Plastindustrien

Miljøstyrelsen
Kemikalier
Strandgade 29
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2. januar 2013

Faglig høring af ni kortlægningsrapporter

Miljøstyrelsen har den 11. december sendt ni kortlægningsrapporter i høring "med henblik på at sikre, at rapporterne indeholder al væsentlig eksisterende viden om de pågældende stoffers anvendelse, regulering, miljø- og sundhedsrisici og alternativer."

Med en høringsfrist på tre uger henover en jul er det ganske urealistisk at forvente faglige input, der i væsentlig grad kan bidrage til at sikre, at rapporterne indeholder al væsentlig viden.

Hvad angår rapporten om BPA og BPA diglycidylether polymer betyder den meget korte høringsfrist, at Plastindustrien samt den europæiske industri har haft meget begrænsede muligheder for at gennemgå og vurdere den ganske omfattende rapport og dermed levere det efterlyste kvalitetstjek.

Vi må også konstatere, at kortlægningsarbejdet har levnet ganske få muligheder for inputs. For BPA's vedkommende er der tale om meget store datamængder og omfattende information om anvendelse, regulering mv. Med ét enkelt opstartsmøde og ét egentligt fagligt møde, hvor 1. udkast blev præsenteret, kombineret med frister for kommentarer på få dage, har muligheden for at levere et kvalificeret indspil derfor været reduceret til nogle overordnede betragtninger.

Dette er naturligvis ikke rimeligt, hvis ønsket er at inddrage de forskellige interessenter i opgaven og forventningen er et kvalificeret fagligt bidrag.

Fra den europæiske plastindustri har vi modtaget vedhæftede bilag med bemærkninger til BPA kortlægningsrapporten. Bemærkningerne er blevet til i processen fra det første udkast til rapporten blev præsenteret og frem til nu. Bilaget rummer derfor kommentarer, som der muligvis allerede er blevet taget højde for, men som vi finder særdeles relevante for rapportens endelige udformning og som vi anmoder miljøstyrelsen om at inddrage.

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Vi opfordrer til, at styrelsen i de kommende kortlægningsprojekter for de resterende LOUS stoffer tilrettelægger processen således, at der bliver rigeligt med tid til at indhente bidrag fra relevante interessenter og at disse får tilstrækkelig mulighed for fagligt at kommentere rapportudkastene.

Venlig hilsen

Helle Fabiansen

BILAG

Comments regarding Survey of Bisphenol A and Bisphenol-A-diglycidylether polymer
Part of the LOUS-review

- The document makes reference several times of Beronius et al: Beronius et al 2012 apparently list potential reference doses ("ADIs") based on "low dose-studies". It is the authorities (e.g. EFSA and others) as well as our position that the studies mentioned are not suitable for setting a reference dose because they have severe shortcomings.
    - ***Carr RL, Bertasi FR, Betancourt AM, Bowers SD, Gandy BS, Ryan PL, Willard ST. 2003. Effect of neonatal rat bisphenol A exposure on performance in the Morris water maze. J Tox Environ Health Part A 66: 2077-2088.***
      EFSA 2010, http://www.efsa.europa.eu/en/efsajournal/doc/1829.pdf: „…Because of these shortcomings, the Panel concludes that this study should be considered of limited value for risk assessment purposes."
      FDA 2008, http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-0038b1_01_02_FDA%20BPA%20Draft%20Assessment.pdf: "…FDA concludes that this study is limited in its utility in determining an assessment for oral exposure to BPA."
    - ***Viberg H, Fredriksson A, Buratovic S, Eriksson P. 2011. Dose-dependent behavioral disturbances after a single neonatal Bisphenol A dose. Toxicology 290: 187-194.***
      The dose tested is an unrealistically high dose and of no relevance to human safety or exposure.
    - ***Jenkins S, Raghuraman N, Eltoum I, Carpenter M, Russo J, Lamartiniere CA. 2009. Oral exposure to bisphenol a increases dimethylbenzanthracene-induced mammary cancer in rats. Environ Health Perspect 117(6): 910-915.***

      EFSA 2010, http://www.efsa.europa.eu/en/efsajournal/doc/1829.pdf: „In consideration of the shortcomings in the design of both studies, in particular the uncertainty regarding the lactational as well as in utero exposure of the offspring to BPA, and of the limitations in reporting the Panel concluded that these results cannot be taken into consideration for derivation of a TDI. However, the Panel noted that at the highest dose level studied there is a shift of the ratio between cell proliferation and apoptosis in favour of cell multiplication in the mammary gland. In view of the mechanistic data obtained upon in utero exposure in other studies (see section 5.3) and the implications of an increased cell proliferation/apoptosis ratio in carcinogenesis, the effects reported by Jenkins and Betancourt deserve further consideration."
      Australian-NZ Authorities 2011:
      http://www.foodstandards.gov.au/_srcfiles/BPA%20Annex%201%20

Table_of_studies_BPA_26October_2011.pdf: “The shortcomings in this study and a lack of concordance with other studies indicate that this study is not useful for hazard assessment.”

- ***Durando et al., 2007; Durando, M., L. Kass, J. Piva, C. Sonnenschein, A. M. Soto, et al. (2007). "Prenatal bisphenol A exposure induces preneoplastic lesions in the mammary gland in Wistar rats" Environ.Health Perspect. 115(1): 80-86.***

  EU Risk Assessment 2010, http://esis.jrc.ec.europa.eu/doc/risk_assessment/REPORT/bisphenolareport325.pdf: “However, due to the small sample size, lack of clarity on statistical analysis and use of a single dose level, it is difficult to establish whether the effects reported were due to chance or were real, treatment-related effects. Furthermore, because of the subcutaneous route of administration, it is questionable whether the reported findings are relevant to normal routes of exposures.”
  US FDA 2008, http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-0038b1_01_02_FDA%20BPA%20Draft%20Assessment.pdf: “The use of only one dose of BPA, the limitations regarding reporting (only select slides are shown), and the lack of progression of reported changes are weaknesses of the study. A major weakness is the use of a non-oral exposure route and that the BPA blood levels were not determined. Complicating this issue is the lack of an indication of the concentration of DMSO used in the mini-pump; pure DMSO is not recommended by the pump manufacturer and could cause its failure.”

- ***Murray et al, 2007:***

  US FDA 2008, http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-0038b1_01_02_FDA%20BPA%20Draft%20Assessment.pdf: “FDA notes that multiple doses were evaluated, care was taken to decrease exposure to environmental estrogens, and the authors used four doses covering a wide range. However, there was no indication of the number of dams treated in each group and the sample size, as noted in the results section, is small (n=4 – 6 for the cribriform-like structures). Additionally, it was not indicated whether the litter or the individual pup was considered the experimental unit. Furthermore, it is unclear if the observations are progressive, the route of administration is non-oral, and according to the manufacturer, 50% DMSO can be used in the Alzet mini-pumps. Lastly, blood levels of BPA were not determined.”
  EU RAR 2008, http://esis.jrc.ec.europa.eu/doc/risk_assessment/REPORT/bisphenolareport325.pdf : “… again, due to the small sample size, lack of clarity on the statistical analysis, absence of a dose-response

relationship and uncertainty about the incidence of the cribriform-like lesions in the controls it is difficult to establish whether the effects reported were due to chance or were real, treatment-related effects. In addition, because of the uncertainty about the significance of the cribriform structures, it is unclear whether real neoplasia actually occurred. Furthermore, because of the subcutaneous route of administration, it is questionable whether the reported findings are relevant to normal routes of exposures."

- The document makes reference to the ANSES interim report.

Key industry comments to the ANSES report are:

The interim report by ANSES concluded that health effects have been proven in animals and suspected in humans, even at doses below the NOAEL of 5 mg/kg/day on which the regulatory TDI of 50 µg/kg/day is set by EFSA. The underlying human and animal data are not sufficiently valid or indicative of adverse effects to support this conclusion and more comprehensive risk assessments conducted by other countries and competent authorities show that BPA is not a risk to human health. The major limitations of the ANSES interim report in contrast to other regulatory evaluations are:

- Conclusions drawn are not consistent in different chapters throughout the interim report.
- ANSES did not perform a comprehensive weight-of-evidence evaluation. The authors did not take into account validity aspects of individual studies and did not take into account the whole database.
- Important and comprehensive key studies are not mentioned throughout the ANSES interim report or not discussed in relevant chapters.
- Important new primary data is not included in the ANSES interim report.
- ANSES panel discussed that non-oral exposure to BPA might be relevant for humans, although, comprehensive and reliable biomonitoring data do not support the suggestion that humans are significantly exposed to non-oral sources of BPA.
- The ANSES panel based their conclusions on non-oral animal studies (e.g., sub-cutaneous injection) that are of limited relevance for human health. New toxicokinetic data reported in the recent US FDA testing program on BPA confirm that the bioavailability of BPA by different routes of exposure under most circumstances are substantially different, with non-oral routes showing much higher bioavailability compared to oral exposure in mice, rats and non-human primates.

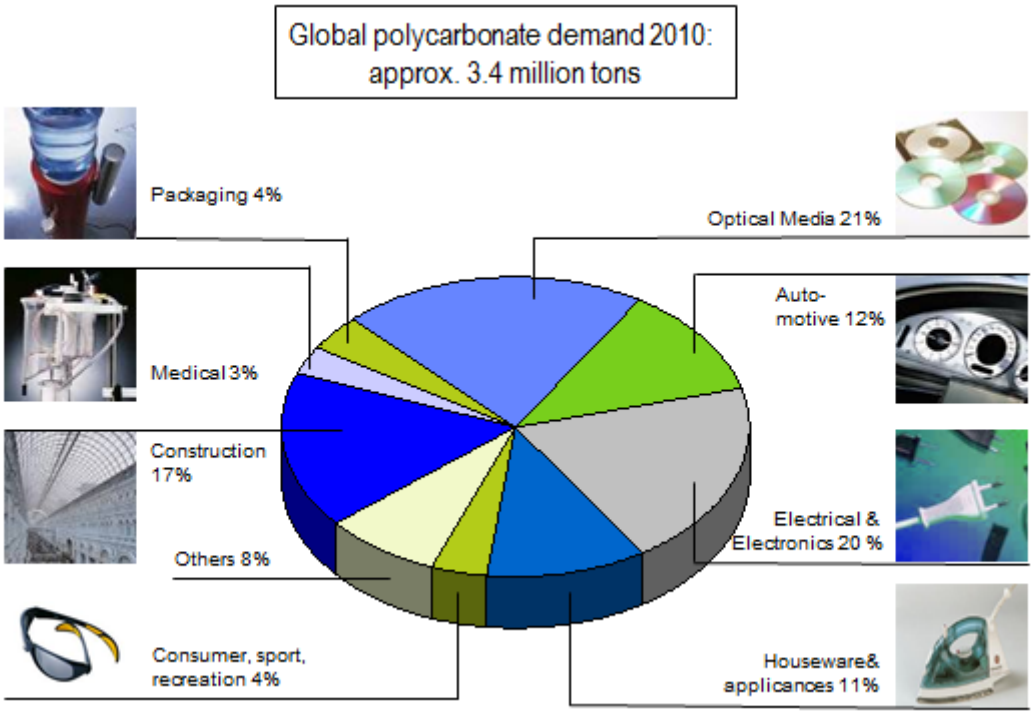
- Page 27, table 3.3:

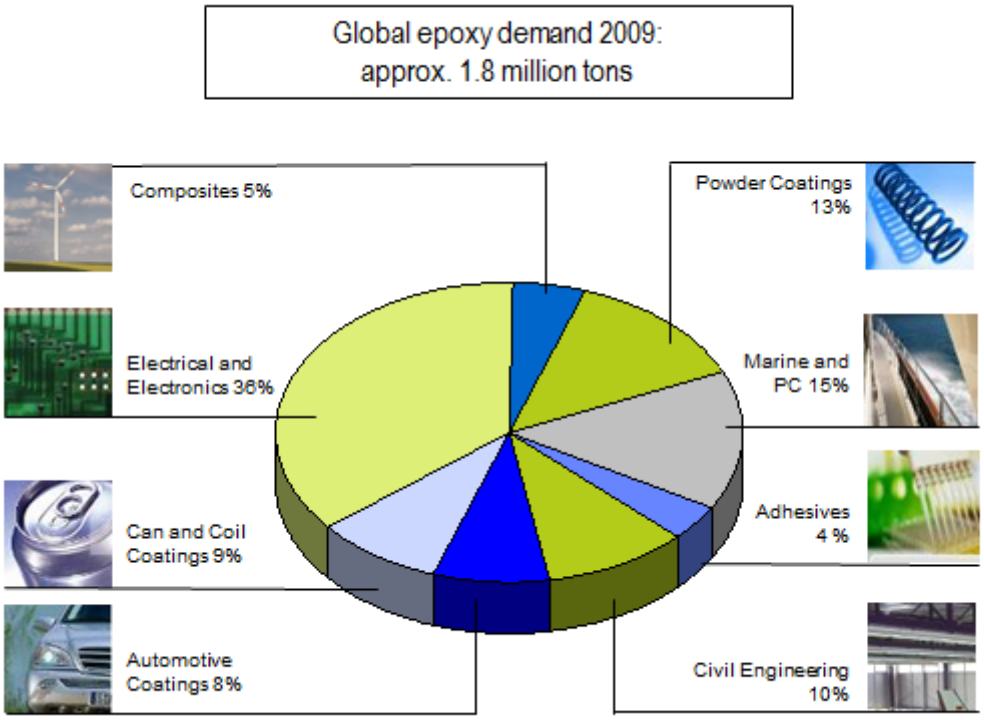
- Japan, Infant products - BPA is banned in infant products in Japan. In force (AU news, 2012).
- This statement is wrong. There is no restriction on BPA in infant products in Japan.

- Page 30: France, Medical devices
  - France suspends medical devices containing BPA or other endocrinal disruptors by July 1st, 2015 (GAIN, 2012).
  - This is wrong: http://www.assemblee-nationale.fr/14/dossiers/conditionnement_alimentaire_bisphenol_a.asp

- Page 32, 4.1.1 Manufacturing sites & volumes: there is production site in the Czech Republic.

- Page 34: 4.3.1 Use volumes, BPA
  - 2010 industry data PlasticsEurope - Global Bisphenol A production volume 2010: app. 4.5 million tons
  - Polycarbonate 69%, Epoxy resins 28%, TBBA 2%, Other Resins 1%





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- Page 41: 4.3.3 Estimated trends in use
  - "Based on the figures below and above the trends show an increase of BPA production in EU from the periods 1996/1999 to 2005/2006 of 64%."
  - This is completely misleading, because it is based on the assumption there has been no BPA production capacity in 1996 in Europe. This is wrong.

- Page 43, 5. Exposure
  - Please find details to the REACH dossier here
  - http://apps.echa.europa.eu/registered/data/dossiers/DISS-9dbe071c-c12d-0fe1-e044-00144f67d249/DISS-9dbe071c-c12d-0fe1-e044-00144f67d249_DISS-9dbe071c-c12d-0fe1-e044-00144f67d249.html
  - http://www.reachcentrum.eu/en/consortiumslt/consortia-under-reach/bisphenol-a-reach-consortium/more-information.aspx

- Page 43
  - "*In general biomonitoring data indicate considerable lower exposures compared to what have been calculated from scenarios using BPA migration data and data on food intake. However, some Japanese urine data indicate measured exposure of children of up to 40% compared to the most conservative calculated BPA exposures*."

- Method, tools and materials of sample-taking, storage and work-up: Several studies have shown that BPA-contamination of samples already through the equipment used to take the samples (syringes, lab-instruments, storage containers etc.) is actually quite a challenge. Therefore, in order to get a "real" result, not confounded by artificial BPA-contamination, specific attention must be placed on how the urine samples are taken, how/in which material containers they are stored, at which temperatures, how the containers were sterilised etc.

- Page 54, 7.1.1
  - "*Limited dermal absorption of BPA was concluded based on an in vitro dermal absorption study with human skin found and from these data an absorption rate of 10% was concluded for use in risk assessments (EU RAR, 2010).*
  - *Later this figure has been challenged as a French in vitro study using pig ear skin and viable human skin explants found a considerable higher absorption and from this an absorption rate of 50% was suggested (Lassen et al, 2011)."*
  - New releavant information is available from authorities which confirmed the EU RAR 2010 rate: Dermal penetration of bisphenol A in human skin contributes marginally to total exposure. Anne-Laure Demierre, Ronald Peter, Aurelia Oberli, Martine Bourqui-Pittet. Toxicology Letters In Press, Accepted Manuscript. Federal Office of Public Health, Division of Chemicals CH-3003 Berne, Switzerland.
  - *http://www.sciencedirect.com/science/article/pii/S0378427412011897?v=s5*

- Page 107, Appendix 4; Overview of risk managements
  - This overview gives a one-sided view of risk management reports focusing on concerns (e.g. regarding environment the Canadian risk assessment is extensively mentioned, but not the EU RAR 2010)

- Page 109, TABLE A4.1, REMARKS ON USE, RISKS, REGULATION AND RISK MANAGEMENT: BPA AND BISPHENOL-A-DIGLYCIDYLETHER POLYMER.
  - Recent information should be taken into account
  - **E.g. US FDA:** http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM297971.pdf
    - "Scientific evidence at this time does not suggest that the very low levels of human exposure to BPA through the diet are unsafe"
    - *" FDA scientists have also recently determined that* ***exposure to BPA through foods for infants is much less than had been previously believed*** *and that the* ***trace amounts of the chemical that enter the body, whether it's an adult or a child, are rapidly metabolized and eliminated****. "*

- *"There have also been studies that contend that BPA is a hazard to people too. But FDA—as well as the European Food Safety Agency (EFSA)— has carefully assessed these studies and finds no convincing evidence to support that belief."*

FDA findings:

- *The level of BPA from food that could be passed from pregnant mothers to the fetus is so low that it could not be measured.*
- *Exposure to BPA in human infants is from 84 to 92 percent less than previously estimated.*
- *…BPA is "exactly the opposite" from some other toxins, like dioxin, that can stay in the body's tissues for months or even years.*
- *The center's toxicology research has not found evidence of BPA toxicity at low doses in rodent studies, including doses that are still above human exposure levels.*

- E.g. Health Canada:
  - http://www.hc-sc.gc.ca/fn-an/securit/packag-emball/bpa/bpa_hra-ers-2012-09-eng.php
  - "*Dietary intake estimations of BPA for both the general population and infants were updated using more recent food occurrence data sets, including results from the Total Diet Study. The updated dietary exposure assessments are lower than those estimated in the assessment of August 2008. Therefore, based on the overall weight of evidence, the findings of the previous assessment remain unchanged and Health Canada's Food Directorate continues to conclude that current dietary exposure to BPA through food packaging uses is not expected to pose a health risk to the general population, including newborns and young children. This conclusion is consistent with those of other food regulatory agencies in other countries, including notably the United States, the European Union and Japan*."
  - http://www.hc-sc.gc.ca/fn-an/securit/packag-emball/bpa/bpa_rm-gr-2012-09-eng.php
  - Risk Management Commitment Updates