European Food Safety Authority

EFSA's approach to hazard assessment

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EFSA opinion on BPA 2010

Review of scientific literature

About 800 recent studies were extensively reviewed by EFSA in a comprehensive risk assessment

Inclusion criteria in 2010

- **Full research papers published in peer-reviewed journals available in public domains since the EFSA 2006 opinion (2007 – July 2010)**
- **Original data** (no reviews, discussions or others)
- **Human studies**
  - The Panel excluded from the selection purely biomonitoring studies, which mainly deal with exposure, and therefore are not useful for TDI setting.

Inclusion criteria in 2010

For the animal toxicity studies the focus was on studies having the following experimental design:

- **Developmental exposure**
  - In view of the possible concern on children's health associated with low dose exposure to BPA, the CEF Panel decided to review the studies where BPA was administered at any stage during the perinatal period
- **Several tested doses (and at least one dose level below the NOAEL of 5 mg/kg bw/day)**
  - The presence of a response at one dose level only is not sufficient to demonstrate a causal relationship between the administration of a substance and an observed change.

Inclusion criteria in 2010

- **Oral route of exposure:**

The CEF Panel considers oral toxicity studies more appropriate for a quantitative risk assessment than non-oral route studies for the following reasons:

  - oral intake is the most relevant route of human exposure, occurring through migration of BPA from food contact materials into food
  - other routes of exposure (e.g. intraperitoneal (i.p.), intracranial (i.c.), subcutaneous (s.c.) injection or through implantation of s.c. pumps), show kinetic differences with respect to oral uptake of BPA (i.e. bypass of intestinal absorption and first-pass detoxifying metabolism), affecting the internal free BPA level

Inclusion criteria in 2010

- The Panel has also considered several studies employing non-oral routes of exposure, in order to properly characterize the potential toxicity endpoint and mode of action of BPA.

Litterature search since 2010

EFSA has outsourced the work on continuous "Review of scientific literature on BPA" through a contract with the University of Parma

1. First contract August 2010-July 2011
2. New contract August 2011-July 2014

EFSA hazard characterication of BPA 2012

(compared with 2010 approach)

Inclusion criteria in 2012

- **Full research papers published in peer-reviewed journals available in public domains since the EFSA 2010 opinion (July 2010-December 2012)**
  - Including papers not evaluated in the 2010 opinion because they did not match the criteria established at that time, e.g. non oral studies
- **Previous governmental risk assessments and reports using original data, as background**
  - Review papers will not be extensively discussed

Inclusion criteria in 2012

- **Human studies**
  - Including ex vivo studies
  - Including biomonitoring studies
- **All animal toxicity studies**,
  - including non-oral routes of exposure
  - single dose studies may be used for hazard identification and as supporting evidence for the risk assessment
- **In vitro studies**
  - Excluding those addressing concentrations above 50-100 nM.
  - Mechanism of action of BPA

Quality criteria 2012

- **points to be considered when assessing the formal status of the study**
  - studies performed under quality assurance system (GLP/other quality assurance system)
  - studies performed according to existing guidelines
  - studies performed with an a priori study protocol/study plan
- **points to be considered when assessing the content of the study**
  - sufficient sample size
  - adequacy of control procedures
  - inclusion of positive controls when applicable
  - statistics
  - adequately detailed study reporting

Quality criteria 2012

- **In *in vivo* animal studies**
  - strain sensitivity, housing conditions, drinking bottle, phyto-oestrogen-containing diet and bedding assessment
  - correlation between morphological and functional changes

Work ongoing

- Nearly 30-40 papers on BPA published every month
- Include papers published until end of December 2012
- Deadline May 2013