EFSA mycotoxin occurrence, data request & exposure assessment

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EFSA – European Food Safety Authority

“Europeans enjoy one of the highest levels of food safety in the world.”

“ensures safe, healthy food for consumers → field to fork”

http://www.efsa.europa.eu/
EFSA

- The European Parliament and the Council adopted Regulation (EC) 178/2002 which sets general principles and requirements of the General Food Law

- EFSA is an agency legally established by the EU under the Regulation 178/2002
  - Operates independently of the EU Member States
  - Responsible for scientific advice (risk assessment) and support (to communicate on risk to the public)

„Food is essential to life. EFSA is working to keep food safe.“

http://www.efsa.europa.eu/
EFSA

- The reason to establish agency like EFSA?
- Why do we need risk assessment in food industry?

- Series of food scandals during the 90’s
- Production and consumption of food is constantly changing
  - Advances in food technology
  - Climate change
  - New eating habits
  - Globalization of trade

http://www.efsa.europa.eu/
EFSA

- EFSA → risk assessor
  - Collects and analyzes data, together with EU Member States → European risk assessment is substantiated by the latest, clear scientific information

- **Only then** the EU legislators (European Commission – EC) will authorize a certain claim

EFSA’s task is also **risk communication**
- To establish the bridge between science and consumers
- To provide accurate information on food safety in time!

http://www.efsa.europa.eu/
Different Scientific Committees and Panels

- Independent scientific experts with a three-year mandate
- Carry out scientific assessments
- Some of them AHAW, ANS, BIOHAZ, CONTAM....
  - AHAW – Panel on Animal Health and Welfare
  - ANS – Panel on Food Additives and Nutrient Sources Added to Food
  - BIOHAZ – Panel on Biological Hazards
  - ...

http://www.efsa.europa.eu/
Panel on Contaminants in the Food Chain (CONTAM)

- Panels engage scientists (chemists, toxicologists, epidemiologists, statisticians, etc. → Panel Members) from all over Europe
- Gives scientific advices and risk assessment on chemical contaminants like mycotoxins, other natural toxicants, or residues of unauthorized compounds to EU risk managers

http://www.efsa.europa.eu/
CONTAM

- CONTAM on mycotoxin-contaminated food and feed
  - Assess human and animal exposure (occurrence data)
  - Exposure for specific population groups
  - Exposure of different animal species
  - Evaluate the toxicity of mycotoxins for humans and animals
  - Recommendations for the collection of further data on mycotoxins that enable better risk assessments

- EU legislation
  - EC Regulation → maximum levels for mycotoxins in food and feed
  - EC Recommendations → agricultural, storage and processing procedures

http://www.efsa.europa.eu/
Risk assessment

- 3 pillars of risk analysis:
  - Risk assessment
    - Hazard identification
    - Hazard characterization
    - Exposure assessment
    - Risk characterization
  - Risk management
  - Risk communication

Hazard assessment + exposure assessment

What is the potential damage?
What is the extent of damage?
What is the probability of damage?

Prof. Dr. S. Godefroy; lecture at IFA-Tulln, 2016
http://www.who.int/en/
Risk assessment

Occurrence data

Consumption

Exposure

Prof. Dr. S. Godefroy; lecture at IFA-Tulln, 2016
http://www.who.int/en/
Call for data

- Upon receiving request from the EC to deliver scientific opinions on risk related to certain mycotoxins calls for data are issued by EFSA

  “Share your data with EFSA. Contribute to food safety in Europe.”

- Collected data are extracted by the EFSA data management system and then used for writing future EFSA scientific opinions

http://www.efsa.europa.eu/
Closed calls for data

- EU Member States, research institutions, academia, national food authorities, industry, trade and any other stakeholders were invited to submit scientific data on occurrence of any of the following substances:

  - Deoxynivalenol (DON), 3-acetyl-deoxynivalenol (3-Ac-DON), 15-acetyl-deoxynivalenol (15-Ac-DON), DON-3-glucoside (DON-3-Glc) → closed in 2012
  - Nivalenol → closed in November 2010
  - Ergot alkaloids, citrinin, sterigmatocystine, beauvericin, enniatines, phomopsins, moniliformin, diacetoxyscirpenol → closed in January 2011
    - Deadline extensions for moniliformin and diacetoxyscirpenol

http://www.efsa.europa.eu/
Open calls for data

“Call for continuous collection of chemical contaminants occurrence data in food and feed” → 1. October each year

- Among them also for the following mycotoxins
  - Aflatoxins (B<sub>1</sub> in feed and B<sub>1</sub> and total in food, M<sub>1</sub> in dairy)
  - Ochratoxin A
  - Deoxynivalenol (and acetylated derivatives)
  - Zearalenone
  - Fumonisins
  - Patulin
  - T-2 and HT-2
  - Nivalenol
  - Ergot alkaloids

- This continuous call includes mycotoxins, for which Commission Recommendations for occurrence surveillance already exist

http://www.efsa.europa.eu/
Open calls for data

- “Main work in progress” → deadline extensions for scientific opinions
  - Deoxynivalenol, its metabolites and masked deoxynivalenol → 31. January 2017
  - Moniliformin → 31. December 2017
  - Diacetoxyiscirpenol → 31. December 2017
    - Deadline extensions for moniliformin and diacetoxyiscirpenol → January 2011
      → September 2014 → December 2017

Deoxynivalenol and its derivatives

- Trichothecene mycotoxin
- Produced by *Fusarium* fungi
- Contaminate grain and cereal-based food and feed

- In 2002, the Scientific Committee on Food (SCF)
  - TDI $\rightarrow$ 1 µg/kg BW/day
- In 2010, Joint FAO/WHO Expert Committee on Food Aditives (JECFA) converted TDI for DON into *DON and its derivatives*
  - Provisional maximum tolerable daily intake (PMTDI) $\rightarrow$ 1 µg/kg BW
  - Acute reference dose (ARfD) $\rightarrow$ 8 µg/kg BW

- Maximum limits and guidance values were set to decrease the presence of DON in food and feed
  - Maximum level for DON up to 1750 µg/kg

http://www.efsa.europa.eu/
EFSA Journal 2013; 11(10):3379
Deoxynivalenol and its derivatives

- Data on the presence of DON should to be reported regularly at the European level
- 26,613 analytical results submitted for DON and its derivatives (3-Ac-DON, 15-Ac-DON, DON-3-Glc)
  - By 21 Member State and Norway
  - Croatia did not submit the results
  - Samples collected between 2007 and 2012
- At the highest levels, also most frequently DON was found in corn, wheat and oat grains and their food and feed products

Deoxynivalenol and its derivatives

- Acetylated DON derivatives were not found frequently, also in lower concentrations
  - DON was also present in most of the samples where 3-Ac-DON and 15-Ac-DON were quantified

- Occurrence data for DON-3-Glc submitted by 1 Member State
  - Found in around 5% of samples, almost always with DON
  - Not taken for the exposure assessment

- Main contributors to chronic exposure were bread and rolls
  - 30.9% to 72.3% of total exposure

Deoxynivalenol and its derivatives

- Main contributors to acute exposure: grain milling products, bread and rolls, fine bakery ware and raw pasta
- CONTAM recommendations
  - Harmonize the sampling
  - Further data on 3-Ac-DON, 15-Ac-DON, and DON-3-Glc to characterize their contribution to the total exposure
  - Precise food description when submitting to EFSA
  - Report only one result which is considered most accurate when one sample analyzed using different analytical methods

Nivalenol (NIV)

- Trichothecene mycotoxin
- Produced by *Fusarium* genus fungi
- Causes general toxicity, haematotoxicity and immunotoxicity

- In 2000, the Scientific Committee on Food
  - Temporary tolerable daily intake (t-TDI) $\rightarrow 0.7 \, \mu g/kg \, BW/day$

- Almost 15 000 results were submitted
  - by 18 European countries

- CONTAM Panel evaluated 13 164 data on food, feed, and unprocessed grains for the Scientific Opinion

Nivalenol (NIV)

- Based on available occurrence data and estimation of chronic dietary exposures → NIV is not of health concern in 17 European countries
  - Highest mean concentrations observed in oats, maize, barley, wheat and their products
- NIV is unlikely genotoxic, therefore TDI was set
  - TDI → 1.2 µg/kg BW/day

Phomopsins

- Produced by *Diaporthe toxica* fungus
- Main host for fungus are lupins
  - Mainly animal consumption, but also for human consumption
- Phomopsin toxicosis (lupinosis) → “disease of sheep”
- Lupinosis reported also in cattle, goats, donkeys, horses and pigs

- No data submitted to EFSA
  - Exposure assessment was not possible
- No data from animal trials → no conclusions on the toxicokinetics

- So far → the oral LD$_{50}$
  - Sheep: 1.0 – 1.3 mg/kg BW
  - Nursling rats: 35 mg/kg BW

Phomopsins

- No risk assessment for either humans or livestock
  - Dose-response information on toxicities missing
  - Exposure/occurrence data missing
- CONTAM recommendations
  - Validate analytical methods for identification and quantification of phomopsins in food, feed, biological animal samples (from animal trials)
  - Collect data on the contamination in lupin-based food and feed with phomopsins
  - Estimate the consumption by human population and animals

Citrinin (CIT)

- Produced by *Aspergillus*, *Penicillium* and *Monascus* fungi
- Nephrotoxic mycotoxin
- Instable in various organic solvents and heat sensitive

- Only results for 30 samples submitted to EFSA
  - By 1 Member State
  - Samples collected in period from 2006 to 2008
  - EFSA investigated CIT occurrence reported in the literature

- CONTAM Panel concluded no-observed-adverse-effect level (NOAEL) of 20 µg/kg BW/day
  - A 90-day toxicity study in rats

Citrinin (CIT)

- Risk assessment not possible
  - Not only grain and grain-based products are source of CIT
  - No conclusion on chronic exposure for nephrotoxicity → not enough data

- CONTAM recommendations
  - Collect more occurrence data
  - Characterize dose-response relationship
  - Have certified reference materials
  - Collect data on carryover of CIT from the feed to animal products for human consumption
  - Validate analytical method in an inter-laboratory study

Sterigmatocystin (STC)

- Produced by *Aspergillus* fungi
- Shares biosynthetic pathway with aflatoxins

- Analytical results from 247 food and 334 feed samples submitted
  - By 2 Member States

- Adsorption of STC is limited after oral exposure
  - Insufficient data to assess the rate of carryover into milk
  - No information about carryover into meat or eggs

- Toxicity
  - Oral LD$_{50}$ between 120 and 166 mg/kg BW
  - Target organs liver and kidneys
  - Genotoxic and carcinogenic

Sterigmatocystin (STC)

- Risk characterization not possible
  - Absence of exposure data
  - An exposure to grains and their products of low health concern would range from 1.5 to 8 µg/kg
  - Bench Mark Dose Low (BMDL$_{10}$) of 0.16 mg/kg BW/day were calculated

- CONTAM recommendations
  - Occurrence data necessary for risk characterization
  - Methods with an LOQ lower than 1.5 µg/kg
  - Certified reference material needed
  - Proficiency tests to support analytical methodology

Beauvericin and enniatins (ENNs)

- Produced by *Fusarium* fungi species
- Predominantly contaminate cereal grains
- Cyclic hexadepsipeptides
  - 29 naturally occurring analogue enniatins identified

- 2147 analytical results for **beauvericin** and 10 538 for **ENNs** in food, feed, and unprocessed grain submitted
  - By 12 European countries
  - Sum of four enniatins (A, A1, B, B1) taken for the assessment
  - Samples collected in period between 2000 and 2013
Beauvericin and enniatins (ENNs)

- The highest mean concentrations of beauvericin found in dried fruits, oilseeds, cereal based food for infants and young children and of ENNs in coffee beans and raw pasta
  - Stable during commercial cereal processing
- Chronic exposure for beauvericin
  - Mean exposure range from 0.003 µg/kg BW/day to 0.050 µg/kg BW/day
- Chronic exposure to sum of ENNs
  - Mean exposure range from 0.42 µg/kg BW/day to 1.82 µg/kg BW/day

Beauvericin and enniatins (ENNs)

- Insufficient data for TDI or ARfD
- Risk assessment not possible
  - lack of toxicity data
- CONTAM recommendations
  - Inter-laboratory validation studies
  - Development of certified reference materials
  - \textit{In vivo} toxicity data needed
  - Co-occurrence of beauvericin with enniatins confirmed → but further data needed, as well as possible combined effects

Ergot alkaloids (EAs)

- Produced by sclerotia of *Claviceps* species
- In Europa most common *Claviceps purpurea*
- St. Antony’s fire, ergotism
- More than 50 EAs identified

- 25 840 analytical data submitted
  - By 14 European countries
  - All samples collected between 2004 and 2011
  - Selected data based on the presence of 4 most abundant EAs (ergotamine, ergocristine, ergocornine, ergosine)

- The highest concentrations reported in rye grains and rye-based products

Ergot alkaloids (EAs)

- Chronic exposure
  - Mean exposure range from 0.007 µg/kg BW/day to 0.080 µg/kg BW/day
- EAs can cause acute as well as chronic effects → appropriate to establish both ARfD and TDI
  - ARfD → 1 µg/kg BW
  - TDI → 0.6 µg/kg BW/day
- Available data do not indicate a health concern
- CONTAM recommendations
  - Continuance of collecting analytical data
  - Need for commercially reference standards

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Take home message:

1. EC, which is responsible for legislation, requests Scientific Opinion from EFSA on certain contaminants (among them mycotoxins)

2. EFSA opens call for data collection → institutions from EU Member States and other European countries are welcome to submit analytical results
   - Croatia did not submit data for the most prevalent mycotoxin before last Scientific Opinion

3. CONTAM Panel members write Scientific Opinions on risks regarding mycotoxins in food and feed

4. New Directives and Regulations are passed if Scientific Opinions proclaim upcoming risks

5. With new Directives and Regulations in force consumers eat safer food
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Thank you!