Rapport nr 8/2016

Endocrine active substances in the food – what is the problem?

Hormonstörande ämnen i maten – vad är problemet?

Documentation of a workshop organiserad by the National Food Agency (NFA, Sweden) and Swedish Chemicals Agency (KemI) held in Uppsala at Uppsala Concert and Congress, 3 November 2015

Livsmedelsverket
National Food Agency

Contents

Abbreviations:

ADI = Acceptable Daily Intake
EDC = endocrine disrupting chemical
EFSA = European Food Safety Authority
KemI = Swedish Chemical Agency
MoE = Margin of Exposure
NFA = National Food Agency Sweden
TDI = Tolerable Daily Intake
WHO/IPCS = World Health Organisation/International Programme on Chemical Safety

Summary

Work is ongoing in the EU (http://ec.europa.eu/environment/chemicals/ endocrine/ index_en.htm) to develop scientific criteria at EU level for the identification and determination of endocrine disrupting chemicals (EDCs) and properties for regulating biocides and pesticides. However, since these criteria are delayed, originally required by 13 December 2013, so-called interim criteria for the protection of human health are still in place and applicable for the pesticide and biocide regulations.

Chemicals that have the ability to act as endocrine disruptors can be found in foods, including drinking water, for different reasons and arising from different sources. They may contaminate food because some of them are contaminants in the environment (e.g. dioxins, PCBs, cadmium, perfluorinated alkyl substances), others migrate from food packaging materials (e.g. phthalates, bisphenol A), are food additives, veterinary drugs or pesticides, or occur as a natural component of some common food plants or fungi (e.g. phytoestrogens in soy, mycotoxins, etc.).

Concerning risk assessment of EDCs, most participants at the workshop were of the opinion that all substance in foods (intentionally added, non-intentionally and natural substances) should be assessed in the same way. However, risk management measures may be different due to various possibilities and needs to reduce exposure. It was considered that intentionally added substances would be easier to handle than naturally occurring substances. For unavoidable natural substances it was suggested to make a risk-benefit assessment. In certain cases, there would be a need to identify dietary patterns and sensitive population groups. However, at least food supplements containing isoflavones (e.g. from soy), do not seem to be a health risk according to a recent Efsa evaluation (2015).

Non-threshold EDCs may be treated as genotoxic substances. For EDCs if an adequately demonstrable unequivocal threshold mechanism can be demonstrated they may be assessed by traditional risk assessment methodology. However, it was emphasised that even if a threshold does exist, it might not be possible in practise to identify that threshold. Other factors that may be considered in the risk assessment process are severity and potency.

Although exposure to EDCs in foods is important, other oral sources (e.g. drugs and dust exposure of children) and other routes of exposures (e.g. inhalation and dermal uptake) may contribute to the overall exposure to EDCs. Also, the same chemical may be taken up via several routes resulting in combined exposure, a consideration that is sometimes overlooked. Some known examples that exemplify this are for phthalates exposure occurring via inhalation and oral intake from e. g. toys for children, and for parabens in cosmetics via dermal uptake and orally as food additives.

In addition, test methods need to be improved in order to detect ED effects and there is a special important need to identify sensitive/critical windows during the human development.

Introduction

Within the framework of the Action plan for a toxic-free everyday environment (Giftfri vardag) the National Food Agency (Livsmedelsverket) and the Swedish Chemicals Agency (Kemikalieinspektionen) organised a workshop on hormone active/ disrupting substances focusing on exposure via food. The purpose of the workshop was to establish a common knowledge base on which the participants would base their discussions on the current challenges and problems regarding the possible identification of hormonally active and potentially endocrine disrupting substances in the food chain. The workshop was also a fora to promote contact and cooperation between researchers and authorities, and to support and improve the authorities' impact on the EU and international processes.

The workshop was primarily aimed at researchers and agencies within the Swedish Chemicals Agency "Network for endocrine disruptors".

Venue: Uppsala Konsert och Kongress
Visiting adress: Vaksala torg 1, 753 31 Uppsala
Date: 3 November, 2015.

Programme

Moderator: *Leif Busk, National Food Agency*

09:00 - 09:10	Introduction *Per Bergman, National Food Agency,. Sweden*
Presentations:	
09:10 - 10:00	Crash course in endocrinology *Olle Söder, Karolinska Institute, Sweden*
10:00 - 10:30	Coffee/tea
10:30 – 11:20	Epidemiology and endocrine disrupting chemicals. The example cadmium *Agneta Åkesson, Karolinska Institute, Sweden*
11:20 – 11:50	Exposure assessment of potential endocrine disrupting chemicals in foods *Per Ola Darnerud, National Food Agency, Sweden*
11:50 – 12:30	Efsa´s opinion on isoflavones *Ursula Gundert-Remy, Efsa*
12:30 – 13:20	Lunch
13:20 – 13:50	Potential endocrine active substances in plant protection products – regulatory aspects *Runa Njålsson, Swedish Chemicals Agency*
13:50 – 14:20	Emerging chemicals in food packaging – toxicological profiling of knowns and unknowns? *Ann-Marie Vinggaard, DTU, Denmark*
14:20 – 14:40	Potential endocrine active substances in food contact materials and as food additives *Kettil Svensson, National Food Agency, Sweden*
Workshop:	
14:40-16:30	Workshop (including coffee/tea) *All participants*
Closing:	
16:30	Concluding remarks *Gregory Moore, KemI*

About the speakers

Prof. Olle Söder:
Olle Söder, MD, PhD, is Professor and Head of the Department of Women's and Children's Health, Karolinska Institutet, and Senior Clinical Consultant of Paediatric Endocrinology at Astrid Lindgren Children´s Hospital, Stockholm, Sweden. He has had multiple national and international assignments in the field of paediatric endocrinology and was the President of the Swedish Paediatric Society, 2012-2014. He has 200 hits on Web of Science on research covering reproductive biology, late adverse effects of pediatric cancer treatment, and health effects and mechanisms of actions of endocrine disrupting chemicals.

Prof. Agneta Åkesson:
Agneta Åkesson, professor of epidemiology specialising in nutrition and toxicology at the Institute of Environmental Medicine (IMM), Karolinska Institute.
She holda a PhD in Environmental Medicine 2000. After a postdoc in nutritional epidemiology, a 4-yr research fellow-position from the Swedish Research Council/Medicine She received a senior lecturer position, 2013. She is Professor from 2015.

Ass. Prof. Per Ola Darnerud:
Per Ola Darnerud, associate professor in toxicology, has a long experience in food toxicology issues at the National Food Agency (NFA). His main present focus is exposure analysis, i.e. using different methods to estimate intake on individual, or population, level for compounds present in food.

Prof. Dr med. Ursula Gundert-Remy:
Ursula Gundert-Remy is a MD with special postdoctoral training in pharmacology and toxicology, clinical pharmacology as well as internal medicine. After 9 years as head of the medical reviewers in German Drug Agency, she became full a professor and chair holder in Clinical Pharmacology at Goettingen University, Germany. She then worked for 15 years at the Federal Institute for Risk Assessment as head of the Department with responsibility for the regulatory assessment of industrial chemicals, pesticides and biocides. After her retirement, Prof. Gundert-Remy is Guest Professor at Charité, the Medical Faculty in Berlin, Germany and Guest Scientist in the Federal Institute for Risk Assessment. She is serving as an expert on several panels, working groups and committees on the European and National Level e.g. for Efsa, and for the German Ministry of Labour.

Dr. Runa Njålsson:
Runa Njålsson is a toxicologist and co-ordinator at the unit for EU co-ordination at the Swedish Chemicals Agency. For the last six years she has represented Sweden at the Commission's Standing Committee on Plants, Animals, Food and Feed (Section Legislation). Amongst other things, this committee votes on the EU authorisations on active substances in plant protection products.

Prof. Ann-Marie Vinggaard:
Ann-Marie Vinggaard, is a professor at the National Food Institute, Technical University of Denmark, where she is heading the Molecular Toxicology group. She has greater than 20 years of experience within toxicology with a focus on endocrine activity of chemicals, cocktail effects of chemicals and mechanisms of toxicant action.

Dr. Kettil Svensson:
Kettil Svensson, risk assessor and toxicologist at the NFA. Focus has been on food contact materials for many years both within Nordic cooperation, Council of Europe (CoE) and Efsa. Other areas include chemicals in drinking water and radioactive contaminants in foods.

Abstracts

Crash-course in endocrinology

***Olle Söder*, Institute of Environmental Medicine, Karolinska Institutet, Sweden**

Multicellular organisms need regulatory systems to integrate and fine-tune cooperation between cells, tissues and organs into functional units at the systemic level. This control is important in the entire life-span from the early prenatal stage to senescence. For such purposes the nervous system is responsible for immediate signaling via nerve fibers and synapses while the endocrine system works through soluble long and medium distance acting messengers (hormones) transported in the blood stream to mediate less rapid responses. Important functions under endocrine control are regulation of energy supply and consumption, reproduction, growth and development, and control of internal environment and homeostasis. More specifically this includes, e.g., glucose metabolism, sexual differentiation and puberty, longitudinal growth, stress response, water and electrolyte balance, and blood pressure. Chemically, hormones constitute a mixed bag of biological substances including proteins, peptides, steroids and low molecular weight factors such as catecholamines and modified amino acids. Hormones act via well-defined receptor systems encompassing two different principles; the plasma membrane bound receptors and the intracellular nuclear receptors.

Endocrine disorders are typically of two major kinds; hypofunction or hyperfunction; which may be due to defective ligands (hormones), receptors or post receptor signaling. The endocrine system is frequently subject to autoimmune perturbations resulting in disease. Many but not all endocrine axes are controlled by feedback circuits. Typical examples are the feedback loops executed by hypothalamic releasing factors acting on the pituitary gland to produce tropic hormones that stimulate peripheral endocrine glands such as the thyroid, adrenals and gonads. The hormones secreted by these glands act on target tissues, but are also sensed at the central levels to control their circulating concentrations by negative feedback. The set points for this control are believed to be programmed in fetal or early postnatal life. Endocrinology is probably the clinical discipline in which the underlying physiology is most tightly linked to pathophysiology and disease. A good knowledge of the basic principles of endocrinology is required for a thorough understanding of endocrine disorders. Disruption of endocrine functions may lead to a multitude of disorders with immediate onset but also to late-onset consequences due to inadequate early programming of endocrine set-points for metabolic control and feedback circuits. The aim of this lecture is to give an overview of the endocrine system to set the scene for the forthcoming presentations and discussions on endocrine disruption.

Epidemiology and endocrine disrupting chemicals. The example cadmium

***Agneta Åkesson*, Institute of Environmental Medicine, Karolinska Institutet, Sweden**

It has been suggested that environmental pollutants mimicking the effects of estrogen contribute to the disruption of the reproductive system of animals and to the high incidence of hormone-related cancers in Western populations. Data supporting this association in humans has hitherto been sparse. This presentation will focus on a potential link between cadmium exposure and hormone-related cancers. In addition, a brief overview of two epidemiological studies on dioxin exposure in relation to non-cancer endpoints will also be given.

Cadmium, a ubiquitous environmental pollutant was shown to induce several well-characterized estrogenic responses in vivo, including increased uterine weight, hyperplasia and hypertrophy of the endometrial lining and increased mammary epithelial density in animals (Johnson et al. Nature Med, 2003). The public health consequences of such effects were, however, not known. We explored, in a collaborative project between experimental toxicologists and epidemiologists, the hormonal effects of cadmium with special focus on the risk of breast, endometrial and prostate cancer in humans. The mechanism of action of the potential endocrine modulative properties of Cd, mimicking the physiological actions of estrogen and androgen was explored experimentally. In experimental settings, using a transgenic mice-model and cell experiments, the hypothesis that the estrogenicity is caused by transcriptional activity of estrogen receptors or mediated via membrane-associated signaling was tested.

Dietary cadmium exposure was statistically significantly associated with increased risk of endometrial cancer; the multivariable-adjusted relative risk was 1.39 (95 % confidence interval (CI), 1.04-1.86; P_{trend}=0.019), comparing highest tertile of exposure with lowest. In sub-analyses among women with low exogenous and endogenous estrogen, a 2.9-fold increased risk (95 % CI, 1.05-7.79) was observed (lean never-smoking women who did not use postmenopausal hormones). A small, but statistically significantly increased risk of cancer of the breast and prostate (localized tumors) (21 % and 13 %, respectively) was also observed.

The experimental the data suggest that cadmium-induced estrogen-like effects do not involve classical estrogen receptor signaling but rather appear to be mediated via membrane-associated signaling. The activation/ transactivation of GPR30/EGFR-Raf-MEK-ERK/MAPKs and Mdm2 represent a general mechanism by which cadmium may exert its effects. Since EGFR, ERK and Mdm2 are all known key players in cancer promotion, cadmium-induced activation of these may have implications for the promotion/development of hormone-related cancers observed in some epidemiological studies.

Exposure assessment of potential endocrine disrupting chemicals in foods

***Per Ola Darnerud*, National Food Agency (Sweden)**

Exposure assessment is a crucial part of the risk assessment procedure, forming the bridge between hazard and risk. Thus, exposure assessment activities play an important role in risk benefit assessments made at the National Food Agency (NFA). In the traditional assessment, the exposure is subsequently compared to reference points for adverse health effects, beneath which the exposure should be without risk. The assessment of carcinogenic compounds is somewhat different, but routines for assessing these compounds have also been developed. However, risk assessment methods for endocrine disrupting compounds (EDCs) are still much debated, including the issue of how exposure data should be dealt with.

At present, exposure studies at NFA are performed by the use of both external and internal methods. External methods use production and purchase statistics or consumer questionnaires to obtain data on estimated consumption on population or individual level. Internal methods for assessing exposure mean that the actual body burden of the actual compound, or its metabolite(s), is measured by analyzing levels in e.g. blood, urine or breast milk. For both these methods, the risk assessment is made by comparing the exposure values with reference points for adverse health effects.

Focusing on exposure assessment of EDCs, there are several challenges, including the low doses and various exposure pathways that must be covered, possible contamination of food samples, the potentially fast degradation, and how to deal with "natural" EDCs, e.g. phytoestrogens. By studying some examples of potential EDCs, i.e. BHA (butylated hydroxyanisole; a food additive), several pesticides and phytoestrogens, the margin of exposure (MOE) seems to be sufficiently high, at least when comparing to generally acknowledged reference points. However, there are much new data questioning the use of only "established" end points in toxicity testing, and the dose-effect relationship is also under debate, as new low dose effects are reported and the dose-effect curve might have new, non-linear shapes. Thus, even if traditional exposure methods in many cases find EDCs in food at relatively safe levels, development of method for risk assessment of EDCs are needed.

Hazard identification and risk assessment – two different questions

The outcome of Efsa's risk assessment on food supplements containing isoflavones

***Ursula Gundert-Remy*, Charité , Berlin**

Isoflavones are naturally occurring substances which can be obtained from a variety of biotanical sources. The main isoflavones are genistein, daidzein, glycitein, formononetin, biochanin A and puerarin. They exert oestrogenic acitivty which is related to their chemical structure, which is similar to 17β-oestradiol. An further activity which is not related to their oestrogenic properties but due to an inhibition of TPO (thyroid peroxidase) is the interaction with the synthesis of thyroid hormone.

Hence, there is the hypothesis of potential adverse effects in peri- and post-menopausal women taking food supplements for relief of menopausal conditions. Three target organs were determined: mammary gland, uterus (estrogenic effects) and thyroid (TPO inhibition). The methodological approach of a systematic review was applied investigating the association between intake of isoflavones from food supplements and adverse effects on the three target organs in peri- and postmenopausal women. Human observational studies did not support the hypothesis of an increased risk of breast cancer from intake of isoflavones in food supplement. Also, no effect was noted in human interventional studies for mammographic density, and for proliferation marker Ki-67. For the effect on uterus endometrial thickness and histopathological changes up to 30 months were investigated without an adverse effect. After 60 months some hyperplastic, but non-malignant findings were reported. Thyroid hormones levels were found not to change with the intake of isoflavones from food supplements.

Animal studies in monkeys and rats were found in the literature in which adverse effects for mammary gland and the uterus were not observed with some exception.

In a weight of evidence approach it was concluded that there is no indication for an adverse effect on the three target organs in postmenopausal women taking isoflavone supplements in daily doses as tested (35-150 mg/da). The data in the literature were not sufficient to give a final assessment for perimenopausal women und for women with having a hormone sensitive tumour or a history of it.

It was not possible to derive a single guidance value for the different preparations containing different isoflavones. The doses used in the intervention studies and the duration of the studies could be help to give guidance for the use of food supplements in postmenopausal women.

Hence, there is clearly a hazard for adverse estrogenic effects which does not result in a risk, given the dose and duration applied by taking food supplements in postmenopausal women.

Emerging chemicals in food packaging – toxicological profiling of knowns and unknowns

***Anna Kjerstine Rosenmai[a], Linda Bengtström[b], Barbara van Vugt-Lussenburg[c], Jens Højslev Petersen[b], Camilla Taxvig[a], Terje Svingen[a], Laurianne Lesne[d], Mona-Lise Binderup[a], Marianne Dybdahl[a], Cecilie Ramskov-Andersen[a], Bernard Jégou[d,e], Kit Granby[b], Xenia Trier[b] & Anne Marie Vinggaard[a]*, DTU, Denmark**

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Thousands of chemicals currently in use are yet to be evaluated for their safety. This includes constituents of food packaging materials (FCM), which represents a significant source of human exposure to chemicals. To address this data gap on potential hazards posed by FCMs, we i) applied a 'bottom up' approach for toxicological profiling of bisphenol analogues and fluorinated compounds and ii) a 'top down' approach to identify new hazardous chemicals in FCMs of paper and board. The bisphenol A analogues (B, E, F, S & cumylphenol) showed generally similar endocrine activity on hormone receptors, hormone production and lipid accumulation in adipocytes. Based on these findings substitution of BPA with any of these analogues is not recommended. The fluorochemicals overall showed endocrine activity *in vitro,* though the effect depended on the fluorinated chain length, the degree of fluorination and the polar head group in the molecule.

We have developed a strategy for evaluating safety of FCMs of paper and board. An initial (Q)SAR screen of 2076 FCM substances predicted a potential for genotoxicity or developmental toxicity for >25 % of them. Twenty FCMs of paper and board underwent in vitro toxicological profiling (ER, AR, AhR, RAR, PPARγ, genotoxicity (p53, Ames) & oxidative stress). All FCMs showed activity in at least one assay, with most showing activity in several. Selected FCMs were fractionated and the active fraction identified by in vitro testing: i) A popcorn bag was Ames positive; ii) A pizza tray showed marked estrogenic activity, which was caused by bisphenol A and the phthalates BBP and DBP; Iii) A sandwich wrapper showed marked androgen receptor antagonism, caused by abietic acid and dehydroabietic acid, chemicals that are added to FCMs and display potent antiandrogenic activity. Migration of these chemicals to foods has been documented.

We suggest that only a fraction of all potential endocrine active chemicals in FCMs have yet been identified and thus that more efforts are required into the future. Our strategy will be a valuable tool for hazard evaluation of FCMs and for identifying emerging endocrine active or genotoxic chemicals.

Potential endocrine active substances in plant protection products – regulatory aspects

***Runa Njålsson*, Swedish Chemicals Agency**

According to Regulation (EC) 1107/2009, the Commission should by 14 December 2013 have presented a draft to the Standing Committee on the Food Chain and Animal Health of the measures concerning specific scientific criteria for the determination of endocrine disrupting properties. The work is delayed, while the Commission performs an impact analysis and discussions with stakeholders take place.

In the meantime, the regulation foresees the use of the interim criteria, as stated in Regulation 1107/2009, Annex II, point 3.5.6., paragraphs 3 and 4. However, as the discussions concerning the scientific criteria for endocrine disruptors are long and extensive, also the discussions on some aspects concerning both the so called 'cut-off' criteria and the interim criteria have been quite extensive. The 'cut-off' criteria implies that substances being (or having to be) classified as carcinogenic category 1A or 1B, toxic to reproduction category 1A or 1B or being identified as endocrine disruptors should not be approved, unless the exposure is negligible. The wording '…substances which *are* or *have to be* classified…' has caused some discussions and the term *negligible exposure* turned out to trigger heated discussions as this term in relation to the groups of substances mentioned above, opens up for approvals despite their hazard profile. In addition to this, Article 4(7) of Regulation 1107/2009 opens up for derogative approvals in certain cases.

A stipulated review of Regulation 1107/2009 is forthcoming, however, this too is delayed. Almost a year ago the Commission should have presented a report to the European Parliament and the Council on the functioning of several aspects of the regulation. The criteria for the approval of active substances are among the provisions specifically mentioned to be reviewed. The report may be accompanied by legislative proposals to amend the specified provisions. At the moment, nothing is known on how far the Commission will go in opening up the regulation for changes, or if anything beside the specified provisions will be included in the review.

Potential endocrine active/disrupting substances in food contact materials and as food additives

***Kettil Svensson*, National Food Agency, Sweden**

Approximately 3000 chemical substances are authorized within national legislations on food-contact materials (FCM) in Europe, but many more are used. Regulation EC No 10/2011 lists approximately 1000-1100 substances for use in plastics. Available lists of potential EDC identify several substances (~30-40) either authorized within national legislations or regulated in plastic within EU. Present EFSA guidance for submission of a FCM substance for evaluation does not fully consider endocrine activity, especially not the so called NIAS; non intentionally added substances such as impurities, metabolites, break-down products and reaction products. Efsa´s new proposed testing strategy for FCM consider to a higher degree new OECD guidelines for testing of chemicals addressing endocrine activity. An example are the OECD Guidelines TG 407 and TG 443 (EOGRTS) at level 4 of the OECD recommendations.

Also among regulated food additives within the EU legislation potential EDC occur. Preservatives such as parabens (hydroxybenzoates) and antioxidants like BHA (butylated hydroxyanisole) and BHT (butylated hydroxytoluene) have elicited interest. Even though the Efsa guidance for submission of a food additive evaluation has been updated to consider endocrine activity to a higher extent when a substance is being tested the system may fail to identify a substance as an EDC. Lack of in vivo data or in vitro data not according to guidelines (e. g. OECD) may delay such a determination.

Efsa is presently referring to the definition of WHO/ICPS, 2002: ”An endocrine disrupter is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organisms, or its progeny, or (sub) populations” in order to decide whether food additives are EDCs. In the absence of the new EU criteria for EDCs, the WHO/ICPS criteria will prevail when evaluating substances.

Workshop:
Summary of questions and answers

The meeting participants were divided into five groups consisting of around six persons per group. Each group was provided with six questions (see below) to answer and after an allotted time each group presented their answers and reflections taking turns either as main presenter or supportive presenters.

For support each group was recommended to be aware of the WHO/ICPS, 2002 definition for endocrine disruptors, i.e.:

"An endocrine disrupter is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)population."

Question 1.
Which endocrine disruptors occurring in food are the most problematic from a health point of view? Food can contain endocrine disruptors which are either intentionally added (e.g. food additives), or of natural origin (e.g. Phytoestrogens in soy products and mycotoxins), or contaminants (e.g. dioxins). Should intentionally added chemicals to be assessed differently from unintentionally occurring substances?

Answer 1.
Most participants were of the opinion that all substances (intentionally added, non-intentionally and natural substances) should be assessed in the same way. However, risk management may be different due to various possibilities to reduce exposure. It was considered that intentionally added substances would be easier to handle than naturally occurring substances.

Question 2.
How important is the exposure to endocrine disrupters in food? Are other routes of exposure more important? In some cases the endocrine disrupting effects occur at doses far higher than the dose that provides the critical effects for the setting of TDI/ADI.

Answer 2.
EDC exposure from foods is important, but other sources (drugs and dust and other routes of exposures (inhalation and dermal uptake) may be important depending on the substance. Some examples are uptake of phthalates via inhalation and oral intake from toys (children) and parabens in cosmetics via dermal uptake.

Question 3.
Is the concept of TDI/ADI appropriate for regulation of endocrine disruptors since that they may have effects at low-doses or no threshold dose? Is it necessary to use other approaches in risk assessment such as specific uncertainty factors or MoE (as for genotoxic carcinogens) or something else?

Answer 3.
Non-threshold EDCs may be treated as for genotoxic substances. EDCs with an adequately demonstrated threshold may be assessed by traditional risk assessment methods. However, it might be practically impossible to identify a threshold.

In addition, test methods need to be improved in order to detect ED effects/critical effects and especially identify sensitive/critical windows during the development.

Question 4.
Should all endocrine disrupting effects be assessed the same way, regardless of the severity and type of health effects?

Answer 4.
No, EDCs should be assessed depending on their potency and the severity of effects.

Question 5.
According to the Swedish Food Agency's dietary guidelines (NFA; www.livsmedelsverket.se) consumers are urged to eat more fruit and vegetables for their general good health. This however presents a potential dilemma when considering naturally occurring endocrine disruptors. For instance, how should we deal with the potential endocrine disrupting effects of phytoestrogens (which is mainly found in legumes) and similar natural substances in food?

Answer 5.
It was considered that a risk-benefit assessment should be conducted. In certain cases it is important to identify dietary patterns and sensitive groups. An example in question might be infant formula based on soy.

However, food supplements containing isoflavones do not seem to be a health risk in post-menopausal women according to a recent evaluation by Efsa (2015).

Question 6.
Food supplements can contain naturally occurring endocrine disrupters at high concentrations e.g. isoflavones that have effects on menopausal symptoms and osteoporosis. Is this a potential health risk which should be regulated?

Answer 6.
Isoflavones in food supplements do not seem to be a health risk in post-menopausal women according to a recent evaluation by Efsa (2015). However, other food supplements may be a health risk and may have to be regulated.

Conclusion

If new EU criteria for identification of EDCs imply restrictions or bans of such substances used or as contaminants in foods from a health point of view in a similar same way as for CMRs (carcinogenic, mutagenic or toxic to reproduction) this may have implications for food production, trade and authorities. Transparent exchange of views at an early stage between stakeholders regarding these challenges as well as possibilities may in addition benefit all parties concerned but more importantly the protection of human health.

Participants

Michael	Reineskog	IKEM - Innovations-och Kemi-industrierna i Sverige
Annika	Hanberg	IMM, Karolinska Institutet
Olle	Söder	Karolinska Institutet
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Christer	Andersson	Livsmedelsverket
Emma	Ankarberg	Livsmedelsverket
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Kettil	Svensson	Livsmedelsverket
Leif	Busk	Livsmedelsverket
Lillian	Abramsson	Livsmedelsverket
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Per	Bergman	Livsmedelsverket
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Rapporter som utgivits 2015

1. Spannmål, fröer och nötter -Metaller i livsmedel, fyra decenniers analyser av L Jorhem, C Åstrand, B Sundström, J Engman och B Kollander.
2. Konsumenters förståelse av livsmedelsinformation av J Grausne, C Gössner och H Enghardt Barbieri.
3. Slutrapport för regeringsuppdraget att inrätta ett nationellt kompetenscentrum för måltider i vård, skola och omsorg av E Sundberg, L Forsman, K Lilja, A-K Quetel och I Stevén.
4. Kontroll av bekämpningsmedelsrester i livsmedel 2013 av A Jansson, P Fohgelberg och A Widenfalk.
5. Råd om bra matvanor - risk- och nyttohanteringsrapport av Å Brugård Konde, R Bjerselius, L Haglund, A Jansson, M Pearson, J Sanner Färnstrand och A-K Johansson.
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