PlasticsEurope
Association of Plastics Manufacturers

Polycarbonate/Bisphenol A group
Epoxy Resin Committee

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ANSES report in contrast to the most recent global scientific consensus on Bisphenol A

Comment of the members of the Polycarbonate/Bisphenol A group (PC/BPA) and Epoxy Resin Committee (ERC) on the four French Food Safety Agency´s (ANSES) reports on Bisphenol A (BPA)

After a more detailed review of the new risk assessment report on BPA issued by ANSES on 9.4.2013, the PC/BPA and ERC members would like to add the following additional comments, expressing concern at the approach taken and conclusions presented by ANSES.

Not a weight-of-evidence approach

ANSES applies *"an innovative mechanism enabling to conduct an extremely detailed risk assessment for the first time taking into account all routes of exposure"*. It is not the first time that such an overall exposure assessment is done, on the contrary: it is official practice since more than a decade in European Chemicals Safety Policy. The ANSES approach deviates from the current method applied in regulatory processes by taking a selective approach to define the safety threshold. The fact that ANSES takes a new approach also means that comparisons are impossible. The results and conclusions drawn remain standing out alone, without an opportunity to validate or put them into perspective.

In its approach, ANSES defines four "effects" of key importance to them, and selects four studies (one per effect) to base its conclusions on, without providing a clear rationale based on transparent criteria for why exactly these four studies were selected. In doing so, ANSES obviously gives strong weight to these four selected studies, while at the same time basically blinding out a lot of other relevant comprehensive studies which reach other conclusions, including solid studies which show no effect. This is not a weight-of-evidence approach. Most worryingly, those four selected studies had already been evaluated and discredited for being unsuitable for regulatory purposes by other regulatory authorities.

Highly selective methodology

ANSES introduces the concept of an *„internal toxicological value"* to take account of the presumed amount of all „active" BPA that may enter the body through oral, dermal or inhalative exposure. While this is indeed a reasonable approach, the focus on the four selected studies leads to setting an extremely low adverse effect level to start with, which is then used to put calculated internal exposure into perspective. In addition, ANSES systematically uses and adds up sometimes irrealistic and arbitrary worst case assumptions (e.g. always using the highest value, not the median) and applies unrealistic calculation methods and figures for internal exposure (e.g. tripling the additionally applied safety factor (100 -> 300), grossly overestimating dermal bioavailability to be 100%, using similar oral bioavailability in rodents and humans although bioavailability is reported to be lower in humans than rats) resulting in a maximal increase of the final figures. Their main area of concern relates to a single study in rats when exposed to a daily dose of BPA at levels over 600 times higher than actual human exposure. It would appear therefore that the employed methodology might lead to an unbalanced conclusion.

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

Four studies of moderate or negligible concern

In addition to noting the ANSES approach of selecting flawed studies and applying unrealistic calculation methods, it is interesting to read the ANSES expert team´s own assessment on the consequences of these studies´ results. The confidence level of the expert panel associated with the results of the *Moral et al study* re potential risk for human health was not united: the majority of their expert group members judged it as *"moderate",* some experts regard it as *"limited".* Concerning the other three studies/types of effects, the panel classifies the confidence level associated with the results re potential risk for human health as *"negligible".*

The ANSES risk assessment on BPA appears to be based on a set of multiple, worst case estimates, which, through the employment of an unclear and seemingly selective approach, could create a conclusion of somewhat limited reliability. Being aware of this assessment, and taking into account the comprehensive amount of existing studies and assessments on BPA, it appears highly surprising how ANSES draws the conclusion as presented in its report.

EU risk assessment and other global safety bodies see no need for additional measures

A well established and reliable Chemicals Safety system is in place in Europe, under which BPA was investigated as extensive as hardly any other substance in the market. The Risk Assessment covers all exposure routes of a chemical to humans and to the environment. For BPA, all exposure routes (oral, dermal, inhalation) were investigated and assessed by European experts. On that basis, the European Risk assessment for BPA (2003, and updated 2008) concluded that BPA poses no risk to consumers and can be safely used in its current applications. A most recent update from FDA of March 2013 reconfirmed the safety of BPA: *"FDA's current assessment is that BPA is safe at the very low levels that occur in some foods. This assessment is based on review by FDA scientists of hundreds of studies including the latest findings from new studies initiated by the agency."* http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm064437.htm.

"We still cannot follow the ANSES interpretation of the existing scientific evidence. It seems to disregard the accepted norms of European risk assessment and is in contrast to the EFSA opinion and the statements made by other regulatory authorities worldwide", says Jasmin Bird of the PC/BPA-group. Consumers and other country authorities and governments alike should wait for the results of the currently running FDA-studies on BPA and for the comprehensive EFSA re-assessment of BPA which has been announced for publication in November 2013.

For more information:

Jasmin Bird
PC/BPA-Group PlasticsEurope
Tel: +32 2 676 17 38
Fax: +32 2 675 39 35

mail: jasmin.bird@plasticseurope.org
website: www.bisphenol-a-europe.org

Background information on the chosen methodology and the four selected studies

Examples of the ANSES **methodology**

- **ANSES applies an additional worst case assessment factor to characterise the "toxicological value" without giving the reasoning for doing so, or giving the criteria for the actual factor selected.**
  In 2006, EFSA considered the database for BPA so strong that an additional uncertainty factor was not warranted any more. The safety factor of 100 applied by EFSA is tripled by ANSES to use safety factor 300, resulting in an even lower level BPA regarded to be of concern.

- **ANSES employs grossly over-estimated bioavailability factors to calculate the internal dose of BPA after exposure.**
  - For **dermal exposure**, ANSES takes 100% of assumed dermal BPA exposure to be entering through the skin. This is completely unrealistic. Comprehensive studies like the recent Swiss authority study on dermal penetration confirmed a penetration of max. 10 %, i.e. a 10 fold lower factor.
  - As calculation basis for **oral bioavailability** ANSES uses 3 % of ingested BPA to enter the body in rats and humans, based a study in rats. However, ANSES does not use the more recent results from valid research data indicating substantially lower bioavailability in monkey and humans compared to rats.

- **ANSES generally calculates with worst case 95th percentiles instead of using the median values, which is common practice.**

Reasons for dismissing **studies** for regulatory purposes generally include methodological flaws, missing reliability of data, too small test groups, inconsistencies or unavailabilities of raw data, unvalidated test procedures etc.

- **Moral et al, 2008,** mammary gland
  The study used by ANSES to justify a potential effect on pregnant women and unborn children had been evaluated by EFSA in its 2010 opinion, by the US FDA in its 2008 interim assessment, as well as by the Japanese AIST in 2011. They concluded: *"However, this study is severely weakened deficiencies in methodology (lack of control for estrogens, the control for litter effects was not documented and the authors rely on data not shown). All of the studies are limited by the nature of the findings (these studies do not demonstrate findings that are clearly relatable to adverse findings in humans and do not demonstrate progression to tumors)."* Claims that link BPA to e.g. cancer are not supported by robust research studies that have thoroughly investigated this question.
  http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-0038b1_01_02_FDA%20BPA%20Draft%20Assessment.pdf

- **Rubin et al, 2001**, female reproductive system ("low dose study")
  The study was assessed by EFSA 2006. It did not lead to a change of the EFSA opinion on the safety of BPA, the current TDI was confirmed: "*The Panel considered that low-dose effects of BPA in rodents have not been demonstrated in a robust and reproducible way, such that they could be used as pivotal studies for risk assessment." (page 4)*
  http://www.efsa.europa.eu/de/scdocs/doc/428.pdf

- **Miyawaki et al, 2007**, metabolism and obesity ("low dose study")
  The study was considered by EFSA 2010. It did not lead to a change of the EFSA opinion on the safety of BPA, the current TDI was confirmed: "*Because of the lack of a common clearly defined mode of action of BPA at low doses, the toxicological relevance of the BPA effects described cannot be evaluated and the results cannot be taken into consideration for derivation of a TDI. While low dose effects of BPA are reported for some biochemical changes the Panel is not aware of any clearly reproducible adverse effect expressed specifically at low BPA doses only*." (page 5)
  http://www.efsa.europa.eu/de/efsajournal/pub/1829.htm

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- **Xu et al 2010a**, brain and behaviour
  This study will be considered by EFSA in their upcoming opinion. It was already considered by WHO 2010: *"There is considerable uncertainty regarding the validity and relevance of these observations. While it would be premature to conclude that these evaluations provide a realistic estimate of the human health risk, given the uncertainties, these findings should drive the direction of future research with the objective of reducing this uncertainty."*