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Polycarbonate/Bisphenol A group

16.8.2010

FDA scientists publish new studies addressing common claims re Bisphenol A (BPA)

FDA studies confirm: BPA is efficiently metabolised already at early days of life; oral exposure is the relevant route for risk assessment

The US Food and Drug Administration FDA is conducting a series of studies in their own laboratories to answer key questions and clarify uncertainties about the risks of BPA. Included are pharmaco-kinetic studies to better understand how BPA is processed in the body, and toxicity studies focused on some of the key claims about health effects from BPA. The first two pharmacokinetic studies from this FDA research program have now been published online in the peer-reviewed scientific magazine Toxicology and Applied Pharmacology. One is a study in rats, the second examines monkeys (see attachment for more information).

Newborns can efficiently metabolise BPA
Both studies, in particular the monkey study, strongly indicate that the ability to metabolize orally administered BPA exists at a very young age already. This reconfirms the findings from earlier studies (reviewed e.g. by EFSA in 2008) and it directly contradicts the common claim that infants do not have the capability to metabolize BPA and were thus more susceptible to effects from BPA. The monkey study in particular showed that the capability of neonates (5 days after birth) to metabolise BPA is equivalent to that of adult monkeys.

Reported levels of (un-metabolised) BPA in human blood likely to be invalid
Another common claim is that significant amounts of un-metabolised BPA are present in human blood, suggesting extremely high exposure, inability to metabolise and eliminate BPA, and the potential for health effects. Based on the efficient metabolism of BPA in monkeys as shown in the new study, the FDA researchers suggest that reported levels of BPA in human blood are likely to be invalid. The authors also stress the importance of robust analytics that are able to clearly distinguish in their measuring between the active and inactive forms of BPA.

Oral exposure is the relevant route for risk assessment
It is often claimed that the many toxicity studies in animals involving non-oral exposure routes are relevant for the assessment of human health since they result in blood levels of BPA similar to what has been reported in people. FDA's findings do not support this claim and suggest instead that studies involving non-oral exposure are of limited relevance to human health risk assessment for oral exposure.

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Key conclusions from FDA pharmacokinetic study in monkeys

Doerge, Daniel R., Twaddle, Nathan C., Woodling, Kellie A., Fisher, Jeffrey W., Pharmacokinetics of bisphenol a in neonatal and adult rhesus monkeys, *Toxicology and Applied Pharmacology* (2010), doi: 10.1016/j.taap.2010.07.009

- BPA is efficiently metabolized by adult monkeys after oral exposure
- The capability of neonatal monkeys to metabolize BPA is equivalent to adult monkeys, which indicates that neonates may not be more sensitive to potential effects from BPA:
  „…minimal pharmacokinetic differences were observed between neonatal and adult monkeys for the (…) active form of BPA"; „…for primates, neonates are able to efficiently detoxify BPA …"
- Studies in rats are likely to over-predict health effects in primates:
  „…any toxicological effect observed in rats from early postnatal exposure to BPA could over-predict those possible in primates of the same age…"
- Reports of high levels of BPA in human blood are likely due to sample contamination rather than indicative of high human exposure levels.
- Rhesus monkeys are a good model for humans.

Key conclusions from FDA pharmacokinetic study in rats

Doerge, Daniel R., Twaddle, Nathan C., Vanlandingham, Michelle, Fisher, Jeffrey W., Pharmacokinetics of Bisphenol A in neonatal and adult Sprague-Dawley rats, *Toxicology and Applied Pharmacology* (2010), doi: 10.1016/j.taap.2010.06.008

- BPA is efficiently metabolized by adult rats after oral exposure
- While neonatal rats are not identical to adults, they also have the capability to efficiently metabolize BPA:
  „…in neonatal rats treated orally, internal exposures to (active) BPA were substantially lower than from subcutaneous injection. The results reinforce the critical role for first pass (…) metabolism of BPA in gut and liver after oral exposure…"
- As a result of efficient metabolism, estrogenic effects from BPA are unlikely due to the very low levels of un-metabolized BPA in the body after oral exposure.
- Because BPA is efficiently metabolized after oral exposure, studies that expose animals by subcutaneous injection are of limited relevance to human health concerns that primarily involve oral exposure.
- Because of efficient metabolism and rapid elimination, BPA does not accumulate in the body.

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