EFSA explains **the Safety of Bisphenol A**

Scientific opinion on bisphenol A (2015)

- What is **bisphenol A** and what has EFSA done?
- What are the **main results** of EFSA's 2015 risk assessment of BPA?
- What **potential** health effects of BPA has EFSA identified?
- What did EFSA find out about **exposure to BPA**?
- What are EFSA's **overall conclusions**?
- **Understanding** EFSA's risk assessment of BPA

What is **bisphenol A** and what has EFSA done?

BPA is a chemical compound used in the manufacture of polycarbonate plastic food contact materials such as re-usable plastic tableware and can coatings (mainly as protective linings. Another widespread application of BPA is in thermal paper commonly used for till/cash register receipts.

EFSA's expert **Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)** decided that the publication of new scientific research on BPA in recent years meant a full re-evaluation of the chemical was necessary.

EFSA's experts estimated the **exposure** to BPA from dietary and non-dietary sources, and assessed the **human health risks** posed by exposure to BPA. The resulting risk assessment was published in January 2015 in the CEF Panel's "*Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs*".

What are the **main results** of EFSA's 2015 risk assessment of BPA?

- BPA poses **no health risk** to consumers because current exposure to the chemical is too low to cause harm.
- Based on new data and methodologies, EFSA has lowered the estimated safe level, known as the tolerable daily intake (TDI), to 4 micrograms per kilogram of body weight per day. This is **twelve and a half times lower** than the previous level.
- The highest estimates for aggregated exposure to BPA from both dietary and non-dietary sources are **3 to 5 times lower than the TDI**, depending on the age group.
- Dietary exposure is from 4 to 15 times lower than previously estimated by EFSA, depending on the age group.
- Based on animal studies, BPA at high doses (more than 100 times the TDI) is likely to cause adverse effects in the **kidney and liver**. It is also likely to have effects on the **mammary glands** of rodents.
- Uncertainties surrounding potential health effects of BPA on the mammary gland, reproductive, metabolic, neurobehavioural and immune systems have been **quantified and factored** in to the TDI.
- **The TDI is temporary** (t-TDI) pending the outcome of an on-going long-term study in rats involving prenatal as well as postnatal exposure to BPA. This study will help reduce the remaining uncertainties about the potential health effects.

efsa
European Food Safety Authority

EFSA's risk assessment in more detail

What **potential health effects** of BPA has EFSA identified?

- Based on animal studies, BPA at high doses (more than 100 times the TDI) is likely to cause adverse effects in the **kidney and liver**. It is also likely to have effects on the **mammary glands** of rodents. How these effects are caused (the 'mechanism of action') is not clear.
- Possible effects of BPA on the reproductive, nervous, immune, metabolic and cardiovascular systems, as well as in the development of cancer are **not considered likely at present** but they could not be excluded. They add to the overall uncertainty about BPA-related hazards and therefore have been considered in the assessment.
- The kidney effects in mice were the reference point for deriving the safe level, known as the tolerable daily intake (TDI), for BPA in food.
- The TDI **has been lowered** from its previous level of 50 micrograms (µg) per kilogram of body weight per day (or *0.05 milligrams per kilogram of body weight per day*) to 4 µg/kg of bw/day. EFSA is making this change because of new data and a refined risk assessment, and because of uncertainty in the database regarding mammary gland and reproductive, metabolic, neurobehavioural and immune systems.
- The TDI is **temporary** (t-TDI) until the results of ongoing research from the US National Toxicology Program can be incorporated in the evaluation. This research is expected to address many of the remaining uncertainties.
- Based on scientific criteria*, EFSA's experts concluded that the available data do not provide evidence that BPA results in non-monotonic dose-response relationships for the health effects considered.

* The three scientific criteria required as evidence of non-monotonic dose-response (NMDR) relationships:

1) At least two adjacent doses departing from monotonicity or support for the NMDR from a similar study (same species, similar treatments, similar sampling time) on the same effect (this criteria reduces the chance for an incidental finding)
2) A plausible underlying mode of action/overarching concept
3) The reliability of the study and the relevance of the effect for human health should be considered as medium or high (as expressed in Appendix B and C); the reliability of the study results should also include an appropriate statistical treatment of the reported data

How did EFSA's experts calculate the new TDI?

In this opinion, EFSA has used a more refined methodology than before supported by new data. EFSA's experts have quantified uncertainty about some potential effects to be able to factor them in to the risk assessment and the derivation of the t-TDI.

- Experts analysed the toxicological studies already available for the previous evaluations, supplemented with new information and used a method known as **benchmark dosing** to calculate the lowest dose (called the "benchmark dose") at which BPA causes a small adverse effect in the kidneys of mice – in this case a 10% change in the mean relative weight of the organ. EFSA established that this effect would occur at a dose of **8960 µg/kg bw/day**.
- New robust studies that have become available since 2010 allowed EFSA to take better account of the differences in the ways in which various animal species and humans metabolise and eliminate BPA. Using this information, EFSA's experts could convert the dose that causes the adverse effect on the kidneys in mice into an oral equivalent dose for humans of **609 µg/kg bw/day**. This "**human equivalent dose**" is applicable to all exposures to BPA, whether they result from diet or from skin contact, provided that the latter is first converted to a corresponding oral exposure.
- The next step normally involves applying an uncertainty factor of 100 to take into account the differences between species and the differences between individual persons.
- Derivation of the human equivalent dose, based on substance specific-data, meant the differences between species in metabolism and elimination were already considered leaving an uncertainty factor of 25.
- Finally, **an extra factor of six** was included to take into account the uncertainty in the 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.
- Thus, an **overall uncertainty factor of 150** (25 × 6) was applied to the equivalent human dose of 609 µg/kg bw per day to derive the new t-TDI of 4 µg/kg bw/day.

What did EFSA find out about **exposure to BPA**?

- Dietary exposure is from **4 to 15 times lower than previously estimated** by EFSA in 2006, depending on the age group considered. This is due to **better data** and less conservative assumptions for the exposure calculations.
- Dietary exposure to BPA is highest among infants and toddlers. The highest estimates are 4 and a half times below the t-TDI. This is explained by their higher food consumption on a body weight basis.
- Dietary exposure for bottle-fed infants aged 0-6 months is 50-fold below the t-TDI for the highest estimates.
- **Canned food** and, to a lesser extent, non-canned meat and meat products were identified as major contributors to dietary BPA exposure for all age groups.
- Aggregated exposure, which reflects the summated exposure to the toxicologically relevant form of BPA – known as 'unconjugated BPA' – through all routes (diet, dust, cosmetics and thermal paper), is highest for adolescents at over 1 µg/kg bw/day.
- **Uncertainty** in the exposure estimates for non-dietary sources is high because of the lack of supporting data. The uncertainty around dietary exposure is relatively low.

What is new about this exposure assessment?

This is EFSA's first review of consumer exposure to BPA to cover both dietary and non-dietary sources. It also considers specific groups of the population, e.g. infants, teenagers (10-18 years) and women of child-bearing age (18-45 years).

EFSA's experts have carried out a considerable refinement of the dietary exposure estimates compared to the previous one in 2006 thanks to the availability of more scientific information.

In contrast to previous opinions, based on extensive new data, the relevance of the various exposure routes (diet, dermal, inhalation) can now be better taken into account.

What are EFSA's **overall conclusions**?

The overall conclusion is that BPA poses **no risk to human health** from foodstuffs because current levels of exposure are well below the t-TDI of 4 µg/kg of bw/day. This also applies to pregnant women and to the elderly.

In addition, EFSA's experts concluded that the health concern from the aggregated exposure to BPA from foodstuff, toys, dust, cosmetics and thermal paper is also below the t-TDI of 4 µg/kg bw/day. The uncertainty in the exposure estimate from toys, dust, cosmetics and thermal paper is considerable due to the very limited availability of data.

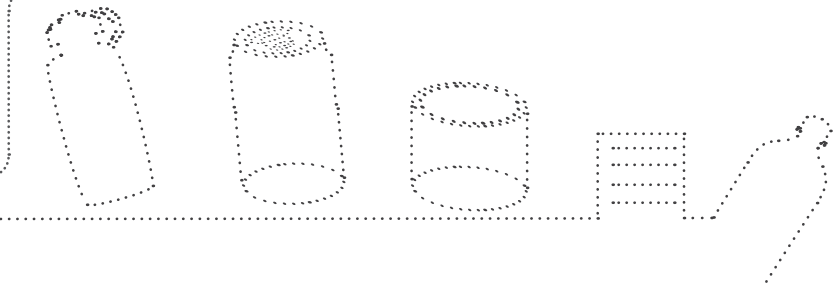
Definitions

What is the Tolerable Daily Intake (TDI)?

The TDI is the estimated quantity of a chemical substance that can be ingested daily over a lifetime without posing a significant risk to health. TDIs are expressed by body weight, usually in milligrams or micrograms (of the substance) per kilogram of body weight, and per day in the case of repeated exposure.

Benchmark Dose
The minimum dose of a substance that produces a clear, low level health risk, usually in the range of a 1-10% change in a specific toxic effect such as cancer induction.

Human Equivalent Dose
The HED is the Benchmark Dose, corrected for differences in kinetics (movement of chemicals) between mice and humans.



Understanding EFSA's risk assessment of BPA

TM-01-15-035-EN-N

EFSA's experts examined both hazards and risks associated with BPA:

1. **Hazard assessment** – uses experimental data from animal and human studies to identify any health effects associated with exposure to BPA.
2. **Risk characterisation** – analyses the extent of the risk posed by the identified hazards to consumers at current levels of exposure to BPA in the population – via oral ingestion, breathing in dust and exposure through the skin.

Are 'hazards' and 'risks' the same?

No, hazards and risks are different. A **hazard** is a possible threat posed to health because of the intrinsic properties of a substance, such as its capacity to damage the kidney or cause cancer. But the **risk** that a substance could cause a harmful effect depends on:

- how much of the substance humans are exposed to
- the length of time of the exposure
- when exposure occurs, i.e. as a fetus, child or adult.

Has EFSA found health hazards associated with exposure to BPA?

Based on animal studies, **BPA at high doses** (more than 100 times the TDI) is likely to cause an adverse effect on the kidney and liver. It is also likely to have effects on the mammary glands of rodents. Effects on fertility and development may be expected at levels of exposure approximately 10,000 times above the t-TDI.

Why has EFSA reduced the Tolerable Daily Intake (TDI)?

Importantly, the reduction of the TDI is not connected to the emergence of new health concerns about BPA. EFSA has reduced the TDI because **the method used to assess the risk from BPA has become more refined** than the one used in evaluations carried out by the Authority between 2006 and 2011.

More accurate data is available now so the calculations used in the risk assessment are based on substance-specific information and less on commonly used standard default values. In addition, an extensive analysis based on new techniques shows uncertainty in the database regarding mammary gland and reproductive, metabolic, neurobehavioural and immune systems, which had to be taken into account.

Does this mean that BPA poses a health risk to humans?

EFSA concludes that BPA poses **no health risk** to consumers because current exposure to the chemical is too low to cause harm. EFSA's scientific opinion shows the level of BPA that consumers of all ages are exposed to through the diet is well below the t-TDI of 4 µg/kg of bw/day; the highest estimates for dietary and non-dietary exposure to BPA are 3 to 5 times lower than the t-TDI, depending on the age group. For all population groups, dietary exposure on its own is more than five-fold below the t-TDI. This also applies to pregnant women and to the elderly.

How did EFSA quantify uncertainty and factor this into the risk assessment?

EFSA's experts used new methodologies to take account of the uncertainties regarding potential health effects, exposure estimates and evaluation of risks for humans. By analysing each uncertainty one by one and combining **expert judgement**, the experts were able to quantify these uncertainties and to factor them in to the risk assessment and derivation of the t-TDI.

European Food Safety Authority

Via Carlo Magno 1A
43126 Parma
Italy

Tel. + 39 0521 036 111
Fax + 39 0521 036 110
www.efsa.europa.eu

ISBN 978-92-9199-642-1
doi: 10.2805/075460

Photo credits :
EFSA, iStockphoto, Shutterstock