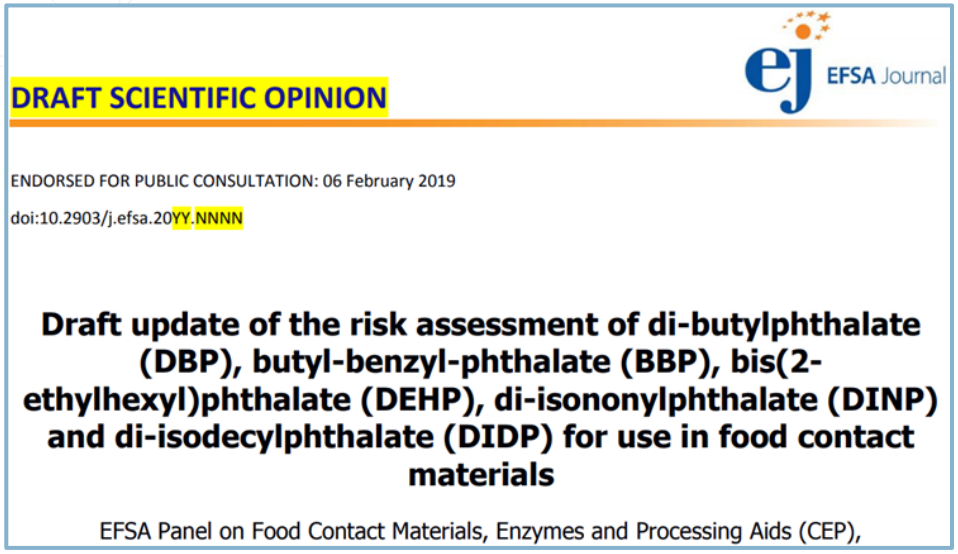
15 March 2019

WEBINAR:

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



EFSA Journal

DRAFT SCIENTIFIC OPINION

ENDORSED FOR PUBLIC CONSULTATION: 06 February 2019

doi:10.2903/j.efsa.20YY.NNNN

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),

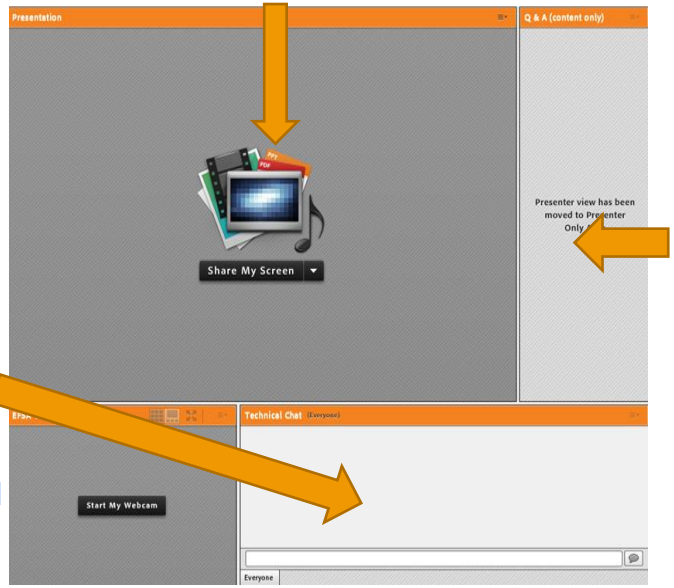
Trusted science for safe food

efsa
European Food Safety Authority

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



Chat box: For technical issues related questions

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

Trusted science for safe food

efsa
European Food Safety Authority

Webinar agenda

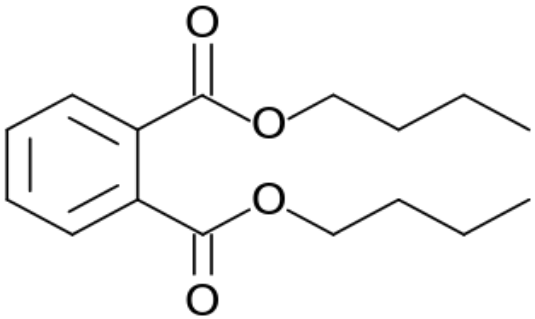
TIME	ITEM
10:30-10:35	Objective and outline of the webinar, introduction of the two presenters
10:35-10:45	Introduction to the mandate
10:45-10:55	Exposure assessment
10:55-11:00	Live Q&A window
11:00-11:15	Hazard identification, hazard characterisation, risk analysis
11:15-11:25	Live Q&A window
11:25-11:30	Closure of the webinar and take home messages

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)

Mandate July 2017 - background

2005:
publication of
EFSA's opinions

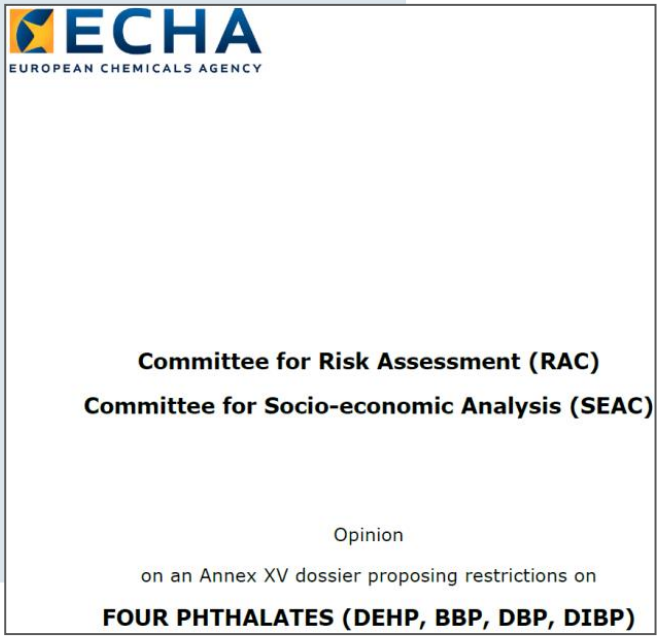
- DBP
  - Di-butylphthalate
- BBP
  - Butyl-benzyl-phthalate
- DEHP
  - Bis(2-ethylhexyl)phthalate
- DINP
  - Diisononyl phthalate
- DIDP
  - Diisodecyl phthalate

Authorised 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


ECHA
EUROPEAN CHEMICALS AGENCY

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)

Mandate from European Commission

- **Update** the EFSA's 2005 **risk assessments of five phthalates**, based on:

All **information** available to the **ECHA** RAC (2017)

- DBP
- BBP
- DEHP

Recent **exposure** and **toxicity** data (focus on reproductive toxicity)

- 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)

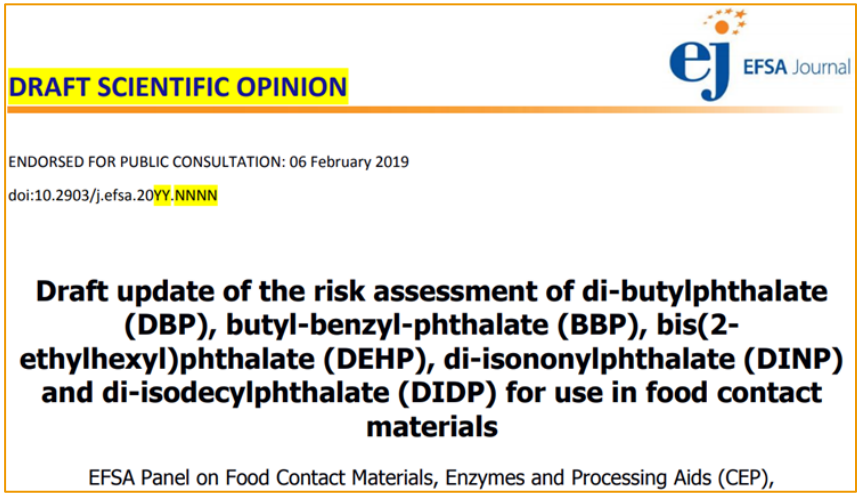
Interpretation of the mandate

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

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

HOWEVER:

recognising the limitations of this approach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EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP),

→**uncertainty** analysis and **recommendations** for future assessments

Dietary exposure assessment

Phthalates occurrence in food

- 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)

x

Food **consumption data** from

EFSA Comprehensive Database

using FoodEx classification (food descriptor for each category)

Estimation of dietary exposure

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

Dietary exposure scenarios

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

Compound	Mean exposure (min-max) (µg/kg bw per day)	P95 exposure (min-max) (µg/kg bw per day)
DBP	0.042 – 0.769	0.099 – 1.503
BBP	0.009 – 0.207	0.021 – 0.442
DEHP	0.446 – 3.459	0.902 – 6.148
DINP	0.232 – 4.270	0.446 – 7.071
DIDP	0.001 – 0.057	0.008 – 0.095
GroupPhthalates	0.865 – 7.205	1.640 – 11.738

Comparing exposure estimates

- 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)

Contribution from plastic FCM to dietary exposure

- 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

Hazard assessment

- **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

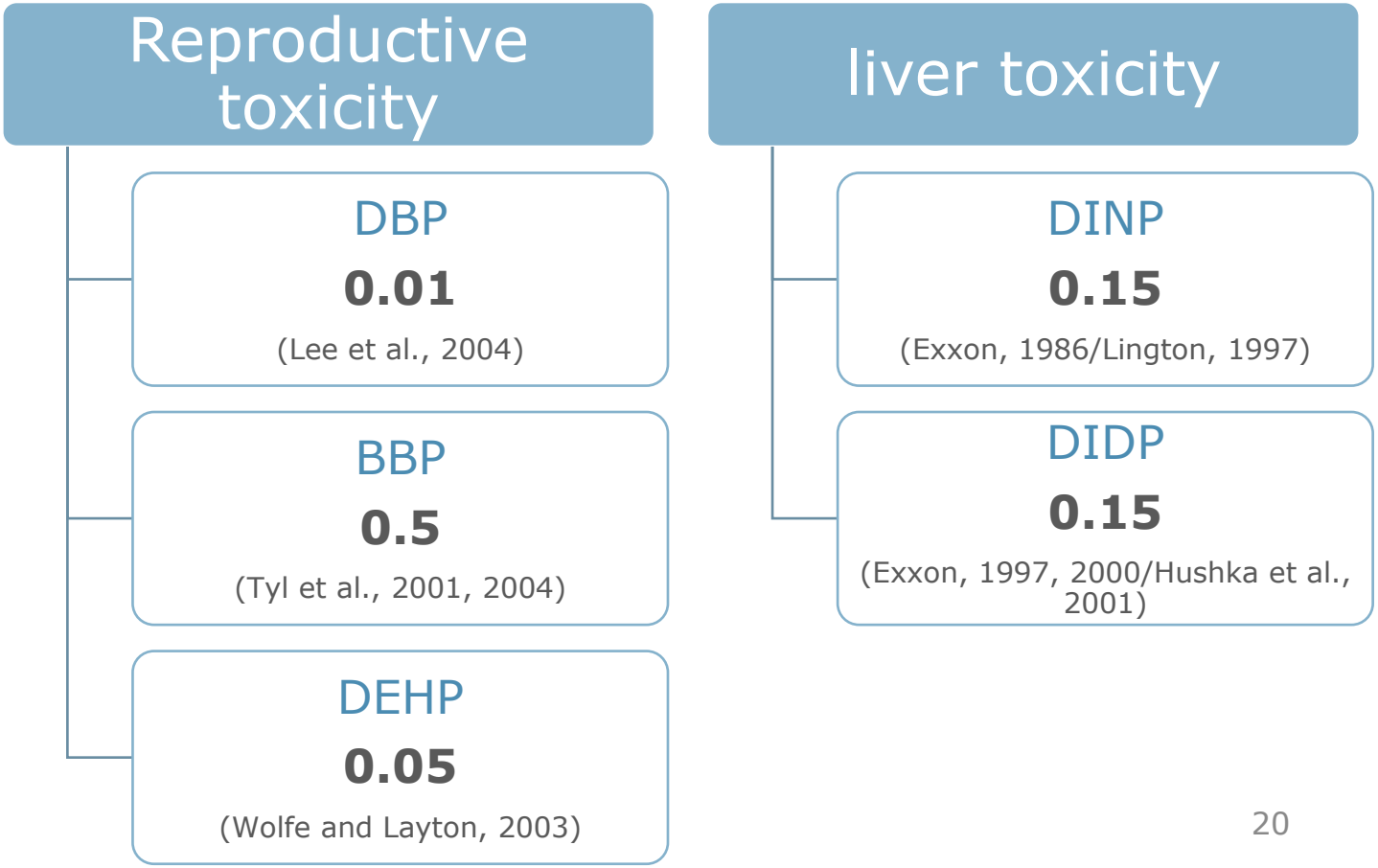
Consideration of the other effects in uncertainty analysis and recommendations of EFSA draft opinion

Hazard assessment – critical effects

- **Confirmation** of critical effects and identified NOAELs/LOAEL from EFSA's **2005 assessments** (also in agreement with ECHA RAC)

→Individual TDIs

(mg/kg bw per day)



Considerations on grouping

- 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

Inclusion in the group-TDI

- Robust evidence for **DBP, BBP and DEHP**
  - Also considering their harmonised classification as **reprotoxicants 1B**

(CLH - Harmonised Classification and Labelling)

Inclusion in the group-TDI

- **DINP** – main considerations:

  1) CLH opinion (**ECHA RAC, 2018**):

  - **No** gross-structural malformations,
    no permantent 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"

Inclusion in the group-TDI

- **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

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**

$$RPF = \frac{HBGV\ index\ compound}{HBGV\ substance}$$

Group-TDI

How to derive a RPF for **DINP**?

Pivotal endpoint **liver toxicity** NOAEL: 15 mg/kg bw per day	But: **group-TDI** based on **reproductive toxicity** NOAEL of DINP: 50 mg/kg bw per day

Hybrid-approach:

additional assessment factor of 3.3 to cover also the more sensitive liver effects

Calculation of RPFs

	DEHP	**BBP**	**DBP**	**DINP** (reproductive effects)
N(L)OAEL	4.8	50	2	50
Uncertainty factors	100	100	200	100
Additional assessment factor	n/a	n/a	n/a	**3.3**
HBGV	0.05	0.5	0.01	0.15
RPF	**1**	**0.1**	**5.0**	**0.3**

RPFs in the exposure assessment

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

Compound	Mean exposure	P95 exposure
DBP	0.042 – 0.769	0.099 – 1.503
BBP	0.009 – 0.207	0.021 – 0.442
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Risk characterisation

	Dietary exposure (µg/kg bw per day)	**Group-TDI** (µg/kg bw per day)
GroupPhthalates	**Mean**: 0.865–7.205 **P95**: 1.640–11.738	50

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

	Dietary exposure (µg/kg bw per day)	**TDI** (µg/kg bw per day)
DIDP	**Mean**: 0.001 – 0.057 **P95**: 0.008 – 0.095	150

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

Uncertainty analysis

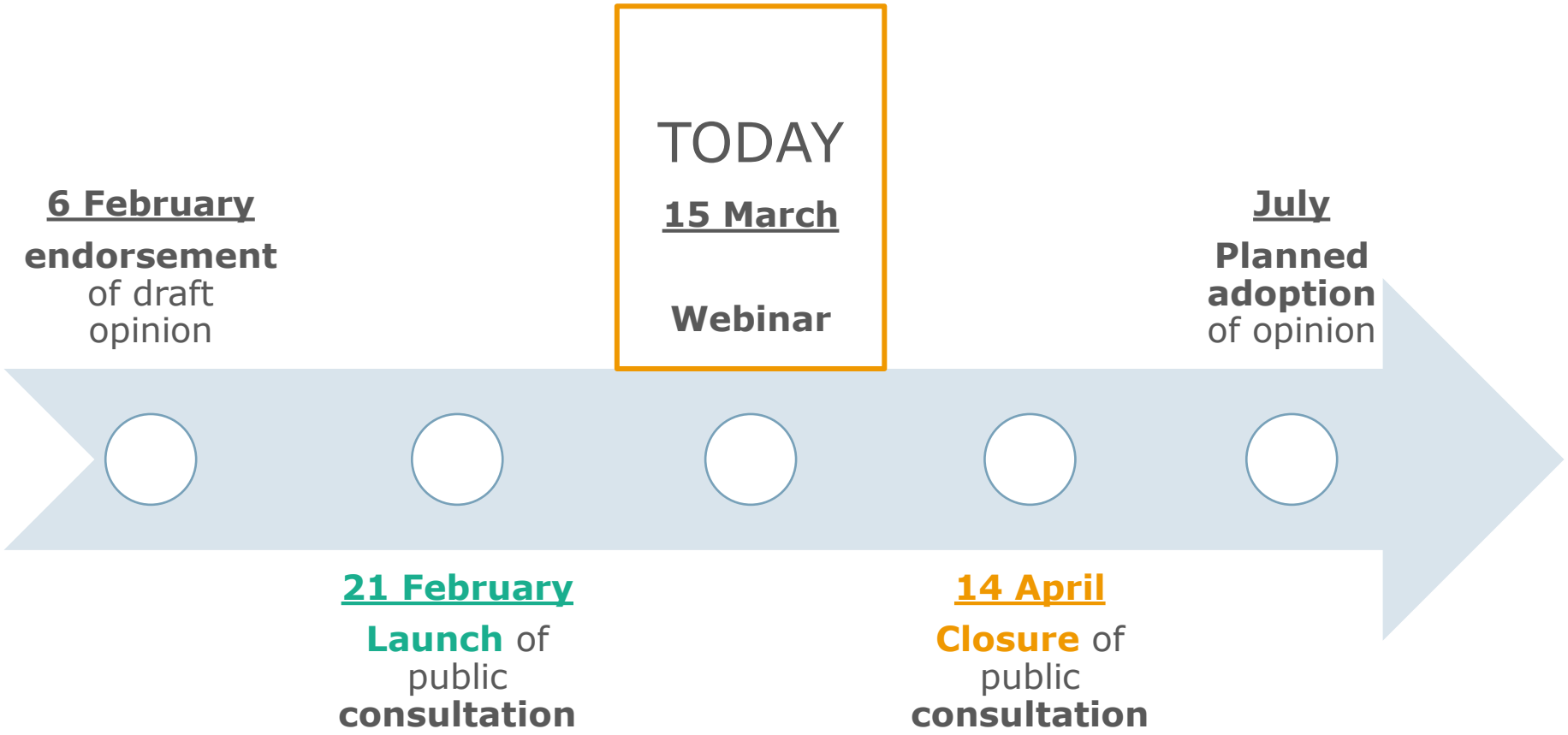
- **Qualitative** approach

- 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?



http://www.efsa.europa.eu/en/consultations/call/190221

- 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@efsa.europa.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!