WEBINAR:
Learn more about the risk assessment of phthalates used in plastic food contact materials

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Draft update of the risk assessment of di-butylphthalate (DBP), butyl-benzyl-phthalate (BBP), bis(2-ethylhexyl)phthalate (DEHP), di-isononylphthalate (DINP) and di-isodecylphthalate (DIDP) for use in food contact materials

EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP),
Webinar guide for attendees

- This webinar is being recorded!
- The webinar is in English and questions should be submitted in English through the platform (see hereunder).
- You are automatically connected to the audio broadcast. One-way audio (listen only mode).

Presentation window

Q&A box: For any questions related to the topic

Chat box: For technical issues related questions

Trusted science for safe food

European Food Safety Authority
## Webinar agenda

<table>
<thead>
<tr>
<th>TIME</th>
<th>ITEM</th>
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<tbody>
<tr>
<td>10:30-10:35</td>
<td>Objective and outline of the webinar, introduction of the two presenters</td>
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<td>10:35-10:45</td>
<td>Introduction to the mandate</td>
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<td>10:45-10:55</td>
<td>Exposure assessment</td>
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<td>10:55-11:00</td>
<td>Live Q&amp;A window</td>
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<td>11:00-11:15</td>
<td>Hazard identification, hazard characterisation, risk analysis</td>
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<td>11:15-11:25</td>
<td>Live Q&amp;A window</td>
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<td>11:25-11:30</td>
<td>Closure of the webinar and take home messages</td>
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</table>
What are phthalates?

→ **additives** that are used in **plastics** as plasticisers (e.g. for gaskets) and as technical support agents

- **migration** from plastics
  → human exposure

- **different exposure routes and sources**
  (environment, food, food contact materials, medical devices, ...)

![Dibutyl phthalate (DBP)](image-url)
### 2005: Publication of EFSA’s opinions

- DBP
  - Di-butylphthalate
- BBP
  - Butyl-benzyl-phthalate
- DEHP
  - Bis(2-ethylhexyl)phthalate
- DINP
  - Diisononyl phthalate
- DIDP
  - Diisodecyl phthalate

Authorized for use as plasticisers and technical support agents in **plastic Food Contact Materials (FCM)** (Regulation (EU) No 10/2011)

### 2017: Publication of ECHA RAC’s opinion

- DBP
- BBP
- DEHP
- DIBP
  - Not authorised for use in FCM

NEW assessment by ECHA including also data from after 2005

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**Committee for Risk Assessment (RAC)**

**Committee for Socio-economic Analysis (SEAC)**

Opinion on an Annex XV dossier proposing restrictions on **FOUR PHTHALATES (DEHP, BBP, DBP, DIBP)**
Update the EFSA’s 2005 risk assessments of five phthalates, based on:

- All information available to the ECHA RAC (2017)
- Recent exposure and toxicity data (focus on reproductive toxicity)

- DBP
- BBP
- DEHP
- DINP
- DIDP
Mandate from European Commission

- Assessing also

  - contribution of plastic FCM

  - potential health risks from consumer exposure to these phthalates from plastic FCMs

  - DBP
  - BBP
  - DEHP
  - DINP
  - DIDP

  Deadline: 31 July 2019
Interpretation of the mandate

DBP, BBP, DEHP

- Review of toxicological data used by ECHA (2017), mainly on reproductive toxicity

DINP, DIDP

- Recent data on reproductive toxicity, including:
  - ECHA RAC assessment of DINP and DIDP (2013)
  - ECHA RAC opinion on a proposal for harmonised classification and labelling of DINP (2018)
Interpretation of the mandate

- analyse the **possibility** of setting a **group health based guidance value**

- **refine** the assessment of **dietary exposure**

**HOWEVER:**
recognising the limitations of this approach

➔ **uncertainty** analysis and **recommendations** for future assessments
Dietary exposure assessment
From EFSA Chemical Occurrence Database

Several limitations, e.g.
• limited number of samples per food category
• high LOD/LOQs
• high percentage of left-censored data

Alternative approach: literature data (after 2008)

- **Lower Bound** approach → values < LOD/Q set to 0
- When several values available for one food category → highest value chosen
Estimation of dietary exposure

Literature **occurrence** data
(pooled European sample)

\( \times \)

Food **consumption data** from
EFSA Comprehensive Database

using FoodEx classification (food descriptor for each category)
Estimation of chronic dietary exposure:

- at individual level per dietary survey and age class (eight population groups)

- by combining the mean/median occurrence value with the average daily consumption for each food type

→ estimates for mean and high (P95) consumers
Scenario 1

Dietary exposure to the five individual phthalates

Scenario 2

Potency-adjusted aggregated dietary exposure to four phthalates included in the group-TDI

(expressed as DEHP equivalents)
## Dietary exposure - results

<table>
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<tr>
<th>Compound</th>
<th>Mean exposure (min-max) (μg/kg bw per day)</th>
<th>P95 exposure (min-max) (μg/kg bw per day)</th>
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<td>Group Phthalates</td>
<td>0.865 – 7.205</td>
<td>1.640 – 11.738</td>
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</table>
EFSA estimates for dietary exposure in **good agreement** with

- Exposure estimates reported in *Total Diet Studies* from UK, Ireland and France

- **Human biomonitoring** data and **exposure modelling** data from ECHA (2017)
Review of papers investigating source of phthalates in food and possible contribution from FCM

→ **did not allow** to conclude on plastic FCM contribution to dietary exposure
Q&A session 1
ECHA (2017): DEHP, DBP, BBP (and DIBP)

- focus on reproductive toxicity (most robust dataset)
- assessment of other endpoints: neuro - metabolic – immune

→ Indications for more sensitive endpoints than reproductive toxicity, BUT: no quantitative risk assessment

→ EFSA agreement with ECHA

Consideration of the other effects in uncertainty analysis and recommendations of EFSA draft opinion
Confirmation of critical effects and identified NOAELs/LOAEL from EFSA’s 2005 assessments (also in agreement with ECHA RAC)

- **Reproductive toxicity**
  - DBP 0.01 (Lee et al., 2004)
  - BBP 0.5 (Tyl et al., 2001, 2004)
  - DEHP 0.05 (Wolfe and Layton, 2003)

- **Liver toxicity**
  - DINP 0.15 (Exxon, 1986/Lington, 1997)
  - DIDP 0.15 (Exxon, 1997, 2000/Hushka et al., 2001)

Individual TDI (mg/kg bw per day)
In **2005**: EFSA concluded on **insufficient evidence** for grouping the five phthalates

**Now**: **new evidence** on

- **dose-additivity** and **mode of action** underlying the **reproductive toxicity**
  (reduction of fetal testosterone production)

→ Considerations on the **plausibility** of deriving a **group-TDI based** on **reproductive toxicity**
Robust evidence for DBP, BBP and DEHP

Also considering their harmonised classification as **reprotoxicants 1B**

(CLH - Harmonised Classification and Labelling)
DINP – main considerations:

1) CLH opinion (ECHA RAC, 2018):

- No gross-structural malformations,
  no permanent decreases of anogenital distance,
  no permanent nipple retention

- Reversible histological changes in foetal testes and effects on testosterone production
  → not considered sufficient for classification

- ECHA conclusion: „No classification for DINP for either effects on sexual function and fertility, or for developmental toxicity is warranted“
DINP – main considerations:

2) **reduction in fetal testosterone**  
(NOAEL 50 mg/kg bw per day)

- **lower potency** compared to DBP, BBP and DEHP and **transient** nature of the effect

- **BUT:** indications for **common mode of action** and **co-exposure**

**Conclusion:** **INCLUDE** DINP in the group-TDI
No inclusion in the group-TDI

- **DIDP**
  - No CLH classification as reprotoxicant
  - No reduction in fetal testosterone levels

→ **NOT INCLUDED** in the group-TDI
EFSA SC Draft guidance on mixtures

- **Index compound** with most robust underlying data set → DEHP

→ group-TDI: 0.05 mg/kg bw per day

- Derivation of **Relative Potency Factors**

\[ RPF = \frac{HBGV \text{ index compound}}{HBGV \text{ substance}} \]
### How to derive a RPF for **DINP**?

<table>
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<tr>
<th>Pivotal endpoint</th>
<th>But: <strong>group-TDI</strong> based on reproductive toxicity</th>
</tr>
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<tbody>
<tr>
<td><strong>liver toxicity</strong>&lt;br&gt;NOAEL: 15 mg/kg bw per day</td>
<td>NOAEL of DINP: 50 mg/kg bw per day</td>
</tr>
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**Hybrid-approach:**
additional assessment factor of **3.3** to cover also the more sensitive liver effects
# Calculation of RPFs

<table>
<thead>
<tr>
<th></th>
<th>DEHP</th>
<th>BBP</th>
<th>DBP</th>
<th>DINP (reproductive effects)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N(L)OAEL</strong></td>
<td>4.8</td>
<td>50</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td><strong>Uncertainty factors</strong></td>
<td>100</td>
<td>100</td>
<td>200</td>
<td>100</td>
</tr>
<tr>
<td><strong>Additional assessment factor</strong></td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td><strong>3.3</strong></td>
</tr>
<tr>
<td><strong>HBGV</strong></td>
<td>0.05</td>
<td>0.5</td>
<td>0.01</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>RPF</strong></td>
<td>1</td>
<td>0.1</td>
<td>5.0</td>
<td><strong>0.3</strong></td>
</tr>
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</table>
aggregated dietary exposure

based on potency-adjusted occurrence data, expressed as DEHP equivalents

GroupPhthalates (µg/kg food) = DEHP*1 + BBP*0.1 + DBP*5 + DINP*0.3

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## Risk characterisation

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→ **Group Phthalates**: Contribution **up to 23%** of group-TDI

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→ **DIDP**: Contribution **far below** TDI (1,500-fold)
Uncertainty analysis

- **Qualitative** approach

- **Main sources of uncertainty:**
  - Focus on reproductive toxicity and **lack of review of other endpoints** (possibly more sensitive)
  - **Co-exposure to other phthalates** with similar effects, e.g. DIBP
Recommendations

- Call for data
  - occurrence of phthalates in food
  - contribution from (plastic) FCM

- Investigation of other, possibly more sensitive effects (immunotoxic, metabolic, neurotoxic)

- Application of Benchmark Dose Modelling approach

- Assessment of co-exposure to other phthalates with similar effects, e.g. DIBP
Where do we stand in the process?

- **6 February**: Endorsement of draft opinion
- **21 February**: Launch of public consultation
- **15 March**: Webinar
- **14 April**: Closure of public consultation
- **July**: Planned adoption of opinion

Q&A session 2
Thank you for attending our webinar!

In case we did not manage to answer all your questions, please feel free to re-submit them via e-mail at: fip@efsaeuropa.eu

Please take 5 more minutes to fill out the evaluation form that you will receive shortly in your inbox. Your feedback will help us improve our service!