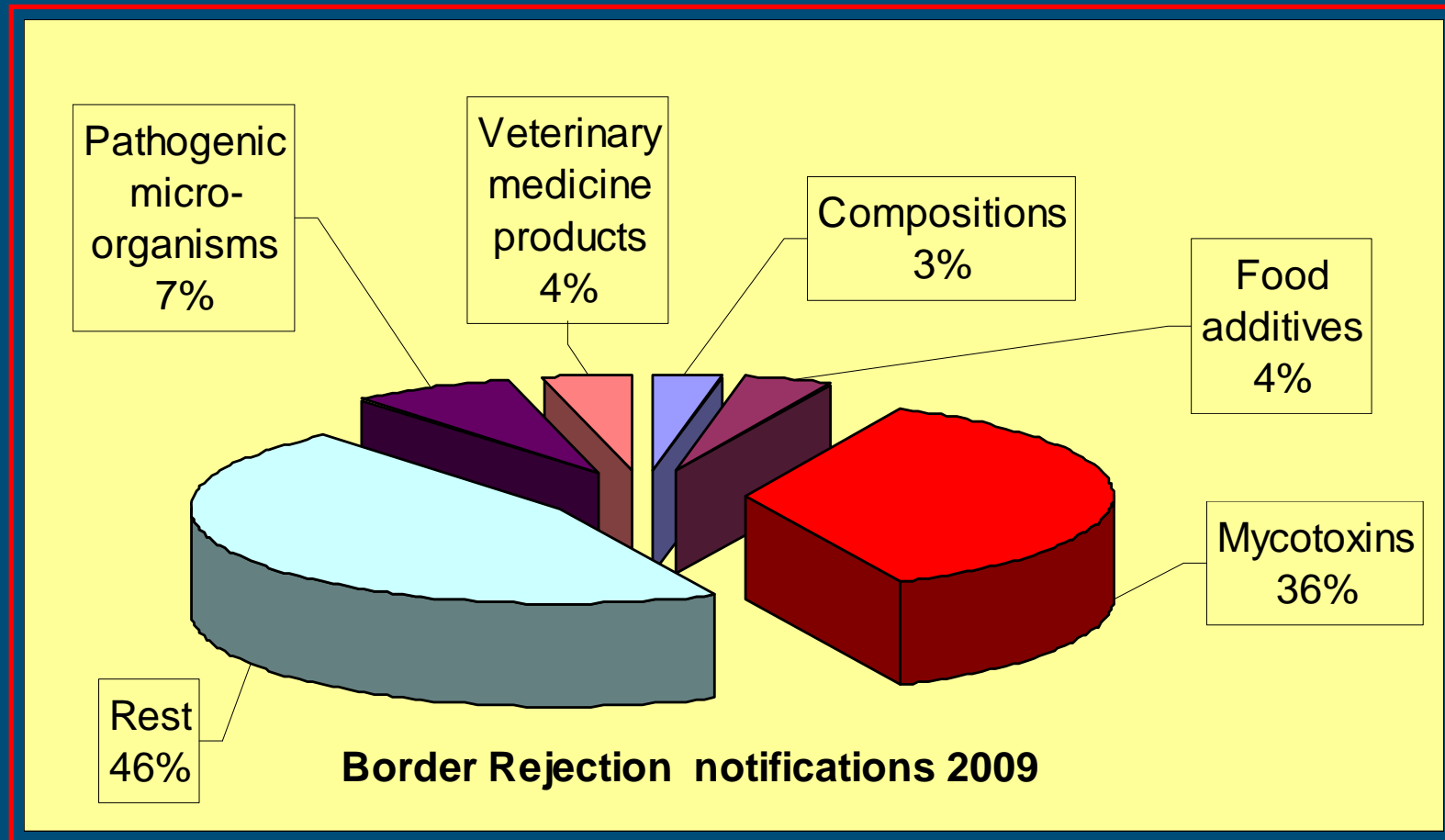
- “We are fairly certain that this ‘*toxic factor*’ in groundnuts is not a new problem”
- “We do not know the chemical composition of the ‘*toxic factor*’, but the source of toxicity is likely related to fungal contamination at a stage before processing”
- “The ‘*toxic factor*’ is present in milk from cows fed with rations containing the toxic groundnut meal, and has shown to be a carcinogen”
- “We think the whole problem is serious from a human and animal health point of view and from economic aspects”

Rapid Alert System for Food and Feed



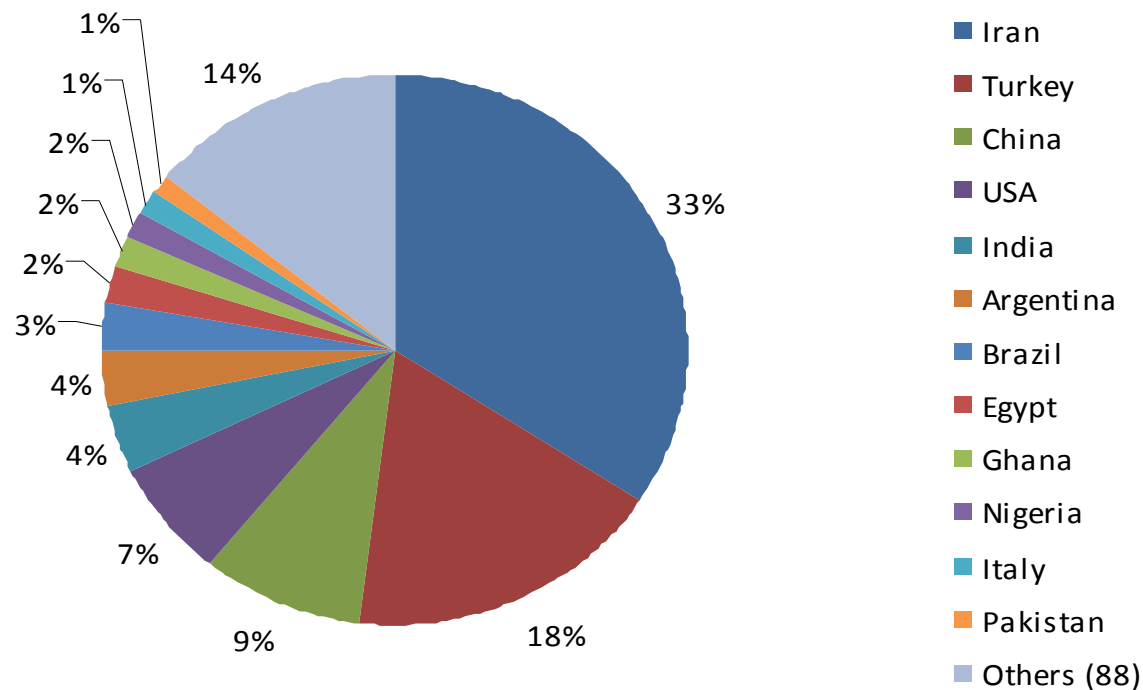
- Quick information-exchange in the EU on risks to human health
- Allows MS to identify potential problems and take measures
- In 2009: 665 mycotoxin issues

RASFF 2009: Border rejection notifications



RASFF trend analysis: mycotoxin reports

Origin of mycotoxin-containing products
RASFF, July 2003 - June 2009



Main products

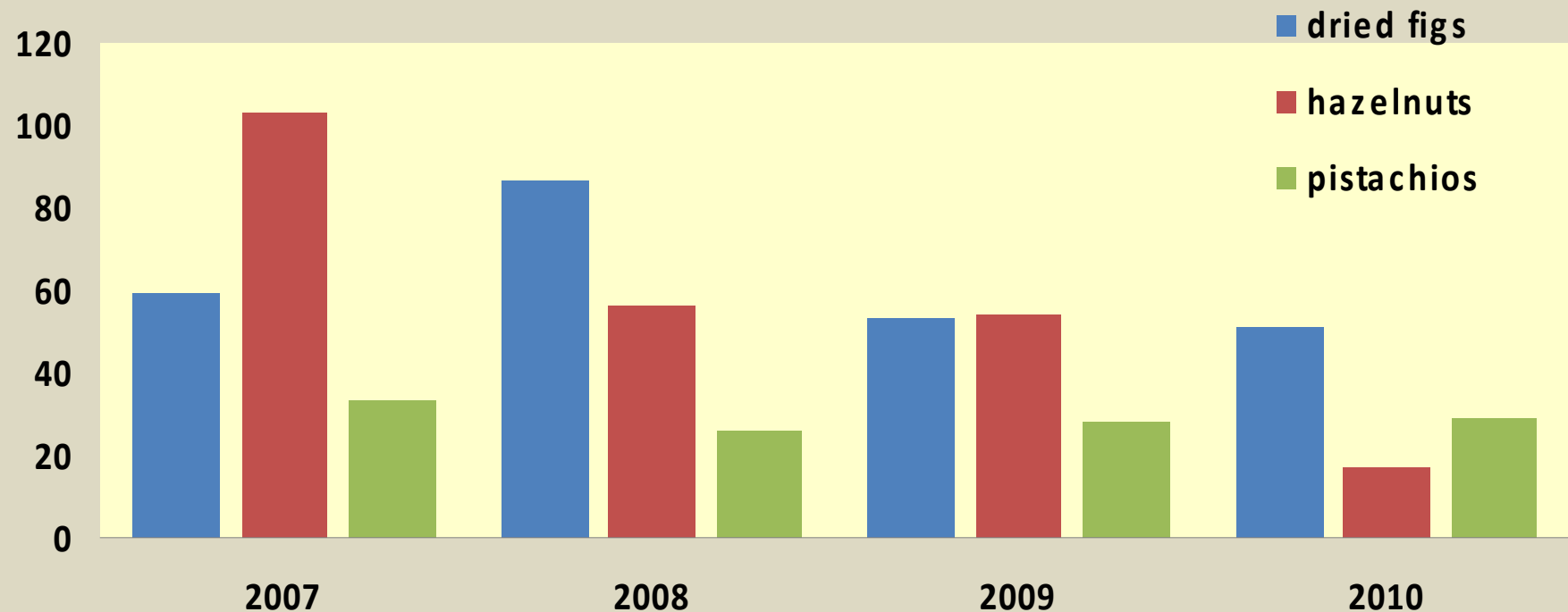
Iran:
pistachio

Turkey:
*dried figs/
hazelnuts/
pistachios*

China:
groundnut

RASFF trends from 2007- 2010

EU Border Rejection Notifications for aflatoxins in products from Turkey



Outline of presentation



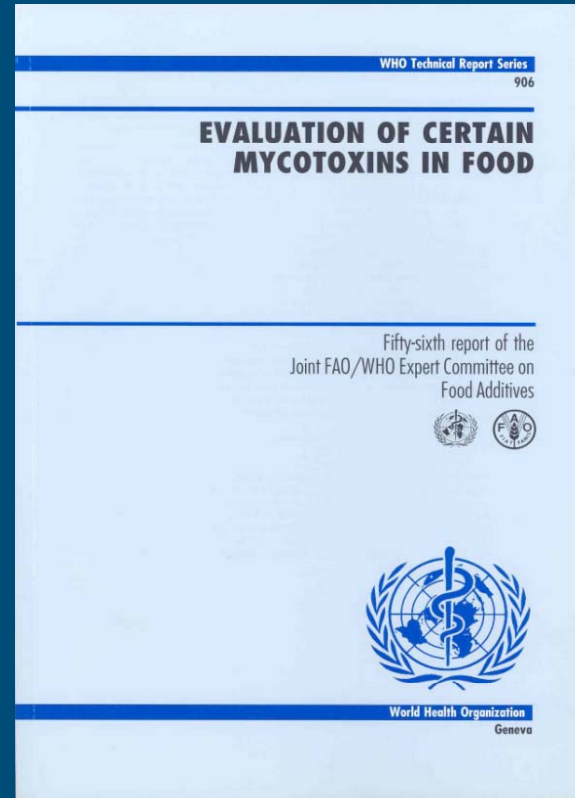
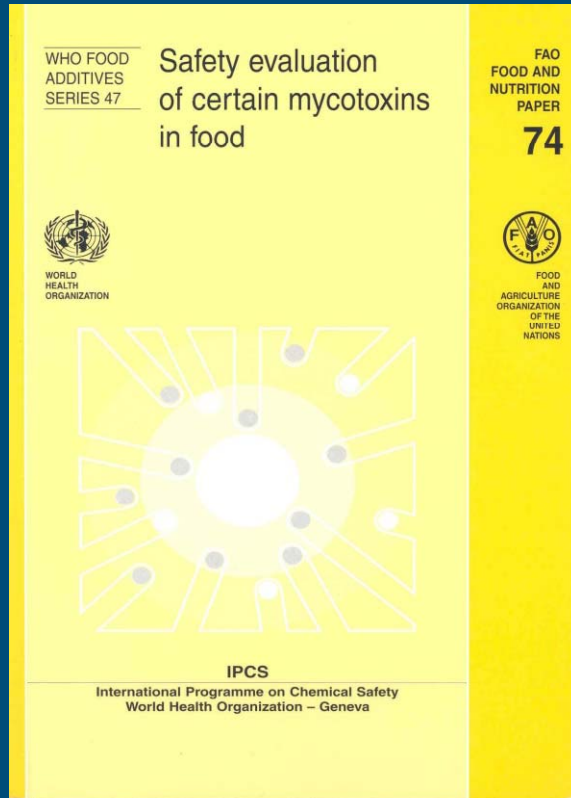
- Introduction
- Risk assessment: scientific basis for regulations
- Other factors influencing mycotoxin regulations
- Mycotoxin regulations
- Summary

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JECFA and EFSA: main players in risk assessment



Risk assessments on mycotoxins

- Opinions published on mycotoxins in animal feed
- New opinions on mycotoxins in human food (and animal feed) in drafting stage
- These risk assessments include:
 - zearalenone (opinion recently published)
 - T-2/HT-2 toxins, nivalenol, diacetoxyscirpenol
 - moniliformin, beauvericin, enniatins
 - ergot alkaloids
 - *Alternaria* toxins
 - sterigmatocystin, phomopsins

Risk Analysis Framework



Risk Assessment

- Hazard identification
- Hazard characterization
- Exposure assessment
- Risk characterization

Risk Management

- Assess policy alternatives
- Select and implement appropriate options

Risk Communication

- Interactive exchange of information and opinions



(after WHO, 1998)

Risk Assessment Process

- **Hazard identification** – Utilization of all available data to establish that a chemical has the apparent capacity to cause an adverse effect
- **Hazard characterization (dose-response relationship)** – Assessment of the relationship between dose, or level of exposure, and the incidence or severity of an effect
- **Exposure assessment** – Estimation of the dose, or level of a chemical in the environment to which various individuals, populations, or ecosystems are exposed
- **Risk characterization** – Estimation of the incidence and severity of adverse effects liable to occur in a population or ecosystem, due to actual or predicted exposure

Risk assessment may lead to

- *Acute reference dose (ARfD)* – For substances with threshold of toxicity, where incidental exposure is relevant (e.g. marine biotoxins)
- *Acceptable daily intake (ADI)* – For avoidable substances with threshold of toxicity, where chronic exposure is relevant (e.g. food additives)
- *Tolerable daily intake (TDI)* – For unavoidable substances with threshold of toxicity, where chronic exposure is relevant (e.g. many mycotoxins)

When these reference points are not exceeded, risk is considered '**not appreciable**'

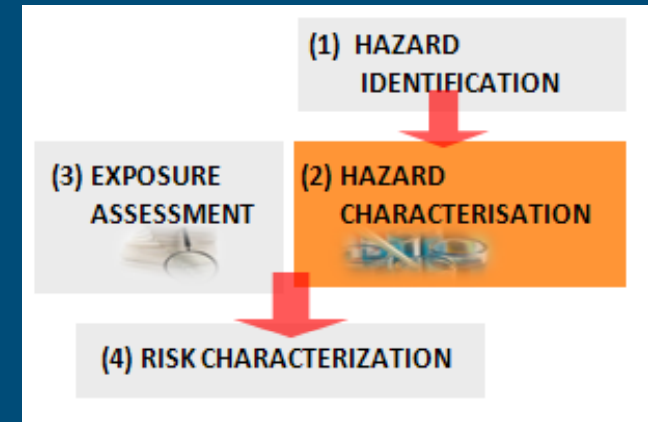
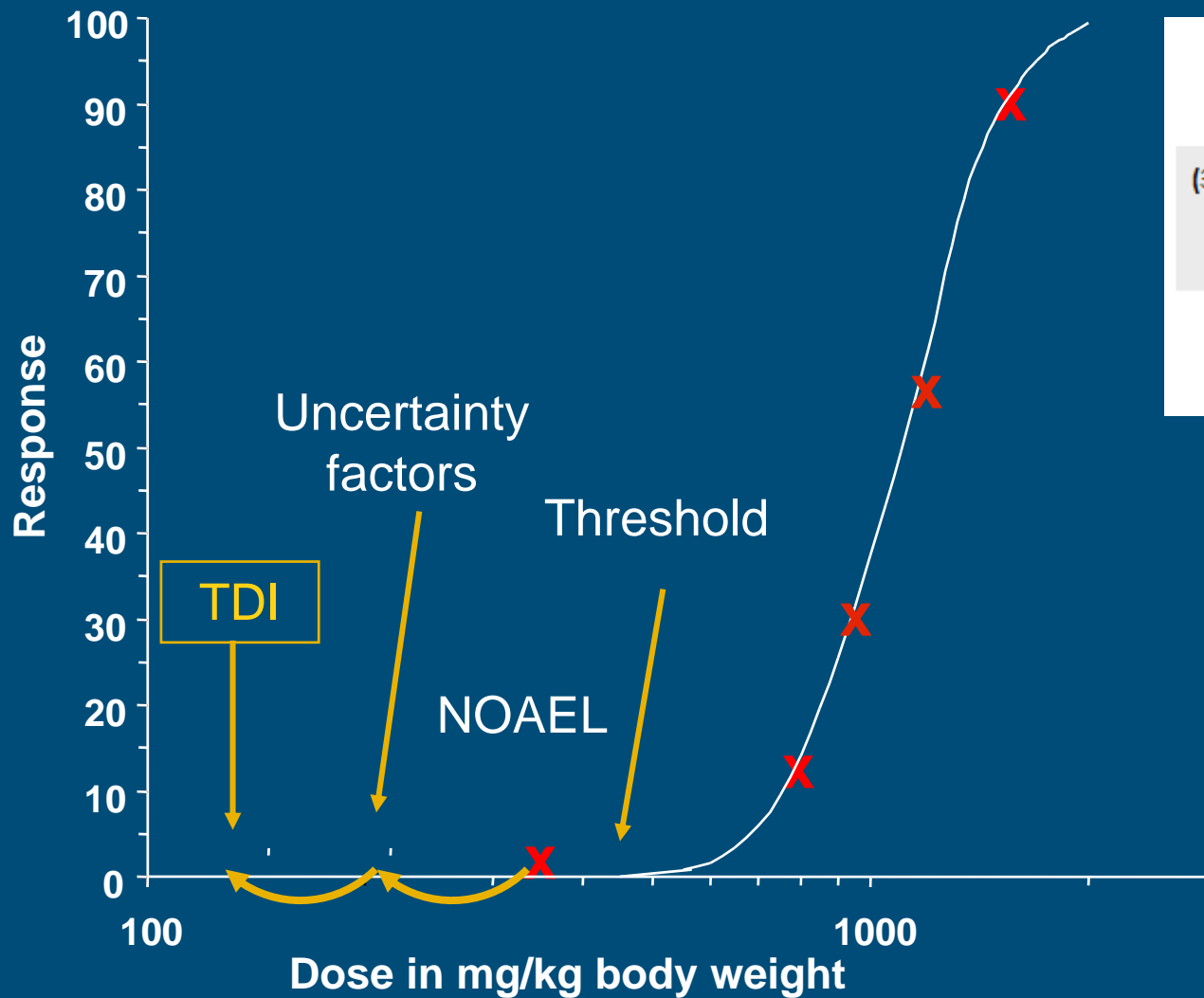
Tolerable daily intake (TDI)

- TDI: an estimate of the amount of an unintended substance in air, food or drinking water that can be taken in daily over a lifetime without appreciable health risk
- TDIs are appropriate for many mycotoxins, with an identified threshold of toxicity

Establishment of tolerable daily intakes

- Databases are evaluated for substances for which a threshold of toxicity exists
- Critical effects are identified
- NOAELs are identified in each study
- Relevance to humans is determined, if possible
- In the absence of other information, the lowest NOAEL is used as the basis for the TDI
- A safety factor is applied to the NOAEL when establishing a TDI (default: 100)

Dose response data for the critical effect



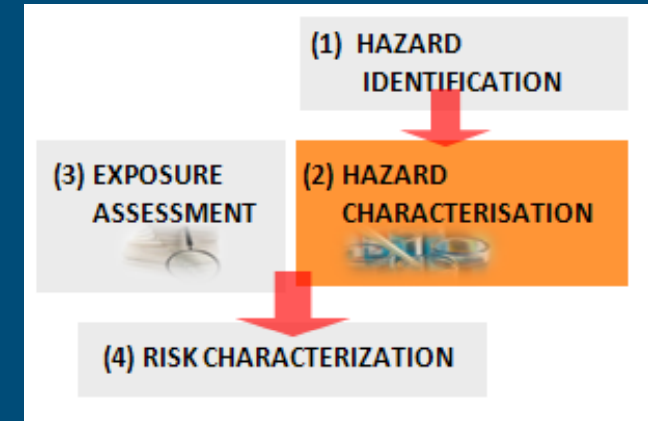
(after M. Eskola, 2011)

Contaminants without thresholds of toxicity

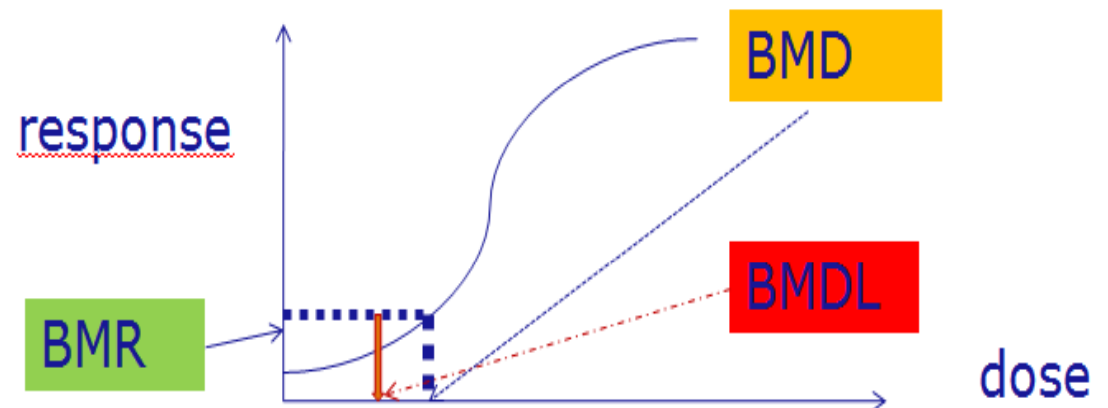
- Aflatoxins: the first carcinogenic contaminants evaluated by JECFA
- JECFA advised that they be present in the food supply at 'irreducible levels': that concentration of a substance which cannot be eliminated from a food without involving the discarding of that food altogether, or severely compromising the ultimate availability of major food supplies
- Other organizations often refer to this as 'ALARA' – "*as low as reasonably achievable*"

Newer concept: Benchmark dose (BMD)

- Used for both thresholded and non-thresholded compounds
- Modelling benchmark dose (BMD) for 10% extra risk of the critical effect
- $BMDL_{10}$ = 95% lower confidence limit of the BMD for 10% extra risk of the critical effect

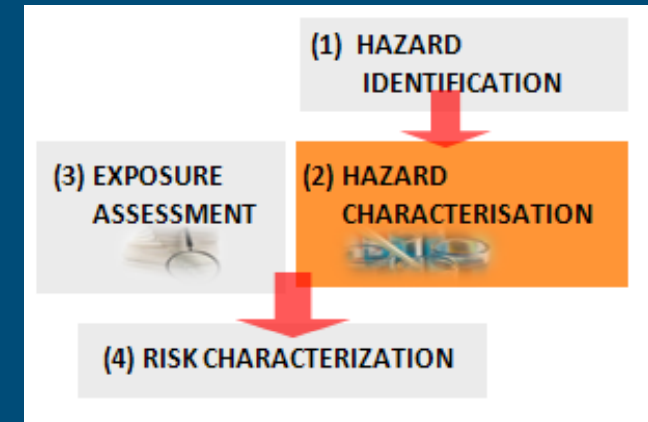


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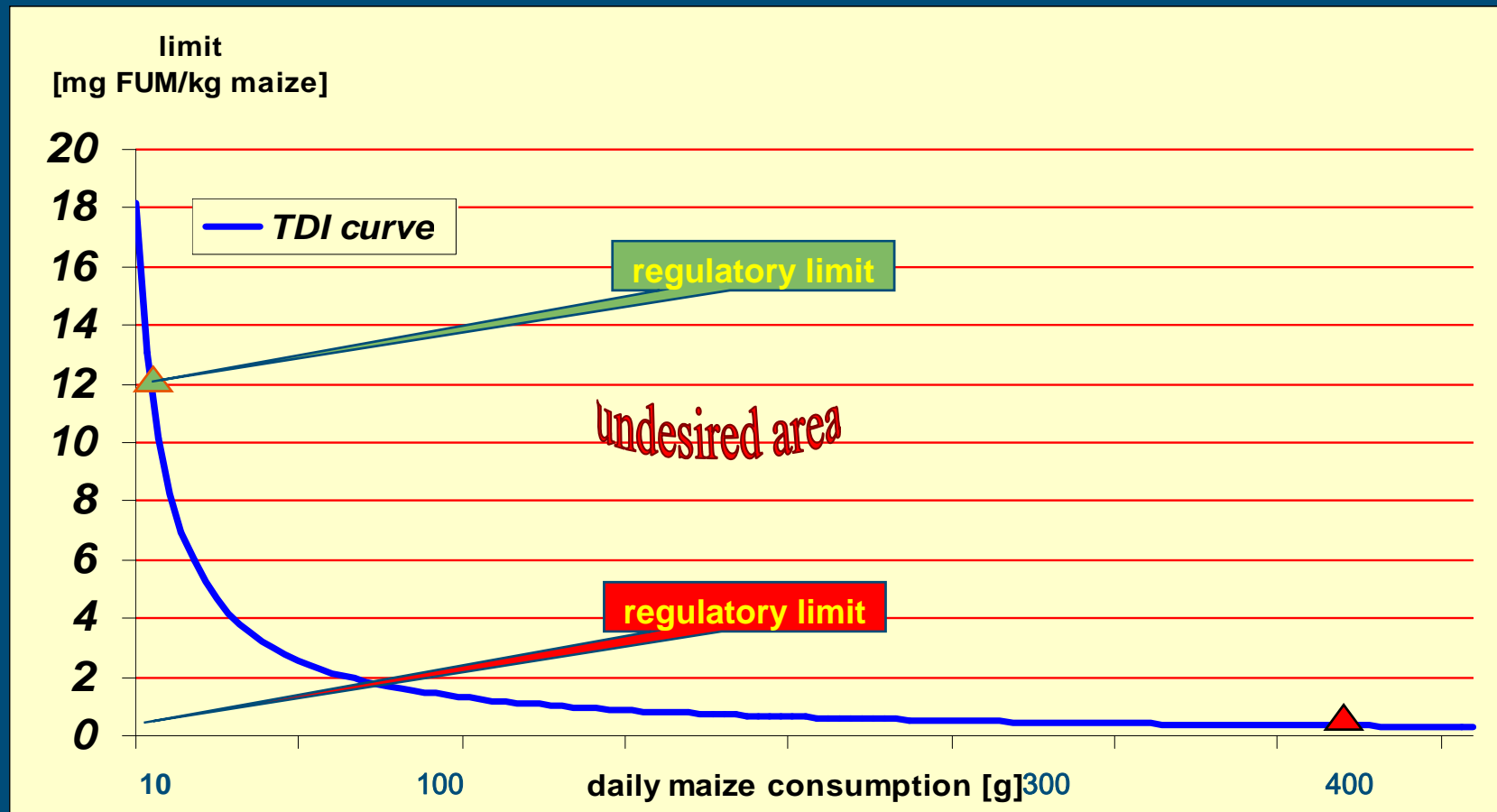


Mycotoxin risk assessment by JECFA or EFSA

- Establishment of the TDI involves the first two steps of risk assessment
- Exposure is assessed by JECFA or EFSA to ensure that it does not exceed the TDI (long-term intake)
- For intake assessment data are needed about occurrence (data collected) and consumption



Consumption data influence setting of limits




Outline of presentation



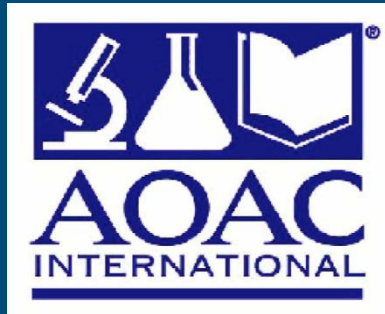
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Other factors influencing mycotoxin regulations

- Hazard assessment:  TDI
- Data on occurrence and consumption
- Availability of methods of sampling and analysis



Analytical methodology for mycotoxins




- US based, international involvement
- Development and validation of methods of analysis and improvement of AQA
- Approx. 45 mycotoxin methods in “OMA”

- European equivalent of ISO
- Performance criteria approach, usually based on interlaboratory studies
- 12 mycotoxin methods standardized
- EU interlaboratory studied methods



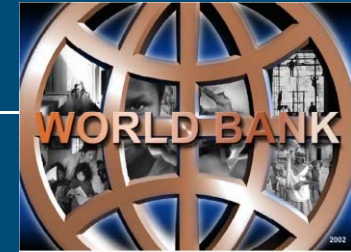
CEN

Other factors influencing mycotoxin regulations

- Hazard assessment:  TDI
- Data on occurrence and consumption
- Availability of methods of sampling and analysis
- Trade contacts with other countries



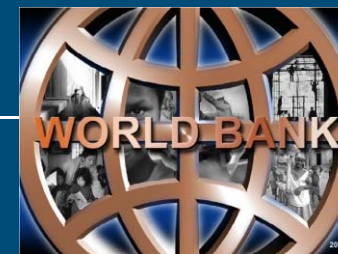
World Bank Report 2001



“Global trade and food safety: winners and losers in a fragmented system” (Wilson and Otsuki, 2001)

- Estimations made on the relationship of aflatoxin B₁ regulatory standards and trade flow
- Scenario studies for cereals and nuts predict significant losses for exporting countries (Africa) if stringent standards are adopted


World Bank Report 2005



“Food Safety and Agricultural Health Standards, Challenges and Opportunities for Developing Country Exports” (Worldbank, 2005)

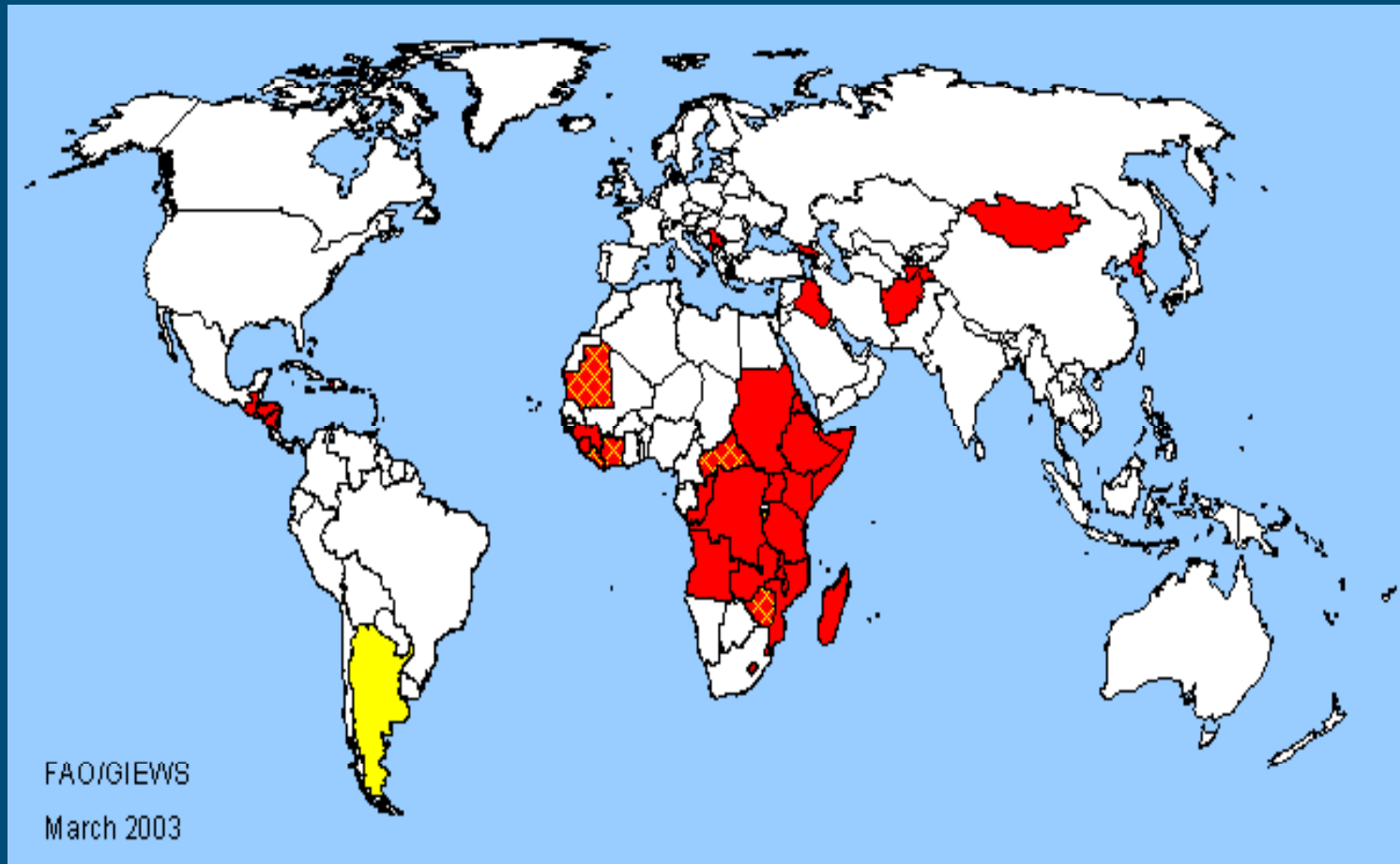
- Actual experience: much different than projected; e.g. African share of EU market for dried fruit increased!
- Border rejections irritating to exporters, but some producing countries got an increase of their EU market share

Other factors influencing mycotoxin regulations

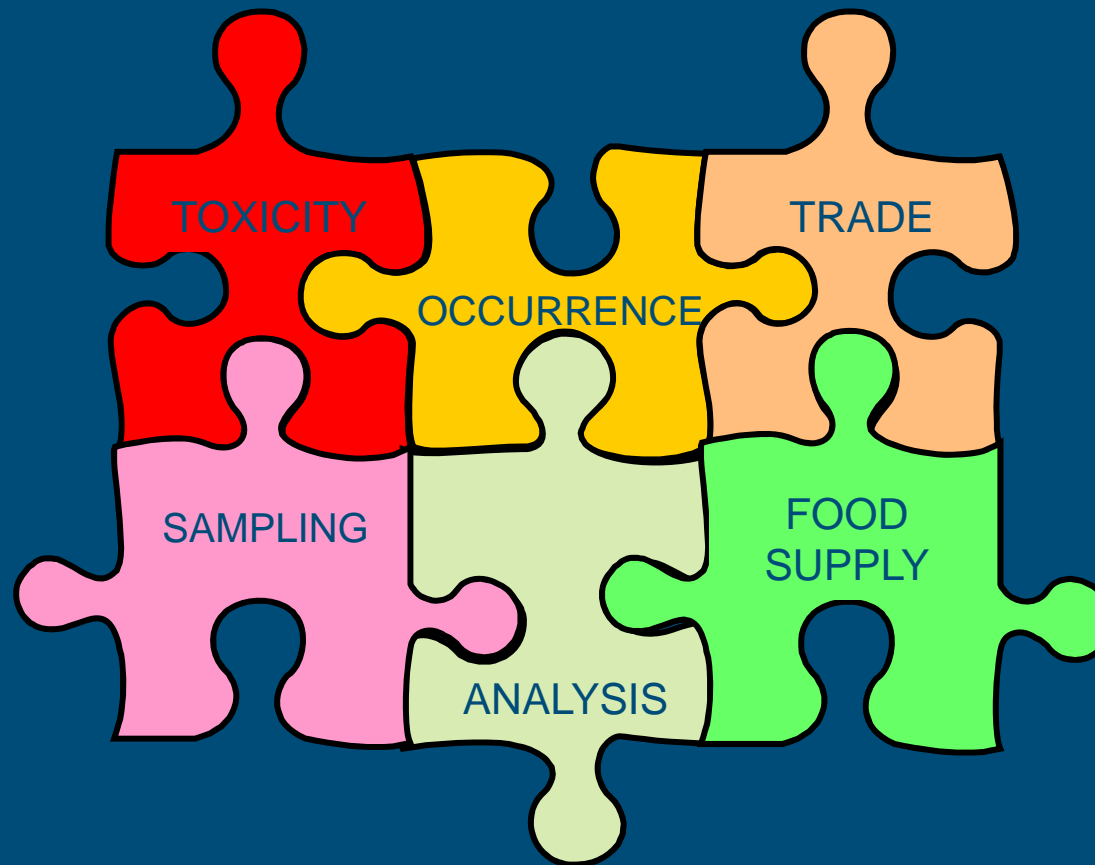
- Hazard assessment:  TDI
- Data on occurrence and consumption
- Availability of methods of sampling and analysis
- Trade contacts with other countries
- Sufficiency of food supply



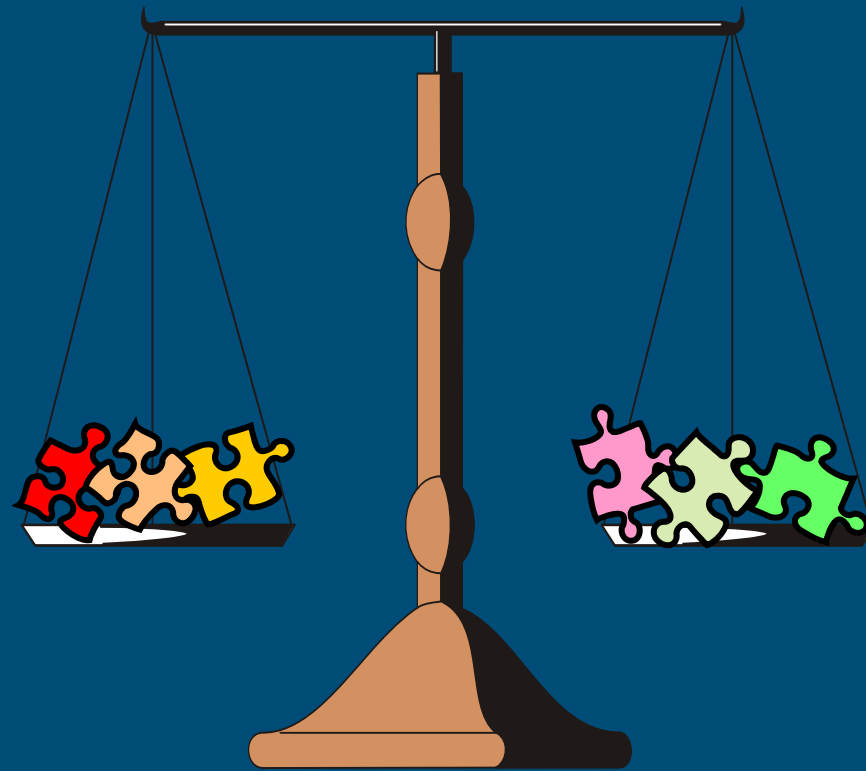
Food shortages in the world



The mycotoxin regulatory puzzle



Weighing the various factors: not trivial



Outline of presentation



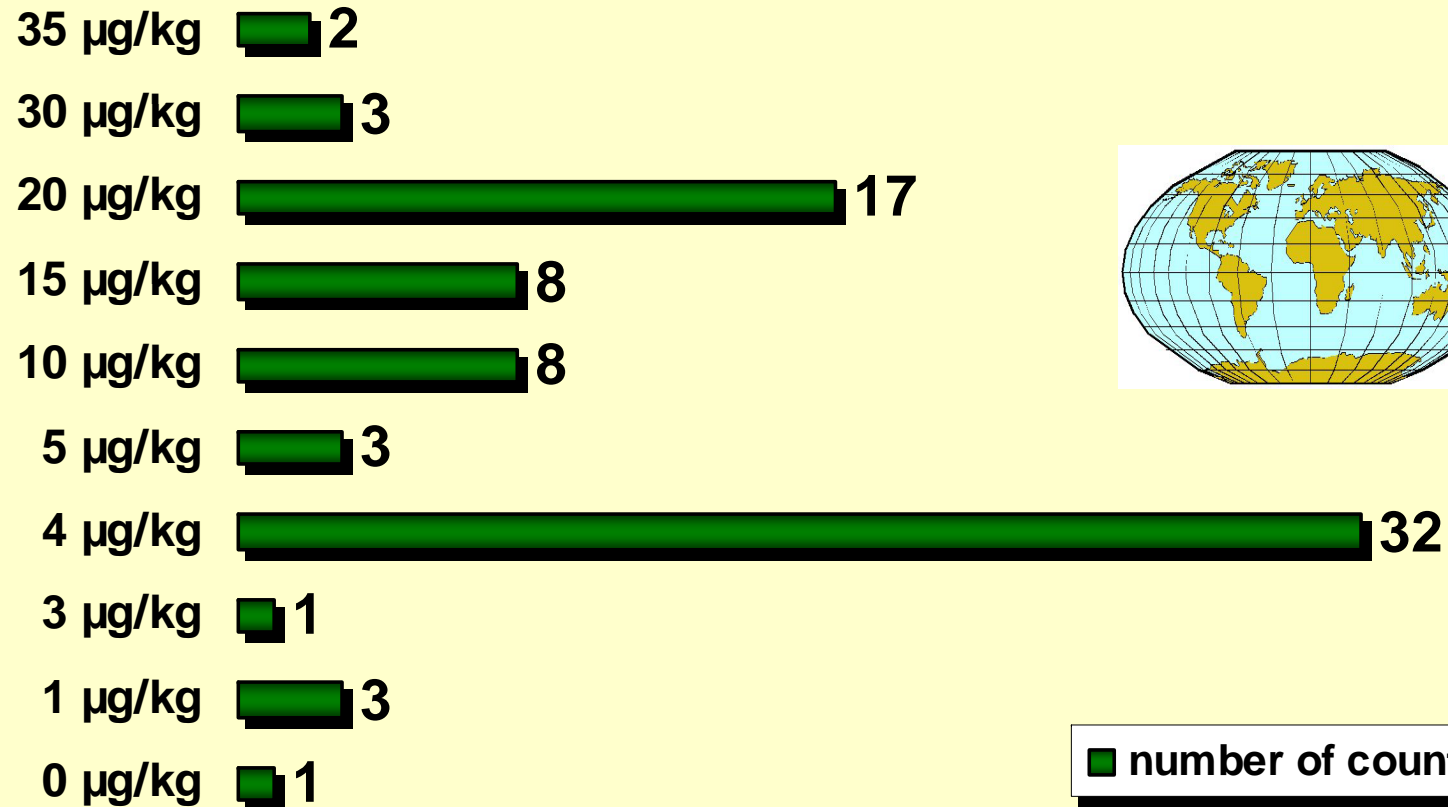
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Inquiries on mycotoxin regulations

- Worldwide inquiries: 1981, 1987, 1995 & 2003, resulting in various publications
- Inquiry 2003 published as FAO FNP 81 (2004)
- Regulations in approx. 100 countries, and for 13 toxins
- French, Spanish and Chinese translations available



Total aflatoxins in food: regulated in 75 countries



Mycotoxin regulatory situation in Europe

- 39 nations with known regulations (99 % of inhabitants of the region)
- EU harmonized limits exist for aflatoxins, ochratoxin A, patulin, DON, zearalenone, fumonisins
- EU food limits expected for T-2/HT-2, ergot alkaloids and other mycotoxins
- EU feed limits exist for aflatoxin B₁
- EU feed guidance values exist for ochratoxin A and some *F.* toxins



Mycotoxin regulations in Turkey

- Regulations exist for mycotoxins in food only
- Max. tolerated levels for 50 different products
- Limits for AFLA, OTA, PAT, DON, ZEA and FUM
- Slight differences exist as compared to EU
- Published in Turkish Food Codex Regulation, 2008 and 2009, Official Gazette 26879 & 27143

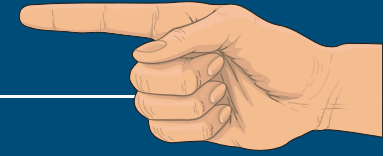


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Summary and conclusions



- Risk assessment: main scientific factor in establishing mycotoxin regulations
- Other factors play a role as well
- Mycotoxin regulations now exist in at least 100 countries and for 13 different toxins
- Details of 2003 inquiry published in FAO FNP 81
- In the EU and Turkey, diverse and detailed mycotoxin regulations exist, in the EU more are expected in the coming years



Risk assessment and regulations for mycotoxins



Gok teşekkür ederim!



Toxic effects of mycotoxins

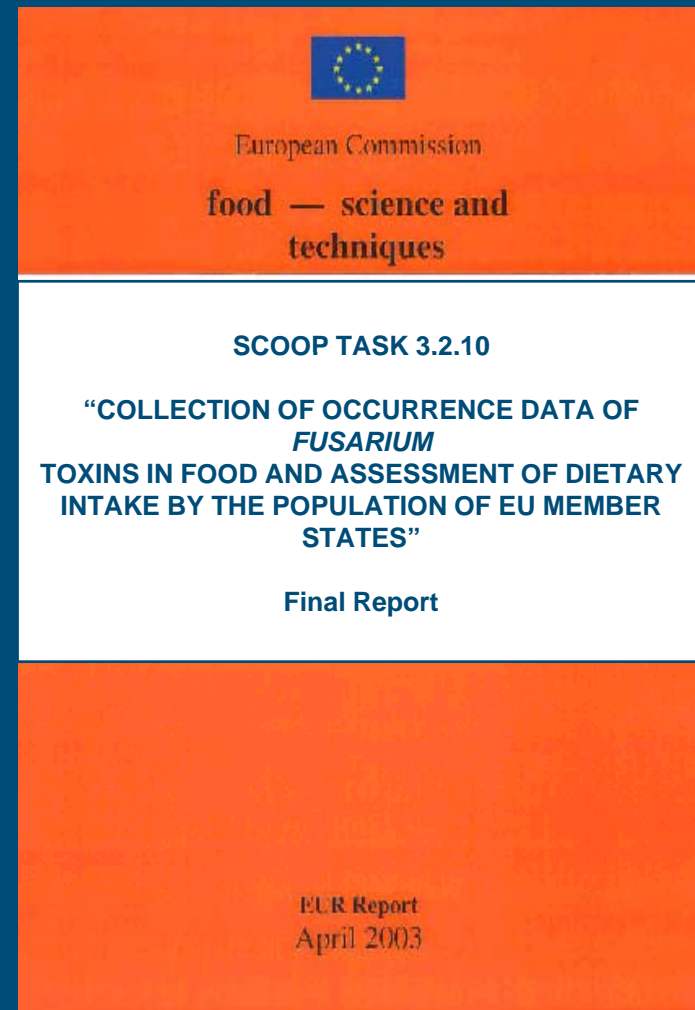
	AFL	OTA	PAT	FUM	TCT	ZEN
carcinogenic	●	●		●		
hepatotoxic	●	●		●		
immunotoxic	●	●	●	●	●	●
nephrotoxic		●		●		
neurotoxic			●	●	●	
oestrogenic						●
teratogenic	●	●				●

Occurrence data are needed



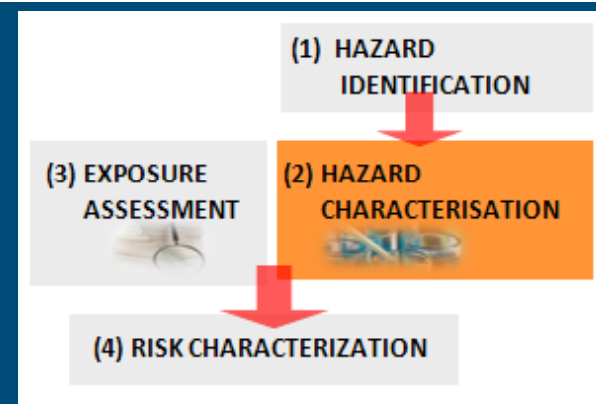
SCOOP:

Scientific Cooperation on
Problems relating to Food



Critical effect and NO(A)EL

- Critical effect
 - the **relevant** adverse effect seen at the lowest dose level
- NO(A)EL - No Observed (Adverse) Effect Level
 - maximum dose that produced no observable effect (usually adverse) in the study identifying the **critical effect** in the most sensitive species (animals, human)
 - human data preferred, if available



Risk analysis

- Risk assessment – primarily the responsibility of scientific committees, e.g. JECFA and EFSA
- Risk management – primarily the responsibility of regulators, e.g. Codex committees and the European Commission/EU memberstates
- Risk communication – between risk assessors and managers, and with the public

About “hazard” and “risk”

- ‘Hazard’ means a biological, chemical or physical agent in, or condition of food or feed with the potential to cause an adverse health effect
- ‘Risk’ means a function of the probability of an adverse health effect and the severity of that effect consequential to a hazard
 - Risk = f (Probability, Severity)
 - Risk = Probability x Severity