Risk assessment and regulations for mycotoxins

Hans van Egmond, MycoRed session 14 October 2011
50 years ago: “Turkey-X disease”
“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
Pathogenic micro-organisms 7%
Veterinary medicine products 4%
Compositions 3%
Food additives 4%
Mycotoxins 36%
Rest 46%

Border Rejection notifications 2009
RASFF trend analysis: mycotoxin reports

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

- **Iran**: pistachio
- **Turkey**: dried figs/hazelnuts/pistachios
- **China**: groundnut

Adapted from Kleter 2010
RASFF trends from 2007-2010

EU Border Rejection Notifications for aflatoxins in products from Turkey

- **2007**: 120 dried figs, 60 hazelnuts, 20 pistachios
- **2008**: 100 dried figs, 80 hazelnuts, 20 pistachios
- **2009**: 40 dried figs, 40 hazelnuts, 20 pistachios
- **2010**: 20 dried figs, 10 hazelnuts, 20 pistachios
Outline of presentation

- Introduction
- Risk assessment: scientific basis for regulations
- Other factors influencing mycotoxin regulations
- Mycotoxin regulations
- Summary
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J ECFA 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
- $\text{BMDL}_{10} = 95\%$ lower confidence limit of the BMD for 10% extra risk of the critical effect

(after M. Eskola, 2011)
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

TDI curve

regulatory limit

undesired area

regulatory limit

limit
[mg FUM/kg maize]

daily maize consumption [g]

0 2 4 6 8 10 12 14 16 18 20

100 200 300 400
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Mycotoxin regulations
Summary
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
“Global trade and food safety: winners and losers in a fragmented system” (Wilson and Otsuki, 2001)

- Estimations made on the relationship of aflatoxin B$_1$ regulatory standards and trade flow
- Scenario studies for cereals and nuts predict significant losses for exporting countries (Africa) if stringent standards are adopted
"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

FAO/GIEWS
March 2003
The mycotoxin regulatory puzzle

- Toxicity
- Trade
- Occurrence
- Sampling
- Food Supply
- Analysis
Weighing the various factors: not trivial
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Inquiries on mycotoxin regulations

- Regulations in approx. 100 countries, and for 13 toxins
- French, Spanish and Chinese translations available
Total aflatoxins in food: regulated in 75 countries

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<th>Level (µg/kg)</th>
<th>Number of Countries</th>
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[Image: Bar chart showing the number of countries regulating aflatoxins at different levels.]
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

Gök teşekkür ederim!
Toxic effects of mycotoxins

- Carcinogenic
- Hepatotoxic
- Immunotoxic
- Nephrotoxic
- Neurotoxic
- Oestrogenic
- Teratogenic
Occurrence data are needed

SCOOP: Scientific Cooperation on Problems relating to Food

SCOOP TASK 3.2.10
"COLLECTION OF OCCURRENCE DATA OF FUSARIUM TOXINS IN FOOD AND ASSESSMENT OF DIETARY INTAKE BY THE POPULATION OF EU MEMBER STATES"
Final Report

European Commission
food — science and techniques

RIKILT WAGENINGEN UR

MycORed
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

(after M. Eskola, 2011)
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 member states
- 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