



CONFIDENCE: Rapid methods: BSc education modules 4 and 11 October 2011



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BSc education modules

4 and 11 October 2011

Risk assessment and regulations for mycotoxins

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Summary

Since the discovery of the aflatoxins, 50 years ago, mycotoxins have caused concern because of their harmful effects to man and animals. Hazards due to mycotoxins include carcinogenic, hepatotoxic, immunotoxic, nephrotoxic, neurotoxic, oestrogenic and teratogenic effects. Depending on the severity and the probability of the adverse health effects, exposure to mycotoxins can pose risks, and these risks can be assessed. Mycotoxin risk assessment is the scientific evaluation of the probability of occurrence of adverse health effects resulting from human (mostly food-borne) exposure. The main authorities in mycotoxin risk assessment are the FAO/WHO Joint Expert Committee on Food Additives (JECFA) and the European Food Safety Authority (EFSA). In the risk assessment process several steps are distinguished, such as hazard identification, hazard characterization (dose-response relationship), exposure assessment and risk characterization.

For unavoidable substances with a threshold of toxicity, where chronic exposure is relevant, risk assessment may lead to the establishment of a tolerable daily intake (TDI). Many mycotoxins belong to this category of substances, and for various mycotoxins JECFA and EFSA have derived (temporary) TDIs. For some mycotoxins the risk assessment process by EFSA is ongoing. For genotoxic carcinogenic mycotoxins (non-thresholded toxicity, e.g. aflatoxins), risk assessment may lead to the establishment of a benchmark dose (BMD).

Risk assessment is the main scientific basis for the setting of mycotoxin regulatory limits in food and feed by national governments or economic communities (e.g. EU, MERCOSUR, Australia/New Zealand). However other factors play a role in the decision-making process focused on setting of regulations for mycotoxins. E.g. the distribution of the concentration of mycotoxins in products is an important factor to be considered in establishing regulatory sampling criteria. In addition reliable analytical methods will have to be available to make enforcement of the regulations possible. Apart from the scientific factors economic factors, such as commercial and trade interests and food security issues, also have an impact. Weighing the various factors that play a role in the decision-making process to establish mycotoxin tolerances is therefore of crucial importance. Despite the difficulties, mycotoxin regulations have been established in at least 100 countries and for 13 different (groups of) mycotoxins during the past decades, and newer regulations are still being issued.

Risk assessment and regulations for mycotoxins

Hans van Egmond, CONFIDENCE presentation 4 October 2011

50 years ago: "Turkey-X disease"

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"

Human aflatoxicosis in Kenya, 2004

317 people in Kenyan villages got ill; 127 died, including many children

FIGURE 1 Districts affected by aflatoxicosis outbreak—Eastern and Central Provinces, Kenya, January-July 2004

Photo: courtesy Henry Njapau and Masja Straetemans

Human aflatoxicosis in Kenya, 2004

Photo: courtesy Henry Njapau and Masja Straetemans

- Village-grown maize suspected to play a causal role
- FDA emergency team confirmed hypothesis of human aflatoxicosis
- New outbreaks occurred in 2005, 2006 and again in 2010

Outline of presentation

- Introduction
- Rapid Alert System for Food and Feed
- Risk assessment: scientific basis for regulations
- Other factors influencing mycotoxin regulations
- Mycotoxin regulations
- Summary



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- **Rapid Alert System for Food and Feed**
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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 (border rejections)

RASFF 2009: Border rejection notifications

Category	Percentage
Rest	46%
Mycotoxins	36%
Pathogenic micro-organisms	7%
Veterinary medicine products	4%
Food additives	4%
Compositions	3%

RASFF trend analysis: mycotoxin reports

Timeline (per quarter-year) of mycotoxin notifications
RASFF, July 2003 - June 2009

Adapted from Kleter 2010

RASFF trend analysis: mycotoxin reports

Mycotoxin notification categories
RASFF, July 2003 - June 2009

Category	Percentage
Information	71%
Border rejections	21%
Alert	8%

Adapted from Kleter 2010

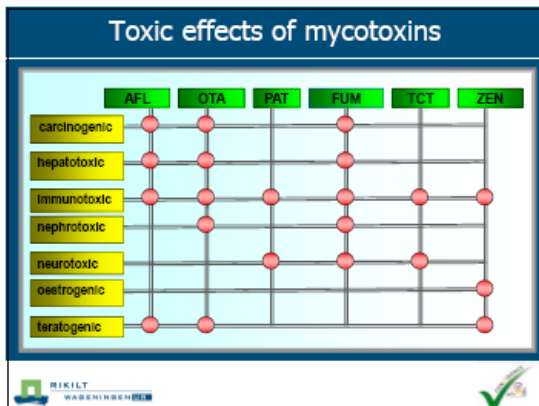
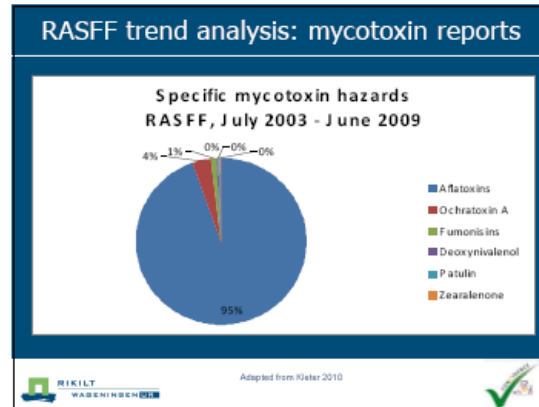
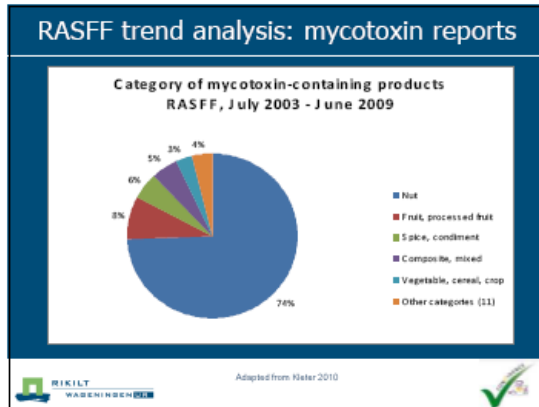
RASFF trend analysis: mycotoxin reports

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

Country	Percentage
Iran	33%
Turkey	18%
China	14%
USA	9%
India	7%
Argentina	4%
Egypt	4%
Ghana	4%
Nigeria	4%
Italy	4%
Pakistan	4%
Others (58)	1%

Main products
Iran: pistachio
Turkey: hazelnut/ pistachio/ dried fig
China: groundnut

Adapted from Kleter 2010



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- ### 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
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- ### 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
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JECFA and EFSA: main players in risk assessment

European Food Safety Authority

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The scientific basis for regulations

- EFSA: the EU's scientific risk assessment body on food and feed safety, nutrition, animal health and welfare, and plant health and protection
- EFSA tackles issues all along the food chain
- To provide science based risk assessments supporting risk management related to food/feed safety
- To provide scientific and technical advice on all matters within these fields
- To communicate all findings publicly

European Food Safety Authority

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Opinions on mycotoxins

- Opinions published on mycotoxins in animal feed
- New opinions on mycotoxins in human food (and animal feed) in drafting stage
- Just appeared: zearalenone
- Coming opinions will include:
 - T-2/HT-2 toxins, nivalenol, diacetoxyscirpenol
 - moniliformin, beauvericin, enniatins
 - ergot alkaloids
 - Alternaria toxins
 - sterigmatocystin, phomopsins

European Food Safety Authority

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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)

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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

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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'

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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)

Critical effect and NOAEL

- Critical effect
 - the **relevant** adverse effect seen at the lowest dose level
- NOAEL - 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

Adapted from Eskola, 2011

Dose response data for the critical effect

Adapted from 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"

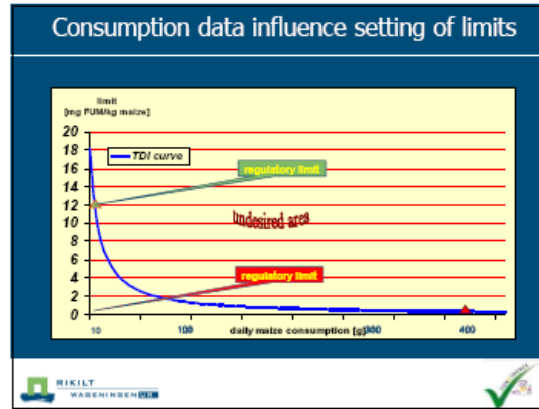
Mycotoxin risk assessment by JECFA or EFSA

- Establishment of the TDI involves the first two steps of risk assessment
- Intake 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 and consumption

Occurrence data are needed

SCOOP:
Scientific Cooperation on
Problems relating to Food

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Other factors influencing mycotoxin regulations

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

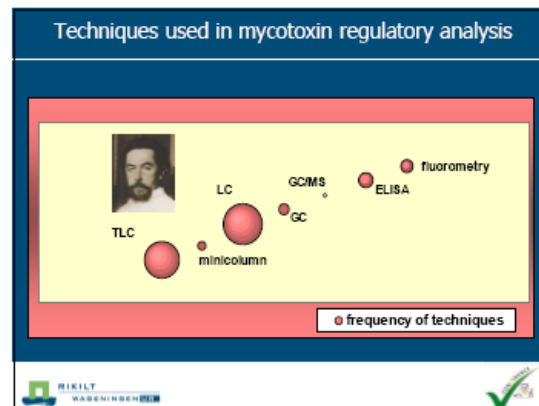
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Analytical methodology for mycotoxins

- 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

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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



Risk-benefit analysis

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The mycotoxin regulatory puzzle

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Weighing the various factors: not trivial

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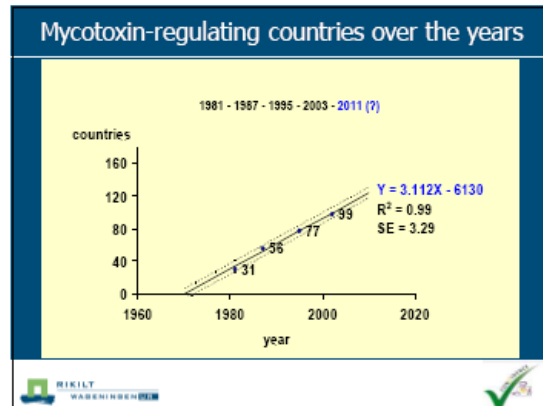
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The mycotoxin regulatory regression equation

$Y = 3.112 X - 6130$


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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)
- Chinese, French and Spanish translations available




Worldwide regulations for mycotoxins in food and feed in 2003





International inquiry 2003

Questionnaire 2003
For an Update of "Worldwide regulations for mycotoxins 1995"
FAO Food and Nutrition Paper 64

- Inquiry 2003: FAO-contracted activity of RIVM
- Information: Dutch Embassies and personal contacts
- Details asked a.o. about tolerance limits, legal bases, responsible authorities, methods of sampling and analysis
- Regulations exist in 100 countries and for 13 toxins
- FAO FNP 81: published in 4 different languages



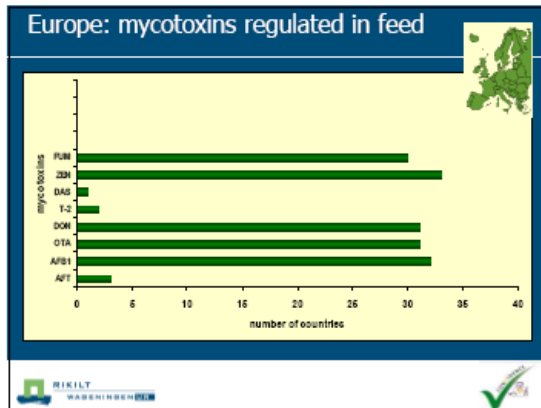
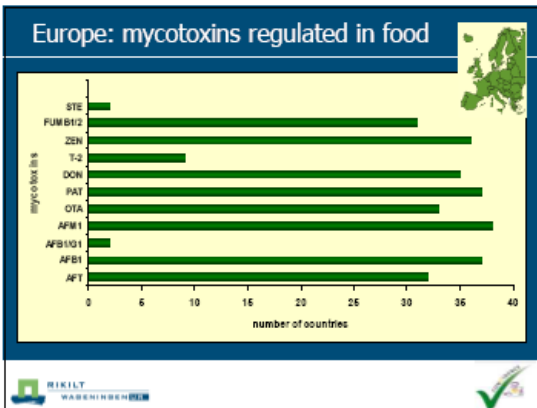


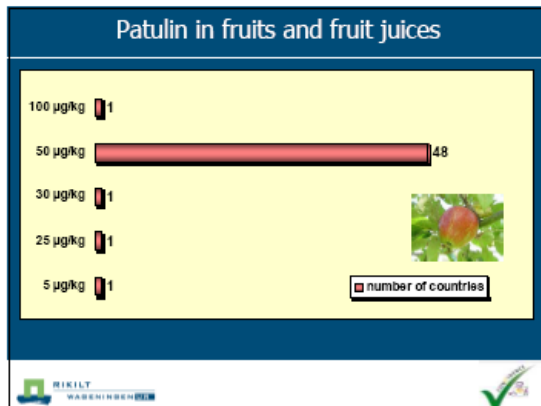
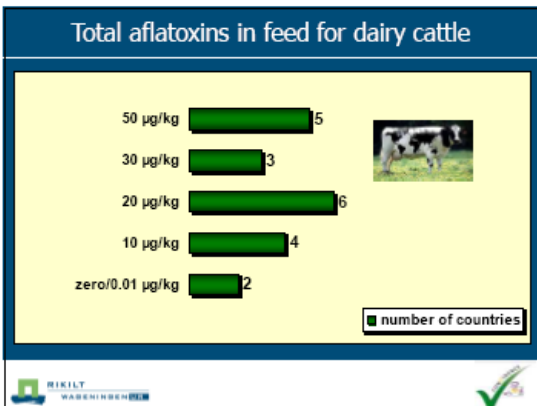
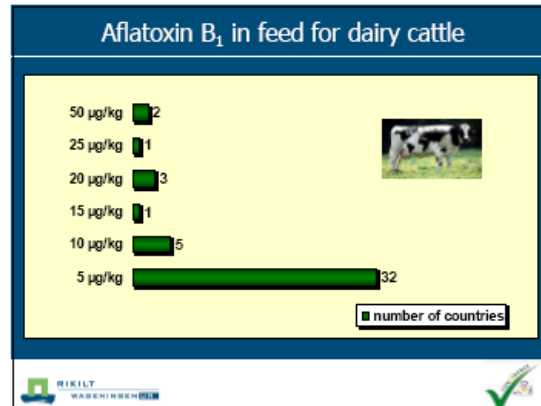
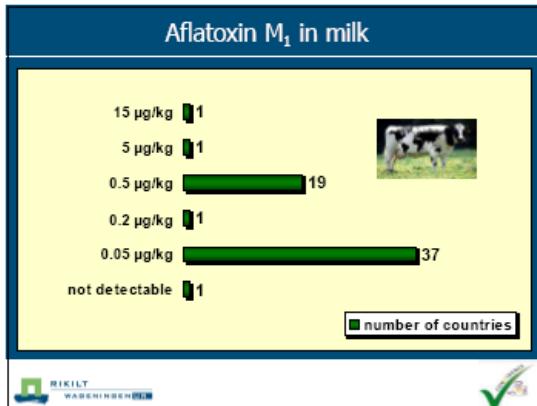
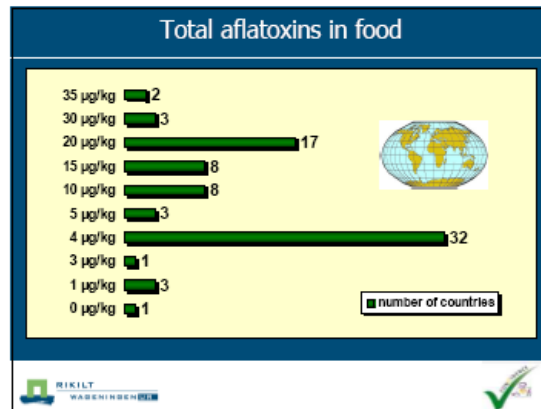
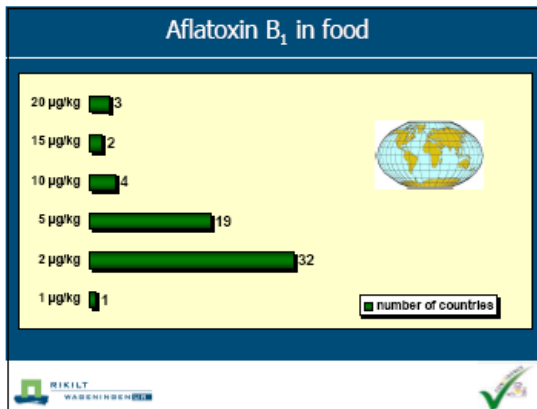
Various translations of FNP 81 available

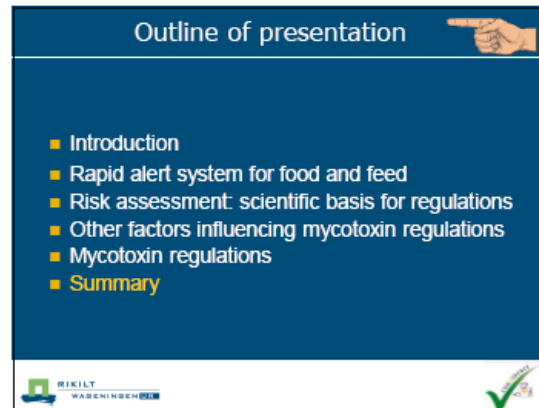
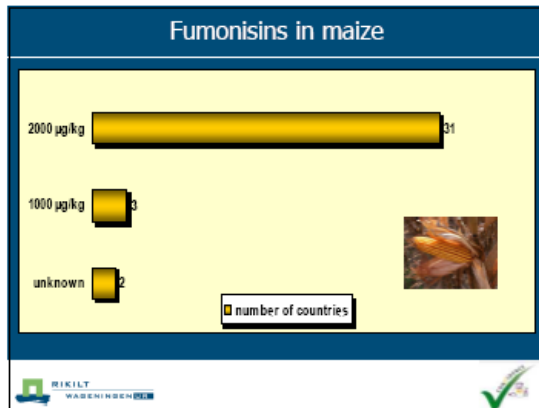
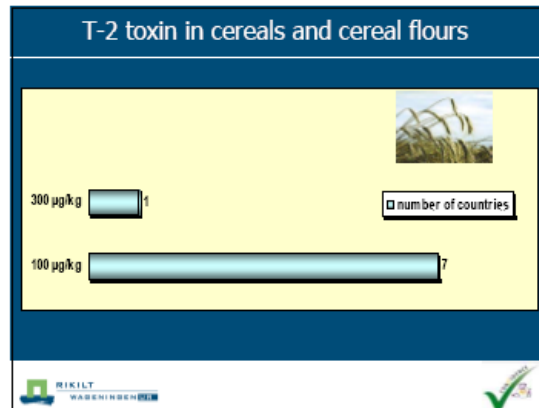
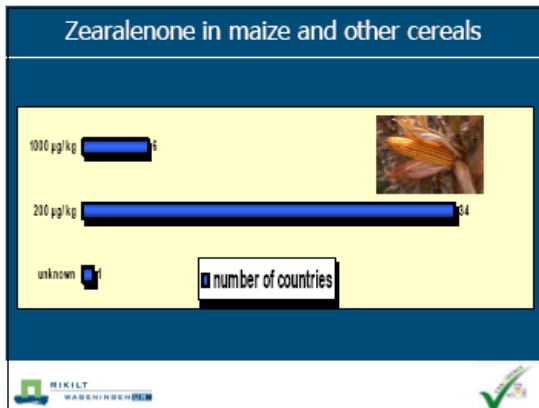
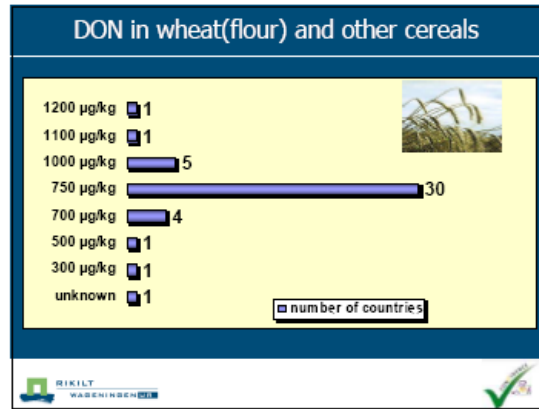
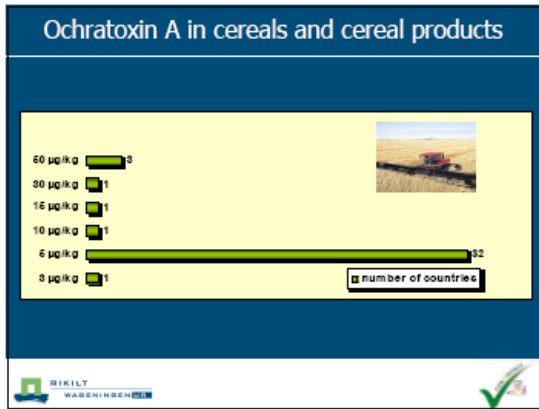



Mycotoxin regulatory situation in Europe

- 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












Summary

- 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, new mycotoxin regulations are expected in the coming years



Risk assessment and regulations for mycotoxins



Hans van Egmond, CONFIDENCE presentation 4 October 2011

