EFSA Draft Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuff

Comments on health effects of BPA

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DTU Food
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Introduction

- We acknowledge the very large and difficult task undertaken by EFSA in a systemic way

Several improvements:

- All studies, incl. non-oral dosing
- Effects on mammary gland development are evaluated as "Likely"
- New (and lower) t-TDI of 5 µg/kg bw per day
- Based on BMDL and mean HED of 113 µg/kg bw per day for effects on kidney weights in adult animals
- Conservative for kidney effects

Overall remark

- For several endpoints:
- "*The endpoint was therefore not taken forward for risk characterisation. The Panel considered nevertheless that the effects described may be of potential concern for human health and add to the uncertainty, which has been taken into account in the risk assessment.*"
- No details on how this potential concern has been taken into account
- Risk estimation or alternatively an additional uncertainty factor would be needed

Hazard identification and characterisation

- Kidney effects in adult animals and effects on mammary gland development are assessed as "Likely"
- Only these effects go on to Hazard characterization
- Excludes effects on e.g. male sexual development as well as neurodevelopmental effects
- Problematic as there are signs of effects at low doses for these types of effects

Mammary gland development

- Benchmark dose (BMD) - a good idea when data permits to do so
- BMD for mammary gland based on the new data in U.S. FDA/NCTR, 2013
- Effects on mammary gland development are excluded due to large variation on BMD
- A "classical" hazard assessment would be relevant, especially for a "likely" effect
- No access to U.S. FDA/NCTR, 2013 via EFSA or U.S. FDA

U.S. FDA/NCTR, 2013 -> Delclos et. al. 2014

Prepubertal female mammary glands

- Only histology –> only small amounts of tissue
- Whole mounts may be more sensitive
- Not possible to make final conclusions

Adult female mammary gland

- Increased incidence of duct hyperplasia at 300 mg/kg
- But: we find significantly more females with "mild" hyperplasia from 80 µg/kg ($p<0.05$, Fisher exact 2x2 test, naïve and vehicle animals pooled)
- Tentative LOAEL at 80 µg/kg and NOAEL at 25 µg/kg

• Hazard characterization, mammary gland

- Effects in rats and Rhesus monkeys at 250 or 400 µg/kg, respectively
- Similar HEDs: rats = 180 µg/kg; monkeys = 168 µg/kg
- Based on Delclos et al (2014), tentative LOAEL at 80µg/kg and NOAEL at 25µg/kg
- A NOAEL of 25µg/kg, the rat HEDF of 0.72 and a factor 25 as used for the kidney weight
- Leads to 0.7µg/kg

Reproductive and developmental effects

"... may be of potential concern for human health and add to the uncertainty... taken into account.."

- Uncertainty - some studies find effects and others do not
- Oral studies indicate effects on male sexual development, LOAELs of 250 or 260 µg/kg/day
- A factor of 5 to go from LOAEL to NOAEL, the rat HEDF of 0.72 and a factor 25 as used for the kidney weight
- Leads to 1.4-1.5 µg/kg day

Effects on male sexual development: "*The gold standard is fertility*"

Far too narrow view because:

- Assessment of fertility has limited sensitivity
- Marked reductions of rat sperm number (to 20%) is needed to see effects on fertility
- Different in humans - smaller reductions may affect fertility
- Effects on male sexual development may lead other severe effects, e.g. hypospadias, decreased penis length and possibly increased risk for prostate cancer

Neurodevelopmental effects

- *"may be of potential concern for human health and add to the uncertainty … taken into account"*
- Oral studies indicate a possible risk for developmental neurotoxicity at 100-250 µg/kg/day
- Using these LOAELs leads to 0.6-1.4 µg/kg

Concluding remarks, TDI

- Substantial uncertainty about the effects of BPA at low doses
- The new t-TDI of 5 µg/kg bw per day has not taken this sufficiently into account
- Studies indicate NOAELs at 25-50 µg/kg
- Margin of safety is only 5-10 – insufficient
- The new TDI should be lower, e.g. 0.7 µg/kg bw/day or lower

Concluding remarks, risk assessment

- *"…. the exposure for the highest exposed groups in the population is well below the t-TDI of 5 µg/kg bw per day, indicating that the health concern for BPA is low at the current level of exposure."*
- 0.7 µg/kg bw/day or lower
- Highly exposed groups: approx. 1.1 µg/kg for women and 1.5 µg/kg for teenagers
- Raise concerns about the health risks of BPA for the highest exposed groups

Thank you to EFSA for inviting me to present these comments

Thank you for your attention