VKM's ranking of substances for monitoring in foods

Inger-Lise Steffensen

7th meeting in EFSA Network on Food Contact Materials (FCM)
Parma, November 6, 2019

Link to the report on www.vkm.no:

https://vkm.no/risikovurderinger/allevurderinger/fremmedstofferimatidentifiseringogrisikorangering.4.3f2ef1ad1674605a4e34ebfc.html

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Ranking of substances for monitoring in foods, drinks and dietary supplements - based on risk and knowledge gaps

Scientific Opinion of the Scientific Steering Committee of the Norwegian Scientific Committee for Food and Environment

Objectives

- To provide the Norwegian Food Safety Authority (NFSA) with a better knowledge base for their **prioritization of monitoring of chemical substances** in foods, drinks and food supplements

- To make a list of potentially harmful substances in foods, drinks and food supplements

- The included substances and the choice of methodology should be determined by VKM using expert judgments

- The basis for the ranking was information obtained from existing risk assessments; from EFSA, VKM or other institutions

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Objectives

- An overview of which foods, drinks and food supplements that should be analysed for the ranked substances
- Sampling procedures, number of samples, special considerations relevant for sampling (seasonal variations, which part of foods, e.g. plants, should be sampled) etc.
- The report should be simple and easy to use
- Substances already part of existing monitoring programs should **not** be included (veterinary medicine residues, illegal pharmaceuticals, pesticide residues)

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The project group

- Inger-Lise Steffensen (SC, Chair of project group)
- Jan Alexander (Chair of the SC)
- Trine Husøy (SC, Chair of Panel 4)
- Helle K. Knutsen (SC, Chair of Panel 5)
- Christiane Kruse Fæste (Panel 6)
- Robin Ørnsrud (Panel 6)
- Gro H. Mathisen (VKM Secretariat)

SC: VKM Scientific Steering Committee

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- Trine Husøy (SC, Chair of Panel 4) – CEP+FAF
- Helle K. Knutsen (SC, Chair of Panel 5) - CONTAM
- Christiane Kruse Fæste (Panel 6) - FEEDAP
- Robin Ørnsrud (Panel 6)
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SC: VKM Scientific Steering Committee – Scientific Committee

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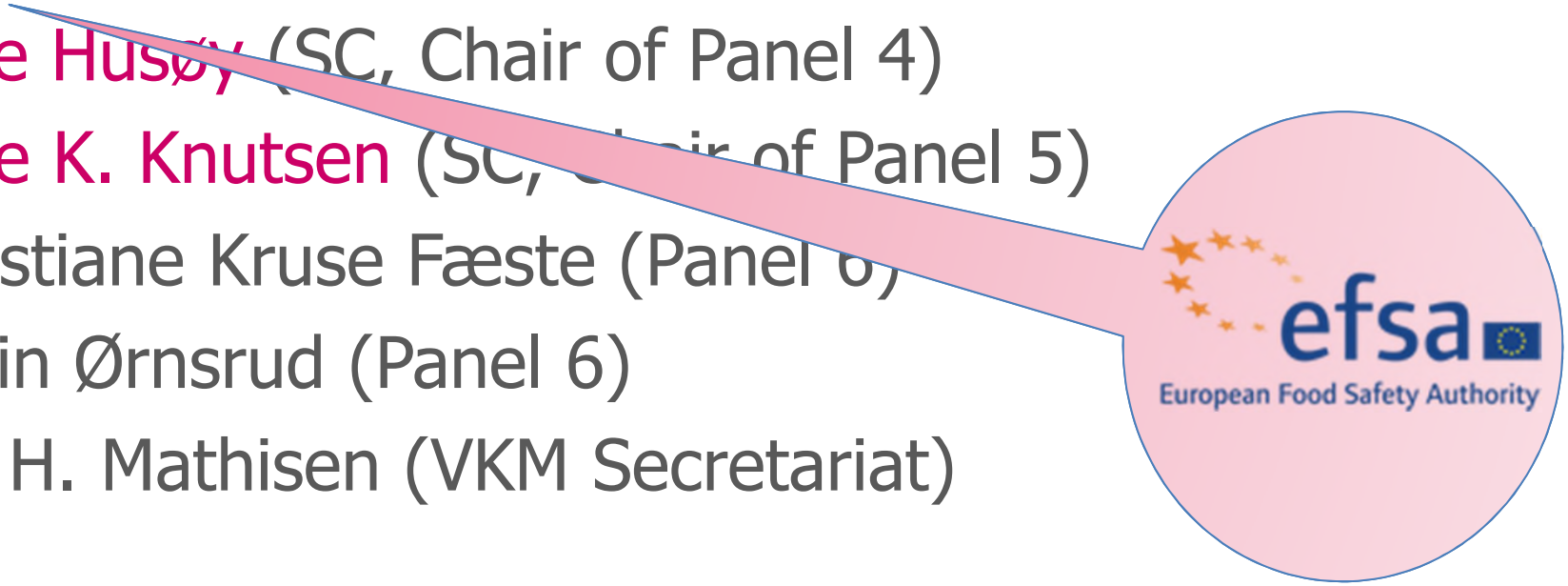

SC: VKM Scientific Steering Committee

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Extensive report on risk ranking methods

EFSA external scientific report Critical review of methodology and application of risk ranking for prioritisation of food and feed related issues, on the basis of the size of the anticipated health impact (EFSA supporting publication 2015:EN-710, URL: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/sp.efsa.2015.EN-710)

EFSA supporting publication 2015:EN-710

EXTERNAL SCIENTIFIC REPORT

CRITICAL REVIEW OF METHODOLOGY AND APPLICATION OF RISK RANKING FOR PRIORITISATION OF FOOD AND FEED RELATED ISSUES, ON THE BASIS OF THE SIZE OF ANTICIPATED HEALTH IMPACT[1]

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ABSTRACT

This study aimed to critically review methodologies for ranking of risks related to feed/food safety and nutritional hazards, on the basis of their anticipated human health impact. An extensive systematic literature review was performed to identify and characterize the available methodologies for risk ranking in the fields of feed and food safety and nutritional hazards, as well as the socio-economic field. Risk ranking methods from the environmental field were studied as well to determine whether approaches used in this field could also be applied for ranking human health risks related to feed and food safety and nutritional hazards. The review used a predefined search protocol. It covered the bibliographic databases Scopus, CAB Abstracts, Web of Sciences, and PubMed over the period 1993-2013. All references obtained were stored into an Endnote database and evaluated for their relevance. All references deemed to be relevant were studied in-depth so as to characterize the risk ranking method described. Characteristics of each method were stored in an Excel database. The methods for risk ranking were then grouped into method categories, which were described in general. These groups included: risk assessment, comparative risk assessment, risk ratio method, scoring method, cost of illness, DALY/QALY, willingness to pay, multi criteria decision analysis, risk matrix, flow charts/decision trees and expert judgment methods. Based on the characteristics of the individual methods and the method categories, an overarching framework was developed for selection of the appropriate method(s) that could be used for risk ranking of feed and food related hazards, on the basis of human health impact. This framework has the format of a decision tool, with which – given the characteristics of the risk ranking question at hand - the most appropriate method(s) can be selected. Application of this overall framework to several case studies showed it can be a useful tool for risk managers/assessors to select the most suitable method for risk ranking of feed/food and diet related hazards, on the basis of expected human health impact.

DISCLAIMER

The methodology used for ranking

- Because of limited time available, a simple methodology was suggested by the project group
- The methodology was discussed in VKM's Steering Committee and tested on a few substances and thereafter slightly modified
- The ranking of the substances was based on scoring of their toxicity, exposure (both occurrence in foods and intake of foods), potential vulnerable groups and the adequacy of data on both toxicity and exposure
- Each of 6 questions was scored in three categories (low, middle, high score) and the total score, i.e. the sum of points in all 6 questions, was used for ranking

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The methodology used for ranking

1. Quantitative data available for both toxicity and exposure; MOE, ADI/TDI/TWI (6, 4, 2)
2. Toxicity of the substance or group of substances (3, 2, 1)
3. Exposure from foods, drinks and food supplements (3, 2, 1)
4. Vulnerable groups (1, 0.5, 0)
5. Adequacy of toxicity data (1, 0.5, 0)
6. Adequacy of exposure data (1, 0.5, 0)

In total 9 – 2 points (high – low priority for monitoring)

Each substance/group of substances was assessed and scored on the basis of either questions 1, 4, 5 and 6, **or** 2, 3, 4, 5 and 6

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1. Quantitative data for both toxicity and exposure

Margin of exposure (MOE) is calculated if sufficient quantitative data are available. If available **acceptable daily intake (ADI)**, **tolerable daily intake (TDI)** or **tolerable weekly intake (TWI)**, it will be scored depending on whether the exposure is below or above these values

MOE = NOAEL or BMDL divided by EXPOSURE

MOE must be interpreted separately for substances without threshold (genotoxic) and substances with threshold (non-genotoxic) since acceptable MOE will be different in these two cases

- High score (6), when MOE is too low or the exposure is above ADI/TDI/TWI
- Middle score (4), when MOE is close to acceptable value or the exposure is close to ADI/TDI/TWI
- Low score (2), when MOE is sufficiently high or exposure is well below ADI/TDI/TWI

NOAEL: no observed adverse effect level

BMDL: benchmark dose lower confidence limit

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2. Toxicity of the substance/group of substances

- High score (3), if the substance(s) has high toxicity based on available knowledge
- Middle score (2), when middle toxicity
- Low score (1), when low toxicity

3. Exposure to the substance/group of substances from foods, drinks or food supplements

- High score (3), when high exposure based on data on **occurrence** of the substance(s) in foods/**intake** of relevant food types or **biomonitoring** showing high total exposure, from food as one important source
- Middle score (2), when middle exposure
- Low score (1), when low exposure

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4. Vulnerable groups

- If the exposure is very high for one or several groups in the population, e.g. because of special food habits, or if one or several groups are especially vulnerable because of having a certain gene variant, disease, drug use or are in a susceptible age/life stage (infants <1 year, puberty, pregnant/breastfeeding women, elders), a high score is given (1)
- If the exposure is somewhat higher for one or several groups in the population or if one or several groups are somewhat susceptible, a middle score is given (0.5)
- If there are no known groups with especially high exposure or there are no known susceptible groups, a low score is given (0)

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5. Adequacy of toxicity data

- High score (1), when there are very little data on toxicity of the substance/group of substances
- Middle score (0.5), when some lack of data on toxicity
- Low score (0), when sufficient/good data on toxicity

6. Adequacy of exposure data (occurrence and/or intake, in Norway and/or EU)

- High score (1), when there are very little data on exposure to the substance/group of substances
- Middle score (0.5), when some lack of data on exposure
- Low score (0), when sufficient/good data on exposure

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Substances included in the ranking

- **Natural toxins**; mycotoxins, plant toxins, marine and freshwater algae toxins
- **Metals and metalloids**
- **Persistent organic pollutants (POPs)**; brominated flame retardants, dechloranes, dioxins and dioxin-like polychlorinated biphenyls (DL-PCBs), non-dioxin-like polychlorinated biphenyls (NDL-PCBs), perfluorinated and polyfluorinated alkyl substances (PFAS) and siloxanes
- **Substances in food contact materials**; bisphenols and phthalates
- **Flavourings**; caffeine
- **Food additives**; nitrites and nitrates, phosphates, sweeteners and synthetic antioxidants
- **Process-induced contaminants**; acrylamide, esterified 3- and 2-monochloropropane-1,2-diol (MCPD), glycidyl fatty esters (GEs), furans, heterocyclic aromatic amines (HAAs) and polycyclic aromatic hydrocarbons (PAHs)
- **'Other substances'**
- **Trace elements**; iodine

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List of ranked substances - scoring 8.5-6.5

Substance	Score
T-2 (T2) and HT-2 (HT2) toxins and modified forms	8.5
Furan, 2-Methylfuran and 3-Methylfuran	8.5
Pyrrolizidine alkaloids (PAs)	8.0
PFOS* and PFOA*	8.0
Dioxines and Dioxin-like PCBs (DL-PCBs)	8.0
Glycidyl fatty acid esters (GE)	8.0
Acrylamide	8.0
Lead (Pb)	7.5
Aflatoxins (AFLAs)	7.5
Phosphoric acid-phosphates	7.5
Methylmercury (MeHg)	7.0
2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP)	7.0
Heterocyclic aromatic amines (HAAs) in general	7.0
Iodine	7.0
Caffeine	6.5
Enniatins (ENNs)	6.5
Ethoxyquin (EQ)	6.5
Solanine and Chaconine	6.5
Azaspiracids (AZAs)	6.5
Tetrodotoxin (TTX) and TTX analogues	6.5
Microcystins (MCs)	6.5
Cadmium (Cd)	6.5
Inorganic arsenic (As)	6.5
PFHxS*, PFNA*, PFDA*, PFUnDA* and PFHpS*	6.5
Bisphenol S (BPS), Bisphenol F (BPF) and Bisphenol AF (BPAF)	6.5

*Perfluorooctane sulfonate (PFOS), Perfluorooctanoic acid (PFOA), Perfluorohexane sulfonic acid (PFHxS), Perfluorononanoic acid (PFNA), Perfluorodecanoic acid (PFDA), Perfluoroundecanoic acid (PFUnDA), Perfluoroheptane sulfonate (PFHpS)

List of ranked substances - scoring 6.0-4.0

Deoksynivalenol (DON) and modified forms	6.0
Alternariol (AOH) and Alternariol methyl ether (AME)	6.0
Tropane alkaloids (TAs)	6.0
Polycyclic aromatic hydrocarbons (PAHs)	6.0
Curcumin	6.0
Lycopene	6.0
Cyanogene glucosides	5.5
Ochratoxin A (OTA)	5.5
Non-dioxin-like PCBs (NDL-PCBs)	5.5
3-Monochloropropanediol (3-MCPD) and its fatty acid esters	5.5
Docosahexaenoic acid (DHA)	5.5
Sodium and potassium salts of nitrite and nitrate	5.5
Erucic acid	5.0
Dechlorane plus (syn-DP and anti-DP)	5.0
Butylated hydroxytoluene (BHT, E321)	5.0
Aluminium (Al)	4.5
Acesulfame K (E950)	4.5
Piperine	4.5
L-Aspartic acid	4.5
L-Tyrosine	4.5
Organic arsenic (As)	4.0
Butylated hydroxyanisole (BHA, E320)	4.0
Glucosinolates	4.0
Dodecamethylcyclohexasiloxane (D6)	4.0
Hexabromobenzene (HBB)	4.0
Decabromo-dipheyl ethane (DBDE)	4.0
1,2-Bis(2,4,6-tribromophenoxy)ethane (BTBPE)	4.0
2,4,6-Tribromophenol (TBP)	4.0
L-Carnithine and L-Carnitine-L-tartrate	4.0
L-Methionine	4.0
Conjugated linoleic acids (CLAs)	4.0

List of ranked substances - scoring 3.5-3.0

Patulin (PAT)	3.5
Octamethylcyclotetrasiloxane (D4)	3.5
Decamethylcyclopentasiloxane (D5)	3.5
Polybrominated diphenyl ethers (PBDEs), including DecaBDE*	3.5
Di-butylphthalate (DBP)	3.5
Butyl-benzyl-phthalate (BBP)	3.5
Bis(2-ethylhexyl)phthalate (DEHP)	3.5
Di-isononyl phthalate (DINP)	3.5
Di-isodecyl phthalate (DIDP)	3.5
Inositol	3.5
L-Cysteine and L-Cystine	3.5
Creatine	3.5
Zearalenone (ZEN) and modified forms	3.5
Nickel (Ni)	3.0
Hexabromocyclododecane (HBCDD)	3.0
Bisphenol A (BPA)	3.0
Sucralose (E955)	3.0
Coenzyme Q10 (CoQ10)	3.0
D-Glucurono-γ-lactone	3.0
Taurine	3.0
Eicosapentaenoic acid (EPA)	3.0
Docosapentaenoic acid (DPA)	3.0
Chromium (Cr)	3.0

*Decabromodiphenyl ether (DecaBDE)

Comments in addition to the scoring

- Especially high exposure for a substance in Norway or differences in exposure in Norway vs. EU
- Large uncertainty in the scoring, including old or temporary ADI/TDI/TWI values
- Indications of other sources of exposure based on biomonitoring not included here (non-foods)
- Anticipated changed/increased exposure because of climate changes or changes in intake habits etc.
- Ongoing risk assessments of a substance by EFSA or others

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The way forward and updates

- NFSA will use this report to plan and prioritize their monitoring projects for 2020
- The report is anticipated to be updated every 3-5 years
- **Updates:** NSFA has announced that they want even more focus on which foods to monitor, sources of exposure, sampling practises etc.
- Literature searches will be needed, expert judgements not sufficient, for selection of substances, and especially for knowledge on sampling?
- Other methodology used for scoring, other weighing in scoring of each question? Not include scoring of data adequacy?

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Thank you for your attention!

Questions?
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1. Quantitative data for both toxicity and exposure

- Too low MOE: **<10 000** based on **BMDL10** (the lower limit of a one-sided 95% confidence interval on the Benchmark Dose (BMD) corresponding to 10% tumour incidence over the control) or **<25 000** based on **T25** (the chronic dose in mg/kg body weight per day that gives tumors in a certain tissue in 25% of the animals during their life-time, after correcting for spontaneous tumors in the negative control group) for **genotoxic** and/or **carcinogenic substances (assumed to be without threshold**)

- Too low MOE: **<100** based on no observed adverse effect level (NOAEL) or **<1 000** based on lowest observed adverse level (LOAEL) for **non-genotoxic substances (with a threshold)**. If NOAEL or LOAEL is from a subchronic, rather than a chronic experiment, an additional **factor 3** may be used

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