PlasticsEurope
Association of Plastics Manufacturers

Polycarbonate/Bisphenol A group
Epoxy Resin Committee

10.11.2015

Position paper regarding the DTU position concerning the EFSA opinion on the safety of BPA

Danish DTU position on BPA only based on limited dataset

In January 2015, the **European Food Safety Authority (EFSA)** published its assessment on the safety of Bisphenol A (BPA) in food contact[1]. Based on a comprehensive assessment of all available scientific data, EFSA clearly concluded that there is no health concern from BPA for any age group including pregnant women and children from dietary exposure to BPA (and low health concern from aggregated exposure based on much higher uncertainty on exposure from non-dietary sources). The current low levels of exposure are confirmed to be significantly below the temporary tolerable daily intake (t-TDI) of 4 microgram/kg bodyweight/day (µg/kg bw/day) for BPA, as established by EFSA.

The **National Food Institute of the Technical University of Denmark, DTU Food**, states that it disagrees with the safety assessment and t-TDI set by EFSA for BPA and continues to advocate for a lower TDI. Contrary to EFSA, DTU proposes a TDI of 0.7 µg/kg bw/day and concludes that there is concern with regard to mammary gland effects of BPA for highly exposed persons.

In response, the PC-BPA Group of PlasticsEurope states that:

1. The DTU position is based on a narrow and selective interpretation of the dataset on BPA

The DTU deduction of a lower TDI is mainly based on the reevaluation of the condensed dataset in the Delclos et al. 2014 publication[2]. Thus, the value proposed by DTU is not a result of the assessment of the full original data of this study, but it originates from the use of an incomplete dataset and a mistaken overreliance on weak evidence. EFSA, on the other hand, assessed the Delclos study´s original full dataset as part of the evaluation and weighing of all available scientific data which lead to the final conclusion that current BPA exposure levels do not raise a concern to human health.

2. The DTU position was assessed by EFSA and not regarded as scientifically substantiated

DTU´s position was fully taken into account and assessed by EFSA in its four year multi stakeholder assessment process. The EFSA process included an intense two-phased public consultation process which involved various national food safety authorities and institutes. During the consultation, the DTU provided its scientific arguments in written as well as in person to EFSA[3]. Like all other comments, the DTU comments were considered in the scientific evaluation and discussed in the EFSA expert working group, as well as being presented in the public stakeholder hearing. The DTU request for a lower TDI was specifically addressed but has not been regarded as scientifically substantiated. Therefore, the EFSA experts did not follow the Danish position.

In fact, based on the full comprehensive dataset, EFSA consistently concluded that there are no low-dose effects observed in the Delclos study in any way, and specifically no low dose effects on the mammary gland. Instead, EFSA considered kidney effects in mice as the most sensitive relevant endpoint (and applied an assessment factor to cover all other endpoints including mammary gland effects), which were therefore taken as the reference point for deriving the TDI for BPA**.** EFSA derived a safe level at 4 µg/kg bw/day – and concluded there is no health risk to consumers because current dietary exposure to the chemical is significantly lower than the TDI and thus causes no harm.

---

[1] EFSA opinion on PBA January 2015 *http://www.efsa.europa.eu/en/efsajournal/pub/3978*

[2] *K. Barry Delclos, Luísa Camacho, Sherry M. Lewis, Michelle M. Vanlandingham, John R. Latendresse, Greg R. Olson, Kelly J. Davis, Ralph E. Patton, Gonçalo Gamboa da Costa, Kellie A. Woodling, Matthew S. Bryant, Mani Chidambaram, Raul Trbojevich, Beth E. Juliar, Robert P. Felton, Brett T. Thorn;* ***Toxicity evaluation of bisphenol A administered by gavage to Sprague-Dawley rats from gestation day 6 through postnatal day 90****; Toxicological Science, Feb 4, 2014*

[3] April 2014 Stakeholder meeting, http://www.efsa.europa.eu/en/events/event/140423.htm
Technical report on the public consultation: http://www.efsa.europa.eu/en/supporting/pub/740e.htm

ASSOCIATION OF PLASTICS MANUFACTURERS IN EUROPE AISBL
Avenue E. Van Nieuwenhuyse 4/3 - B -1160 Brussels – Belgium
Tel (32-2) 675 32 97 - Fax (32-2) 675 39 35
VAT BE 416 155 338 - WWW.PLASTICSEUROPE.ORG

PlasticsEurope
Association of Plastics Manufacturers

3. The EFSA opinion is based on a comprehensive and sophisticated 'weight of evidence' approach

The EFSA panel published its conclusion in January 2015, confirming that BPA poses no health risk to consumers. The EFSA opinion is the result of an extensive weight of evidence assessment of all available data, intense scientific discussions, the involvement of independent scientific advice and a broad public stakeholder consultation process. The t-TDI was derived with a more sophisticated methodology than before. Remaining uncertainties concerning potential effects (including mammary gland effects) were analysed one by one, and by combining the Panel's expert judgement, EFSA's experts were able to quantify these uncertainties. These were factored into the derivation of the t-TDI and applied in the final risk assessment.

In conclusion, the multinational scientific expertise of the European scientific expert committee, which operates in global exchange with other key scientific bodies and experts from across the world, should outweigh a single standing assessment based on a minor selected part of the available scientific data.

The case for a lower TDI for BPA in food as presented by the Danish DTU is therefore unjustified.

Contact:

Jasmin Bird
PC/BPA-Group PlasticsEurope
mail: jasmin.bird@plasticseurope.org
website: www.bisphenol-a-europe.org

Annex: Comments on scientific data

Mammary gland effects arguments:

Availability and assessment of Delclos data
The TDI proposed by DTU ("*the TDI for BPA should be 0.7 µg/kg bw/day or lower to be sufficiently protective with regards to endocrine disrupting effects of BPA on mammary gland development")* is mainly based on an evaluation of the results in the peer-reviewed paper Delclos et al. 2014.

The Delclos et al study, done in 2013 by researchers of the U.S. Food and Drug Administration´s (FDA) National Center for Toxicological Research (NCTR), was conducted according to Good-Laboratory-Practice (GLP). Thus, all data, including data on individual animals and individual scoring of all endpoints investigated, are documented and available in the full study report. As is usual in such comprehensive studies, in the peer-reviewed publication only summary data are published, based on the limited space in this scientific journal. This is also the case for Delclos et al 2014.

DTU based its assessment on this limited set of data. Additionally, DTU applied a different statistical assessment of the study data. In contrast, EFSA and the FDA authors themselves took into account all comprehensive information on this study. Based on all data and additional statements, i.e. the entire study report and separate histopathology statements of independent reviews (explicitly NOT taken into account by DTU as mentioned in its evaluation) the FDA study authors and EFSA concluded that there are no low-dose effects observed in this study on any parameter, i.e. no low dose effects on mammary gland histopathology.

DTU discussion of mammary gland (hyperplasia)
Based on a statistical re-evaluation of the results in the published paper Delclos et. al. 2014, DTU claims evidence of mammary gland effects (hyperplasia) at low doses of BPA administered. There is a high likelihood of these findings being equivocal though: The FDA authors report a high variability of the hyperplasia effects, both in the groups exposed to BPA as well as in the control groups (that were not administered a BPA dose), and therefore conclude "*the evidence for duct hyperplasia in the mammary gland of females on either PND 21 or 90 is weak. We consider it to be an equivocal finding that may be a reflection of normal biological variability and/or a reflection of limits in tissue processing.*"

Is the DTU methodology applied to the Delclos study appropriate?

As there is no detailed description of the methodology applied by DTU given in their paper, the methodology cannot be assessed. However, generally it is scientifically questionable to re-assess the results of a study without taking all relevant data into account.

Why is it important to apply a weight of evidence approach in deriving a TDI?

A weight of evidence (WOE) approach assesses the strengths and weaknesses of experimental data or a study regarding their ability to provide a scientifically rigorous answer to a specific question. For deriving a safe level, known as the tolerable daily intake (TDI), the most sensitive endpoint is taken as reference point.

Applying a weight of evidence approach on all available data, EFSA considered the kidney effects in mice as the most sensitive endpoint (covering all other endpoints including mammary gland effects), which were therefore taken as the reference point for deriving the t-TDI for BPA in food. Contrary to the EFSA assessment, DTU regards mammary gland effects as the most sensitive endpoint. However (see also above), the DTU proposal is based on a limited set of summary data of Delclos et al..

Based on all data and additional statements, the EFSA expert panel concluded that there are no low-dose effects observed in this study on any parameter, i.e. no low dose effects on mammary gland histopathology. Therefore EFSA did not judge mammary gland effects as the most sensitive one.

Nevertheless, in deriving the t-TDI, EFSA applied an extra factor of six to take into account the remaining uncertainty in the entire database related to effects on mammary gland and reproductive, neurobehavioural, immune and metabolic systems. The Panel derived this factor of six by performing a detailed uncertainty analysis based on expert judgement. Based on the resulting safe level at 4 µg/kg bw/day – EFSA concluded there is no health risk to consumers because current dietary exposure to BPA is significantly lower than this TDI and thus causes no harm.

Excerpt from EFSA Q&A http://www.efsa.europa.eu/en/faqs/faqbisphenol.htm

Q 14: What is a weight of evidence approach?

A weight of evidence (WOE) approach assesses the strengths and weaknesses of experimental data or a study in being able to provide a scientifically rigorous answer to a specific question.

In EFSA's 2015 opinion on BPA, this approach estimated the degree to which the newly considered evidence strengthened or weakened the likelihood of an association between BPA exposure and a certain health hazard. The conclusions of earlier assessments of BPA by EFSA in 2006 and/or 2010 were taken as the starting point for the new evaluation. EFSA assessed the strength of the evidence linking BPA to each hazard and graded them on a six-point sliding scale. This ranged from 'very likely' and 'likely', to signify the strongest links, to 'unlikely' and 'very unlikely' where the link was considered weakest. EFSA said that only those health hazards evaluated as having a likely or very likely link to BPA exposure would be considered directly in characterising the risk posed by the chemical.