FCM NETWORK MEETING/
21-23 OCTOBER 2025

EFSA FCM NOTE FOR GUIDANCE UPDATE: *ASSESSMENT OF HAZARDOUS BISPHENOLS & THEIR DERIVATIVES*

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EUROPEAN FOOD SAFETY AUTHORITY

OUTLINE

- Background
- EU Regulation 2024/3190
- FCM note for guidance for applicants
- EFSA self-task mandate, ToRs
- EFSA technical report on BPS (2020)
- ECHA screening assessment of Bisphenols (2025)

BACKGROUND

SCIENTIFIC OPINION

efsa JOURNAL

ADOPTED: 6 December 2022

doi: 10.2903/j.efsa.2023.6857

Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs

EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), Claude Lambré, José Manuel Barat Baviera, Claudia Bolognesi, Andrew Chesson, Pier Sandro Cocconcelli, Riccardo Crebelli, David Michael Gott, Konrad Grob, Evgenia Lampi, Marcel Mengelers, Alicja Mortensen, Gilles Rivière, Vittorio Silano (until 21 December 2020†), Inger-Lise Steffensen, Christina Tlustos, Laurence Vernis, Holger Zorn, Monika Batke, Margherita Bignami, Emanuela Corsini, Rex FitzGerald, Ursula Gundert-Remy, Thorhallur Halldorsson, Andrew Hart, Evangelia Ntzani, Eugenio Scanziani, Henri Schroeder, Beate Ulbrich, Dina Waalkens-Berendsen, Detlef Woelfle, Zainab Al Harraq, Katleen Baert, Maria Carfì, Anna F Castoldi, Cristina Croera and Henk Van Loveren

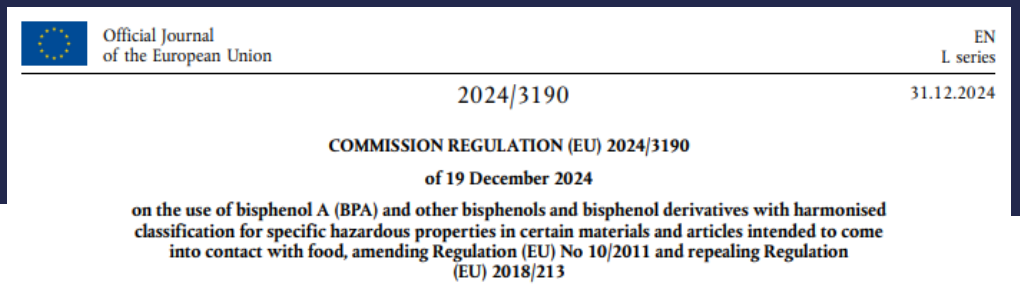
Abstract

In 2015, EFSA established a temporary tolerable daily intake (t-TDI) for BPA of 4 μg/kg body weight (bw) per day. In 2016, the European Commission mandated EFSA to re-evaluate the risks to public health from the presence of BPA in foodstuffs and to establish a tolerable daily intake (TDI). For this re-evaluation, a pre-established protocol was used that had undergone public consultation. The CEP Panel concluded that it is Unlikely to Very Unlikely that BPA presents a genotoxic hazard through a direct mechanism. Taking into consideration the evidence from animal data and support from human observational studies, the immune system was identified as most sensitive to BPA exposure. An effect on Th17 cells in mice was identified as the critical effect; these cells are pivotal in cellular immune mechanisms and involved in the development of inflammatory conditions, including autoimmunity and lung inflammation. A reference point (RP) of 8.2 ng/kg bw per day, expressed as human equivalent dose, was identified for the critical effect. Uncertainty analysis assessed a probability of 57–73% that the lowest estimated Benchmark Dose (BMD) for other health effects was below the RP based on Th17 cells. In view of this, the CEP Panel judged that an additional uncertainty factor (UF) of 2 was needed for establishing the TDI. Applying an overall UF of 50 to the RP, a TDI of 0.2 ng BPA/kg bw per day was established. Comparison of this TDI with the dietary exposure estimates from the 2015 EFSA opinion showed that both the mean and the 95th percentile dietary exposures in all age groups exceeded the TDI by two to three orders of magnitude. Even considering the uncertainty in the exposure assessment, the exceedance being so large, the CEP Panel concluded that there is a health concern from dietary BPA exposure.

EFSA BPA opinion (EFSA, 2023)

- ✓ A **TDI** was established based on a **RP** identified as the lowest BMDL associated with the most sensitive effect to BPA exposure, i.e. **T helper 17 cells** percentage increase in mouse' splenocytes (**Immunotoxicity**).
- ✓ The EFSA Panel concluded that there is a **health concern** from **dietary exposure to BPA**.
- ✓ On **19 December 2024**, the Commission released the **Regulation (EU) 2024/3190** on the **ban of BPA** and the provisions on the **use of hazardous bisphenols other than BPA and their derivatives**.
- ✓ As of **20 January 2025**, the use of BPA in FCMs is prohibited.

REGULATION (EU) 2024/3190 (LINK)



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COMMISSION REGULATION (EU) 2024/3190

of 19 December 2024

on the use of bisphenol A (BPA) and other bisphenols and bisphenol derivatives with harmonised classification for specific hazardous properties in certain materials and articles intended to come into contact with food, amending Regulation (EU) No 10/2011 and repealing Regulation (EU) 2018/213

Article 6

Authorisation for the use of hazardous bisphenols other than BPA or hazardous bisphenol derivatives in the manufacture of food contact materials and articles for a specific application

1.To obtain an authorisation for the use of a hazardous bisphenol other than BPA or hazardous bisphenol derivative in the manufacture of a food contact material or article for a specific application, an application shall be submitted in accordance with Article 9 of Regulation (EC) No 1935/2004.

2. In accordance with Article 10 of Regulation (EC) No 1935/2004, the Authority shall issue an opinion for the use of the hazardous bisphenol or hazardous bisphenol derivative in the manufacture of a food contact material or article for a specific application for which a valid application was submitted in accordance with Article 9 of Regulation (EC) No 1935/2004. In case the Authority receives several applications regarding the same hazardous bisphenol or hazardous bisphenol derivative, the Authority may publish a single opinion concerning that hazardous bisphenol or hazardous bisphenol derivative.

…

4. For the purpose of paragraph 1, and before ***20 January 2027****, the Authority shall publish* ***scientific output detailing the information necessary for the assessment of the use of hazardous bisphenols or hazardous bisphenol derivatives****, in the manufacture of food contact materials and articles for a specific application, supplementing or updating where necessary the detailed guidelines referred to in Article 9(2) of Regulation (EC) No 1935/2004*. The Authority and the European Chemicals Agency shall collaborate with each other for this purpose.*

5. Upon request by the Authority, business operators using bisphenols or bisphenol derivatives in the manufacture of food contact materials and articles shall provide data on the use of the bisphenols and bisphenol derivatives in the manufacture of food contact materials and articles to inform the preparation of the information referred to in paragraph 4.

*Link to the *Regulation (EC) no 1935/2004 of the European parliament and of the council on materials and articles intended to come into contact with food.*

EFSA NOTE FOR GUIDANCE FOR FCM APPLICATIONS

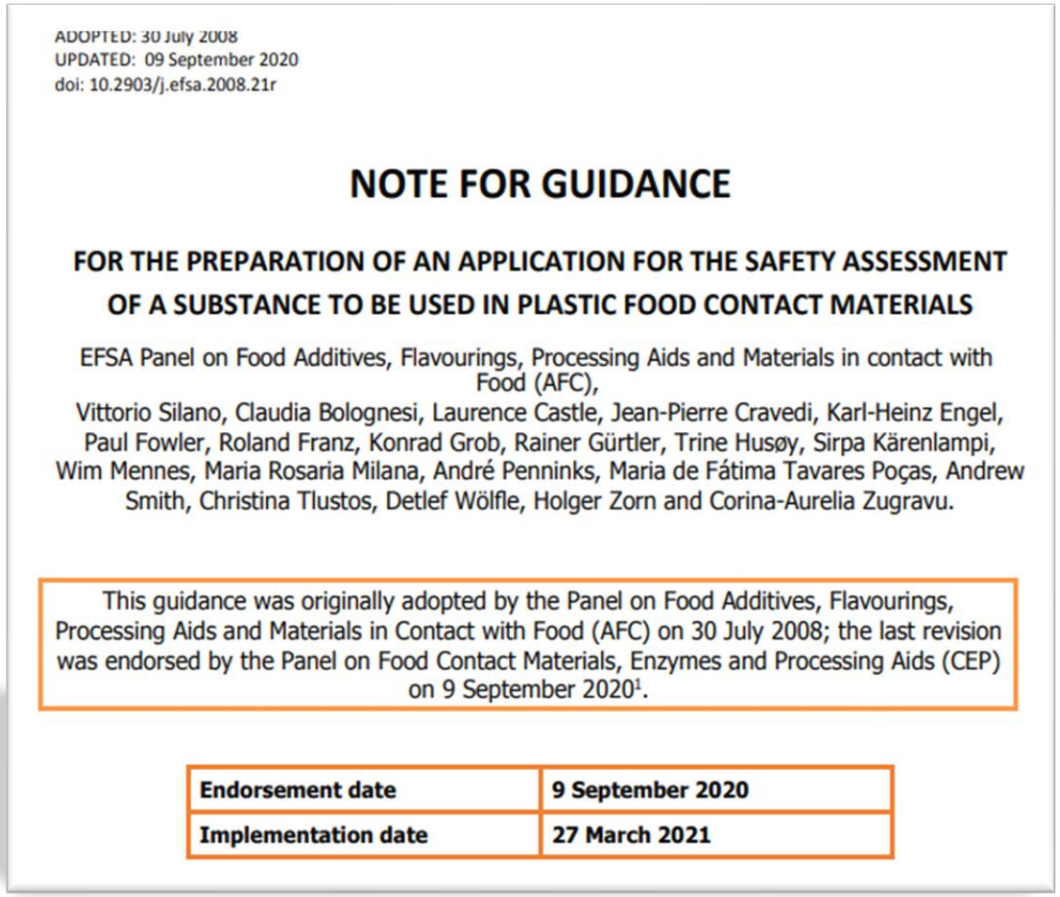
"… the greater the exposure through migration, the more toxicological data is required for the safety assessment of a substance."

Three tiers with different thresholds:

I. **Low** migration (**< 0.05** mg/kg food), only a limited dataset is needed.

II. Migration **between 0.05 and 5** mg/kg food, a reduced dataset may suffice.

III. High migration (**5–60** mg/kg food), an extensive dataset is needed.



ADOPTED: 30 July 2008
UPDATED: 09 September 2020
doi: 10.2903/j.efsa.2008.21r

NOTE FOR GUIDANCE

FOR THE PREPARATION OF AN APPLICATION FOR THE SAFETY ASSESSMENT OF A SUBSTANCE TO BE USED IN PLASTIC FOOD CONTACT MATERIALS

EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in contact with Food (AFC),
Vittorio Silano, Claudia Bolognesi, Laurence Castle, Jean-Pierre Cravedi, Karl-Heinz Engel, Paul Fowler, Roland Franz, Konrad Grob, Rainer Gürtler, Trine Husøy, Sirpa Kärenlampi, Wim Mennes, Maria Rosaria Milana, André Penninks, Maria de Fátima Tavares Poças, Andrew Smith, Christina Tlustos, Detlef Wölfle, Holger Zorn and Corina-Aurelia Zugravu.

This guidance was originally adopted by the Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) on 30 July 2008; the last revision was endorsed by the Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) on 9 September 2020[1].

Endorsement date	**9 September 2020**
Implementation date	**27 March 2021**

EFSA NOTE FOR GUIDANCE FOR FCM APPLICATIONS

I. In case of **migration below 0.05 mg/kg** of food/food simulant:

- At least **two in vitro genotoxicity tests** are needed, in line with the testing strategies of the EFSA Scientific Committee recommendations on genotoxicity testing strategies:
  - i) A bacterial reverse mutation test
  - ii) An in vitro mammalian cell micronucleus test

II. In cases where **migration is in the range from 0.05 to 5 mg/kg** of food/food simulant, the following data are needed:

- At least **two genotoxicity tests**, as indicated above
- A **90-day oral toxicity study**
- Data to demonstrate the absence of potential for accumulation in man

EFSA NOTE FOR GUIDANCE FOR FCM APPLICATIONS

III. In case of high migration (**5–60 mg/kg** food/food simulant)**, a full dataset** is needed:

- At least **two genotoxicity tests**, as indicated above
- A **90-day oral toxicity study**
- Studies on **absorption, distribution, metabolism and excretion**
- Studies on **reproduction and developmental toxicity**
- Studies on **long-term toxicity/carcinogenicity**

EFSA'S SELF TASK MANDATE & TERMS OF REFERENCE

- **Mandate**: EFSA self-task to update the FCM note for guidance to include the assessment of the use of hazardous bisphenols in FCM.

- **ToRs:** The FCM Panel is requested by EFSA to update the Note for Guidance for the preparation of an application for the Safety Assessment of a Substance to be used in Plastic Food Contact Materials (2021), specifying the requirements needed by the Panel to assess the safety of hazardous bisphenols and their derivatives in their use in FCM (plastic and non-plastic).

The task should be completed by **19 January 2027** (including public consultation, webinar).

APPROACH & OUTPUT DEVELOPMENT

- The EFSA's scientific output will be a **Statement** complementing the FCM NfG with the information and data requirements necessary for the assessment of BPs.
- It will be based on the EFSA opinions and all other assessments on BPs, including the ECHA assessments (screenings, CLH opinions, etc..).

Datasets identified as relevant to be considered:

I. Immunotoxicity
II. Metabolic effects
III. Reproductive toxicity
IV. Toxicokinetics
V. Any other endpoint that could trigger effects at a dose level that is not currently covered by the FCM NfG tiered approach.

Technical Report

2020 EFSA ASSESSMENT OF NEW INFO ON BPS

In 2019, the **Commission asked EFSA to assess the impact** on the current authorisation of BPS in plastic FCM **of the newly generated studies** submitted by the Registrant(s) of BPS in response to the ECHA's Decision **on the substance evaluation under the REACH** Regulation (EC) No 1907/2006.

These studies include a **Reproductive Toxicity Study** (EOGRTS), with **developmental- neurotoxicity** (DNT) and **-immunotoxicity** (DIT) cohorts (OECD test guideline (TG) 443), and a **toxicokinetic** (TK) study (OECD TG 417) in rats.

The **lowest NOAEL** from the EOGRTS was identified **for developmental toxicity and developmental immunotoxicity** at the lowest BPS dose tested of **20 mg/kg bw per day**.

The mid-dose of 60 mg/kg bw per day was the NOAEL for general systemic toxicity, whereas developmental neurotoxicity, fertility and reproductive performance were not affected even at the high dose tested of 180 mg/kg bw per day. The new kinetic data support that BPS is rapidly metabolized and eliminated from rats.

Based solely on the studies above, EFSA concluded that the lowest **NOAEL of 20 mg/kg bw per day from the EOGRTS neither affects the current SML for BPS of 0.05 mg/kg food nor BPS current authorisation** under Regulation (EU) No 10/2011.

EFSA is nonetheless aware that other toxicological studies have been published since BPS authorisation. This report **does not take into consideration the full toxicological dataset** available for this compound.

2025 ECHA SCREENING ASSESSMENT OF BPs

Source: ***ECHA RAC BPA opinion_Sep.2025 -*** *[opinion published*]*

- Besides the request to revise the existing OEL for BPA, DG EMPL requested ECHA to perform a screening of other BPs relevant for occupational health.

- ECHA identified **BPS, BPF, BPAF** as most relevant BPs, screened the existing information and whether they are similar to BPA:
  - BPS (as BPA) is indicated as SVHC (EDs) for HH and ENV, while BPF and BPAF only for ENV (currently), based on their endocrine properties.
  - Because of similar structures, toxicokinetics properties and MoA are similar to BPA's (but some differences also exist)
    - For an equivalent oral exposure, all 3 BPs show a higher internal exposure to the unconjugated bisphenol than BPA.
    - It cannot be excluded that **effects noted** for BPS, BPF and BPAF could occur **at lower dose levels** compared to BPA.
  - Focus on Reproductive toxicity endpoints – **effects at lower doses** for BPS, BPF and BPAF compared to BPA:
    - BPS (eg. decrease in fertility index and number of implantation sites) at 300 mg/kg bw per day (oral gavage).
    - BPF (eg. low number of implantation sites) at 100 mg/kg bw per day
    - BPAF (eg. no or fewer pregnancies) at 300 mg/kg bw per day, and at 30 and 100 mg/kg bw per day.
    - These types of effects are not noted with BPA up to 640 mg/kg bw per day.

*Opinion published on ECHA website: https://echa.europa.eu/oels-activity-list/-/substance-rev/72807/term

2025 ECHA SCREENING ASSESSMENT OF BPs

Source: ***ECHA RAC BPA opinion_Sep.2025***

- Immunotoxicity (Comparative study - Malaise et al., 2020 – developmental immunotoxicity):
  - BPS exposure induced an **increase of anti-E.Coli IgG** in plasma at **5 µg/kg** bw per day (oral exposure).
  - BPF exposure induced prominent changes at low dose in offspring mice, in term of intestinal and systemic immune responses, provoking an **intestinal and systemic Th1/Th17 inflammation** (**5 or 50 µg/kg** bw per day).
- Metabolic effects (Varghese & Hall. 2023). :
  - BPF: obesogenicity effect unclear - no effect on lipid accumulation in a murine preadipocyte (instead decreased the expression of several adipogenic markers) - function as a PPARg agonists differentiation assay
  - BPAF is suggested to have **pro-inflammatory effects in human adipocytes.**
- Genotoxicity:
  - Similar to BPA, there are **no clear indications of a mutagenic/ genotoxic activity for BPS, BPF or BPAF**
- Carcinogenicity:
  - No studies are available for BPS, BPF or BPAF

Thank you for your attention