Webinar | 11 December 2025

EFSA'S CONTAM PANEL UPDATE OF THE OPINION ON DIOXINS AND DL-PCBs IN FOOD AND FEED

STARTING AT 10:00 CET

efsa
EUROPEAN FOOD SAFETY AUTHORITY

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You are automatically connected to the audio broadcast.

The event is in **English**

This event is **being recorded** for internal purposes

After the event, attendees will receive a **link to a survey** to evaluate the EFSA's event & services

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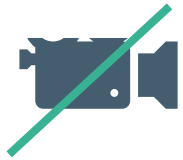
- Please **switch off your camera** and **mute your microphone**.
- Use the **dedicated Q&A chat box** to write your questions and comments.
- Participants **may not intervene** without being granted the floor by the Chair.
- **Recording or transcribing** the meeting **is not permitted**.
- If you experience technical issues, please contact the **Meeting Moderator via the chat.**



Q&A SESSION

- **Priority** will be given to questions submitted at the time of registration.
- Additional questions raised during the meeting will be addressed during the **Q&A session**.
  - Write in the **dedicated Q&A chat box** or raise your hand if you have a question.
  - When invited to speak by the Chair, please **turn on your camera and microphone**.
- **Questions outside the scope** of the webinar or EFSA's remit (e.g. risk management) will not be addressed.

AFTER THE EVENT

- Questions posted in the **dedicated Q&A chat** box not answered during the webinar, will be answered in written form after the webinar.

- If you have **further questions** after the webinar, please submit them via:
  - **#AskEFSA** service on the EFSA website https://www.efsa.europa.eu/en/applications/askaquestion

- If you have **comments to the draft updated Opinion**, please submit them via:
  - the **public consultation platform** on EFSA website: https://connect.efsa.europa.eu/RM/s/consultations/publicconsultation2/a0lTk000006Nv0X/pc1724

- The **presentation** will be published on the EFSA website after the meeting at EFSA's website

AGENDA

- Welcome and introduction to the Webinar
- Why is EFSA updating its 2018 risk assessment on PCDD/Fs and DL-PCBs in feed and food
- How EFSA approached the update of the exposure assessment
- How EFSA approached the update of the TWI
- Draft conclusions of the risk characterisation
- Questions and answers

TODAY'S MODERATORS AND SPEAKERS

Mary Bridget Gilsenan
Moderator
Head of Unit, FEEDCO Unit

Chantra Eskes
Team Leader
FEEDCO Unit, EFSA

Ron Hoogenboom
Chair of of EFSA WG Dioxins update

Helle Katrine Knutsen
Chair of the EFSA CONTAM Panel

Francesca Riolo
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Luisa Ramos Bordajandi
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TODAY'S CONTRIBUTORS

Evi Ntzani

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Welcome and introduction to the Webinar

Mary Gilsenan (Head of Unit FEEDCO, EFSA)

EFSA vision and mission

SCIENCE
SAFE FOOD
SUSTAINABILITY

Protecting consumers, animals, plants and the environment through independent and transparent scientific advice on risks in the food chain from farm to fork

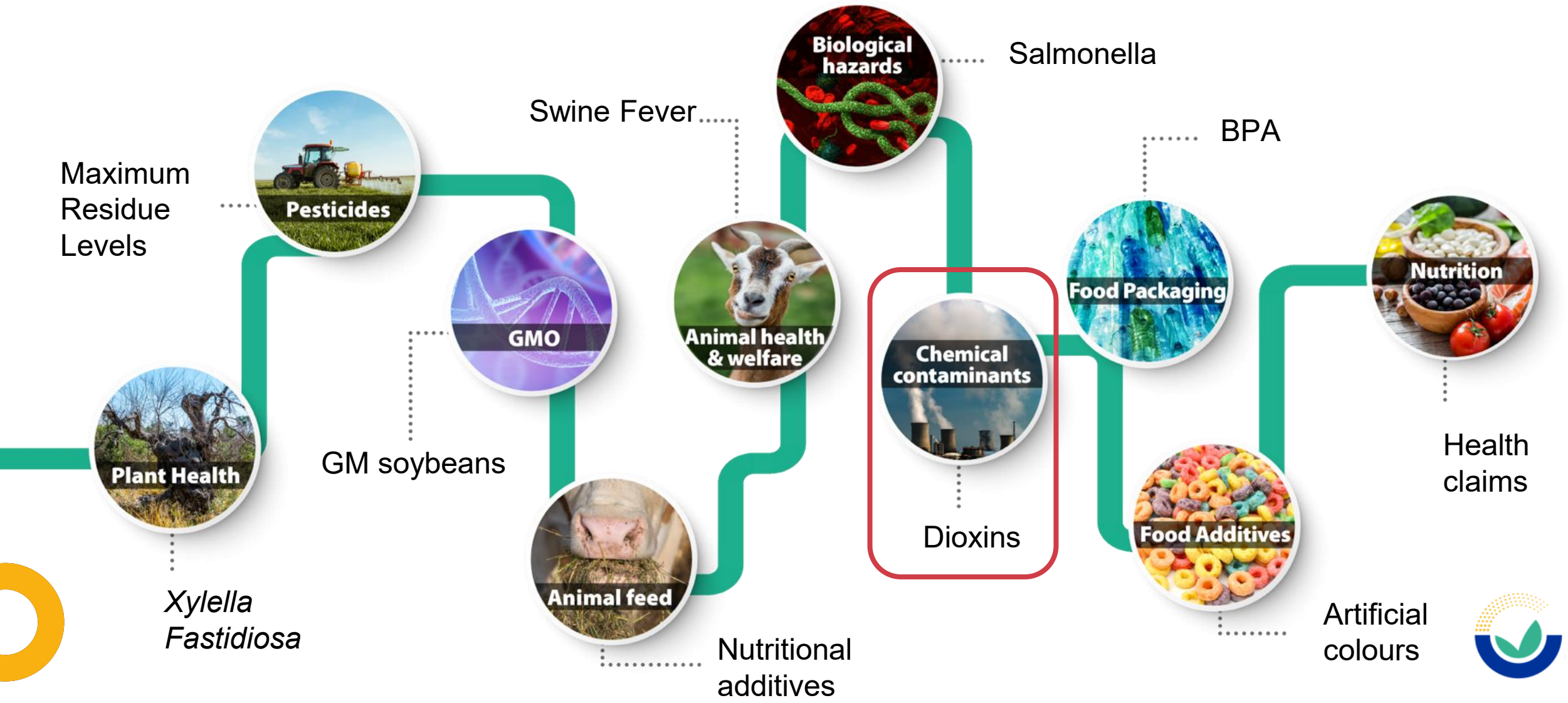
What EFSA does

- Provides independent scientific advice and support for EU risk managers and policy makers on food and feed safety
- Provides independent, timely risk communication
- Promotes scientific cooperation

What EFSA does NOT do

- Develop food safety policies & legislation
- Adopt regulations, authorise marketing of new products
- Enforce food safety legislation

SCIENCE – FOOD SAFETY FROM FARM TO FORK



HOW DOES EFSA WORK?

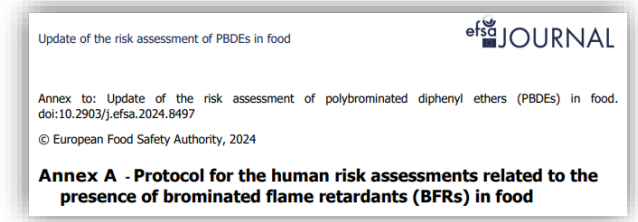
Who sends requests to EFSA

- European Commission
- European Parliament
- Member States
- EFSA self mandate

Once the request is received

EFSA RISK ASSESSMENT

- **Problem formulation and protocol development**
- **Data collection**
- **Evidence appraisal Data validation**
- **Evidence synthesis/ integration Data analysis**
- **Expert Knowledge Elicitation**
- **Publication**
- **Communication**


Update of the risk assessment of PBDEs in food

efsa JOURNAL

Annex to: Update of the risk assessment of polybrominated diphenyl ethers (PBDEs) in food. doi:10.2903/j.efsa.2024.8497

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Annex A - Protocol for the human risk assessments related to the presence of brominated flame retardants (BFRs) in food


SCIENTIFIC OPINION

efsa JOURNAL

Update of the risk assessment of polybrominated diphenyl ethers (PBDEs) in food

EFSA Panel on Contaminants in the Food Chain (CONTAM) | Dieter Schrenk | Margherita Bignami | Laurent Bodin | James Kevin Chipman | Jesús del Mazo | Bettina Grasl-Kraupp | Christer Hogstrand | Laurentius (Ron) Hoogenboom | Jean-Charles Leblanc | Carlo Stefano Nebbia | Elsa Nielsen | Evangelia Ntzani | Annette Petersen | Salomon Sand | Tanja Schwerdtle | Heather Wallace | Diane Benford | Peter Fürst | Andy Hart | Martin Rose | Henri Schroeder | Martine Vrijheid | Sofia Ioannidou | Marina Nikolić | Luisa Ramos Bordajandi | Christiane Vleminckx


Public hearing on plant lectins in food

9 September 2025, 11.30 - 13.00 (CEST)

Add to Calendar

Share:

Online

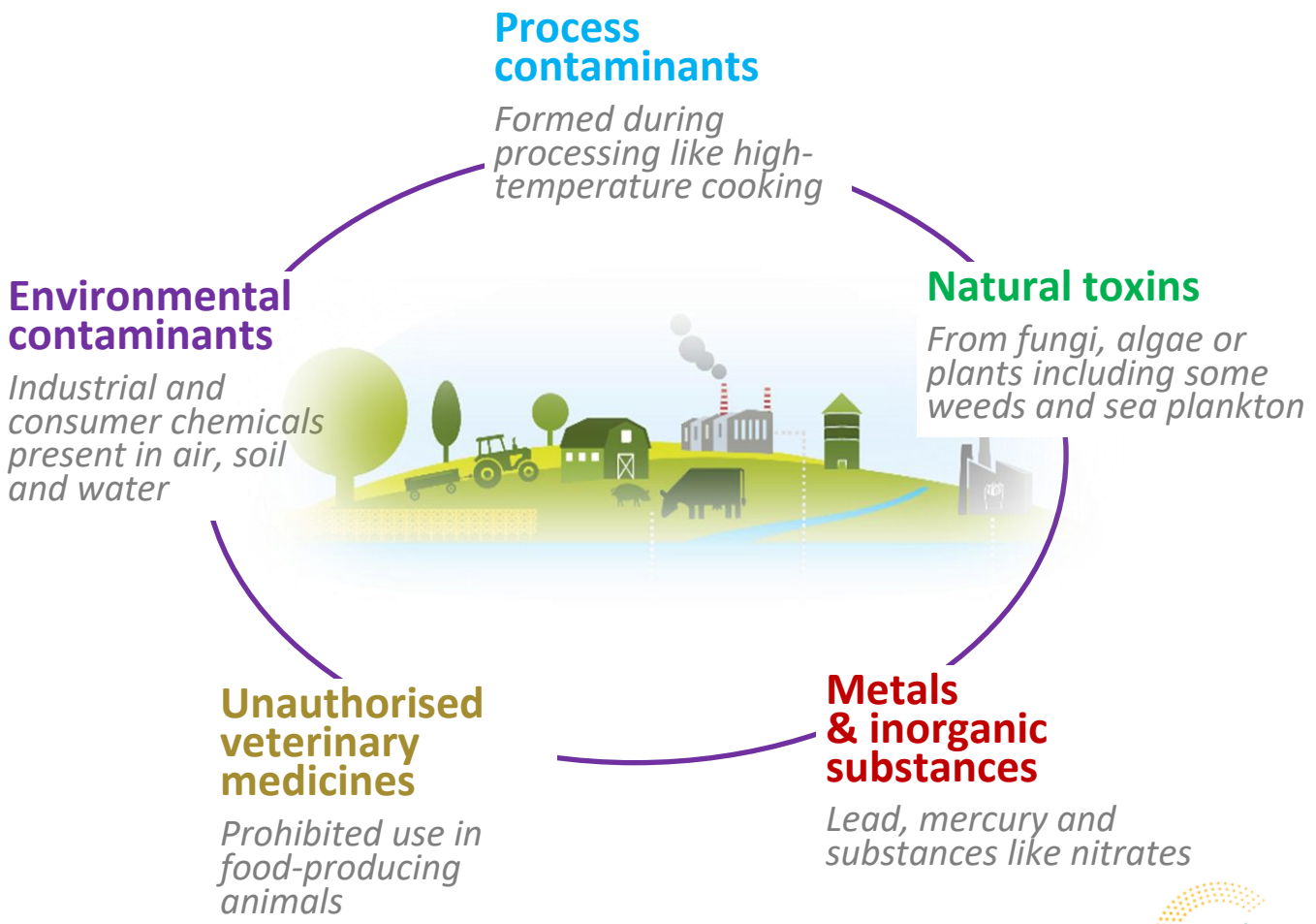
Receipt of the Mandate → Allocation to Scientific Panel (10 Scientific Panels + Scientific Committee) → Acceptance → Register of questions (OpenEFSA portal)

THE CONTAM PANEL

The CONTAM Panel and the EFSA CONTAM Team provide scientific advice on **contaminants in the food chain** and **undesirable substances** such as natural toxins, mycotoxins and residues of unauthorised substances, mainly through **generic mandates.**

19 Panel members with expertise in:

✓ Chemistry
✓ Exposure assessment
✓ Human and veterinary toxicology
✓ Epidemiology
✓ Statistics / PBK modelling
✓ Animal nutrition



THE CONTAM PANEL (2024-2029)

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Why is EFSA updating its 2018 risk assessment on PCDD/Fs and DL-PCBs in feed and food, and what are the main objectives of the update?

Luisa Ramos Bordajandi (WG coordinator, EFSA)

THE 2018 CONTAM OPINION

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 14 June 2018

AMENDED: 18 February 2019

doi: 10.2903/j.efsa.2018.5333

Risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food

Tolerable Weekly Intake (TWI) of 2 picograms/kg bw per week, expressed using the 2005 WHO Toxic Equivalency Factors (**2005 WHO-TEFs**), and based on decreased sperm concentration in boys from the Russian Children's Study cohort.

- When comparing the **mean and P95 exposure** to polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (DL-PCBs) of the different age groups, **exceedance of the TWI was observed**.
- The TWI was based on the association with PCDD/Fs in the critical human study. No significant association for DL-PCBs or the sum of PCDD/Fs and DL-PCBs observed.
- **Recommendation to update the 2005 WHO-TEFs**, based on data showing that DL-PCBs are less potent in human cells (expectation that association for the sum of PCDD/Fs and DL-PCBs would improve with new TEFs)

SINCE THE 2018 OPINION

- **In 2022**, a WHO Expert Group met, and updated the 2005 WHO-TEFs.
- **The new 2022 WHO-TEFs were published in 2024** (DeVito et al., 2024)

17 PCDD/Fs	2005 WHO-TEFs	2022 WHO-TEFs
2,3,7,8-TCDF	0.1	0.07
1,2,3,7,8-PeCDF	0.03	0.01
2,3,4,7,8-PeCDF	0.3	0.1
1,2,3,4,7,8-HxCDF	0.1	0.3
1,2,3,6,7,8-HxCDF	0.1	0.09
2,3,4,6,7,8-HxCDF	0.1	0.1
1,2,3,7,8,9-HxCDF	0.1	0.2
1,2,3,4,6,7,8-HpCDF	0.01	0.02
1,2,3,4,7,8,9-HpCDF	0.01	0.1
OCDF	0.0003	0.002
2,3,7,8-TCDD	1	1
1,2,3,7,8-PeCDD	1	0.4
1,2,3,4,7,8-HxCDD	0.1	0.09
1,2,3,6,7,8-HxCDD	0.1	0.07
1,2,3,7,8,9-HxCDD	0.1	0.05
1,2,3,4,6,7,8-HpCDD	0.01	0.05
OCDD	0.0003	0.001

non-*ortho* PCBs	2005 WHO-TEFs	2022 WHO-TEFs
PCB-81	0.0003	0.006
PCB-77	0.0001	0.0003
PCB-126	0.1	0.05
PCB-169	0.03	0.005
mono-*ortho* PCBs	**2005 WHO-TEFs**	**2022 WHO-TEFs**
PCB-123	0.00003	0.00003
PCB-118	0.00003	0.00003
PCB-114	0.00003	0.00003
PCB-105	0.00003	0.00003
PCB-167	0.00003	0.00003
PCB-156	0.00003	0.00003
PCB-157	0.00003	0.00003
PCB-189	0.00003	0.00003

Decision to keep the 2005 WHO-TEFs

MANDATE AND TERMS OF REFERENCE

- **In 2024,** EFSA received a mandate from the EC to **update the 2018 Opinion on the basis of the new 2022 WHO-TEFs**:

- The update should relate to all aspects of the risk assessment where the change in WHO-TEF values has an impact
- Deadline: **30th April 2026**

https://open.efsa.europa.eu/questions/EFSA-Q-2024-00227

MANDATE AND TERMS OF REFERENCE

Using 2022 WHO-TEFs,

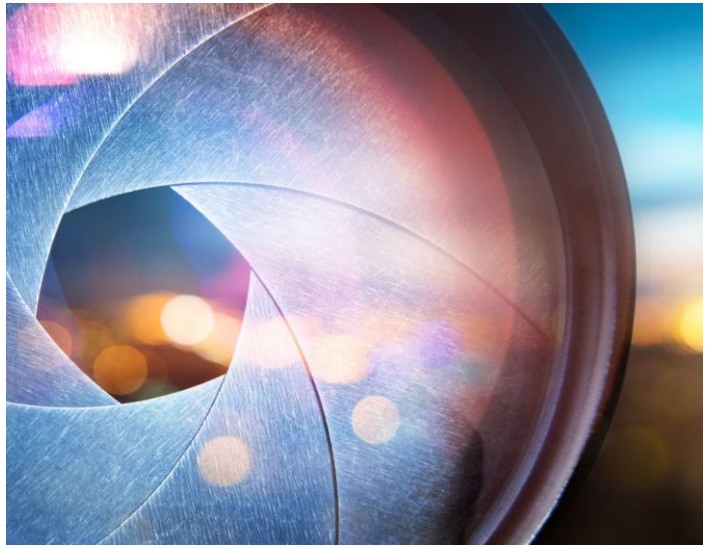
- Update of the **human dietary exposure assessment**
- Update of the **exposure for food-producing animals via feed**
- Update of the **human hazard identification/characterisation**
- Update of the **transfer from feed to food of animal origin**

→ Understand the impact of the change in WHO-TEFs

- **Occurrence data in food and feed** submitted to EFSA for the period 2013-2023
- **New evidence available in the public literature since the 2018 Opinion** on the toxicokinetics, toxicity, studies in humans, and mode of action of PCDD/Fs and DL-PCBs.

FOCUS OF THE WEBINAR

This Webinar focuses on the **approach and draft conclusions** related to the **human risk assessment**:



- Human dietary exposure assessment
- Hazard characterisation (health-based guidance value)
- Risk characterisation conclusions

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How EFSA approached the update of the exposure assessment to PCDD/Fs and DL-PCBs in food

Francesca Riolo (exposure assessor, EFSA)

FOOD OCCURRENCE DATA SUBMITTED TO EFSA

- A total of 83,031 food samples on PCDD/Fs and DL-PCBs **sampled from year 2013 to 2023** were available in the EFSA database by the 4th of September 2024.
- **Only the samples that were analysed for all 29 congeners** were retained for further validation steps:
  - 17,767 incomplete samples were excluded (mainly samples for which only PCB-118 was analysed)
- **After data validation**, **54,177 food samples** were used to estimate the dietary exposure.
- The food samples included in the final dataset:
  - were submitted by 24 Member States, plus Norway and Iceland
  - Germany and France submitted 64% of the samples.
  - sample distribution across the sampling year was comparable among the years.

FOOD OCCURRENCE DATA USED IN THE DIETARY EXPOSURE ASSESSMENT

FOODEX2_L1	N samples
Meat and meat products	22,737
Fish and seafood	13,647
Eggs and egg products	7399
Milk and dairy products	6293
Animal and vegetable fats and oils and primary derivatives thereof	1730
Food products for young population	810
Legumes, nuts, oilseeds and spices	409
Vegetables and vegetable products	326
Products for non-standard diets, food imitates and food supplements	303
Sugar and similar, confectionery and water-based sweet desserts	163
Grains and grain-based products	110
Composite dishes	90
Major isolated ingredients, additives, flavours, baking and processing aids	51
Fruit and fruit products	40
Coffee, cocoa, tea and infusions	20
Amphibians, reptiles, and terrestrial invertebrates	19
Seasoning, sauces and condiments	17
Starchy roots or tubers and products thereof, sugar plants	11
Fruit and vegetable juices and nectars (including concentrates)	1
Water and water-based beverages	1

FOOD OCCURRENCE DATA USED IN THE DIETARY EXPOSURE ASSESSMENT

- The highest occurrence levels were found in **fish meat** and **fish liver**.
- The data indicate that levels of both PCDD/Fs and DL-PCBs in **farmed fatty fish** are lower than those in **wild-caught fatty fish**.
- Higher levels of PCDD/Fs and DL-PCBs were found in **fish samples of Baltic origin** than in those of non-Baltic origin or unknown origin.

- In general, **eggs from hens with outdoor (including organic production)/free range access** showed higher levels of both PCDD/Fs and DL-PCBs than those kept indoors.

DIETARY EXPOSURE ASSESSMENT TO PCDD/Fs AND DL-PCBs

- **Chronic dietary exposure** was estimated for:
  - ➢ the sum of the 29 PCDD/Fs and DL-PCBs
  - ➢ the sum of the 17 PCDD/Fs
  - ➢ the individual 29 PCDD/Fs and DL-PCBs
- Comparison between dietary exposure estimates for the current Opinion (occurrence data submitted to EFSA from 2013-2023), **based on 2005- vs 2022 WHO-TEFs**

→ Understand the impact of the change in WHO-TEFs

TEFs = Toxic Equivalency Factors

DIETARY EXPOSURE BASED ON 2022 WHO-TEFs

Range of mean dietary exposure (pg WHO-TEQ/kg bw per day) using WHO_{2022}-TEFs

		Minimum		Median		Maximum	
Age group	**N surveys**	**LB**	**UB**	**LB**	**UB**	**LB**	**UB**
Infants	14	0.26	0.60	0.57	1.15	1.19	1.87
Toddlers	17	0.62	1.22	0.95	1.68	1.57	2.35
Other children	21	0.51	1.02	0.72	1.25	1.11	1.71
Adolescents	23	0.29	0.48	0.38	0.65	0.66	1.02
Adults	23	0.27	0.43	0.36	0.56	0.56	0.81
Elderly	21	0.25	0.42	0.37	0.55	0.68	0.91
Very elderly	16	0.24	0.41	0.35	0.57	0.63	0.87

Range of P95 dietary exposure (pg WHO-TEQ/kg bw per day) using WHO_{2022}-TEFs

		Minimum		Median		Maximum	
Age group	**N surveys**	**LB**	**UB**	**LB**	**UB**	**LB**	**UB**
Infants	13	0.60	1.23	1.55	2.57	3.13	4.39
Toddlers	16	1.23	1.96	2.04	3.08	3.30	4.72
Other children	21	0.97	1.74	1.52	2.31	2.40	3.28
Adolescents	22	0.61	1.08	0.87	1.33	2.10	2.54
Adults	23	0.59	0.90	0.92	1.25	1.65	2.09
Elderly	21	0.57	0.86	1.03	1.28	1.92	2.11
Very elderly	12	0.57	0.90	0.88	1.17	1.40	1.71

Dietary exposure in pg TEQ/kg bw per day (using the 2022 WHO-TEFs) ranged across surveys as follows:

- **Mean LB exposure**: from 0.24 in 'Very elderly' to 1.57 in 'Toddlers'
- **Mean UB exposure**: from 0.41 in 'Very elderly' to 2.35 in 'Toddlers'

- **P95 LB exposure**: from 0.57 in 'Elderly' and 'Very elderly' to 3.30 in 'Toddlers'
- **P95 UB exposure:** from 0.86 in 'Elderly' to 4.72 in 'Toddlers'

LB: Lower Bound
UB: Upper Bound

COMPARISON DIETARY EXPOSURE 2022 VERSUS 2005 WHO-TEFs

- Ratio (median and ranges) between the mean dietary exposure estimates based on 2022 WHO-TEFs and based on 2005 WHO-TEFs:

Age Group	N	Median LB	Range Ratio LB	Median UB	Range Ratio UB
Infants	11	0.73	0.68 – 0.87	0.78	0.72 – 0.89
Toddlers	14	0.69	0.64 – 0.77	0.72	0.69 – 0.83
Other children	20	0.69	0.62 – 0.79	0.72	0.66 – 0.79
Adolescents	19	0.69	0.61 – 0.78	0.72	0.65 – 0.78
Adults	18	0.66	0.60 – 0.78	0.7	0.64 – 0.79
Elderly	19	0.65	0.58 – 0.78	0.69	0.63 – 0.79
Very elderly	13	0.66	0.60 – 0.81	0.7	0.65 – 0.79

  - The median Lower Bound ratio ranged between 0.65 and 0.73 across age groups.
  - Lower Bound exposure estimates with the new 2022 WHO-TEFs are between **27% and 35% lower** than those obtained using 2005 WHO-TEFs.

CURRENT DIETARY EXPOSURE - CONTRIBUTION DIFFERENT FOOD GROUPS

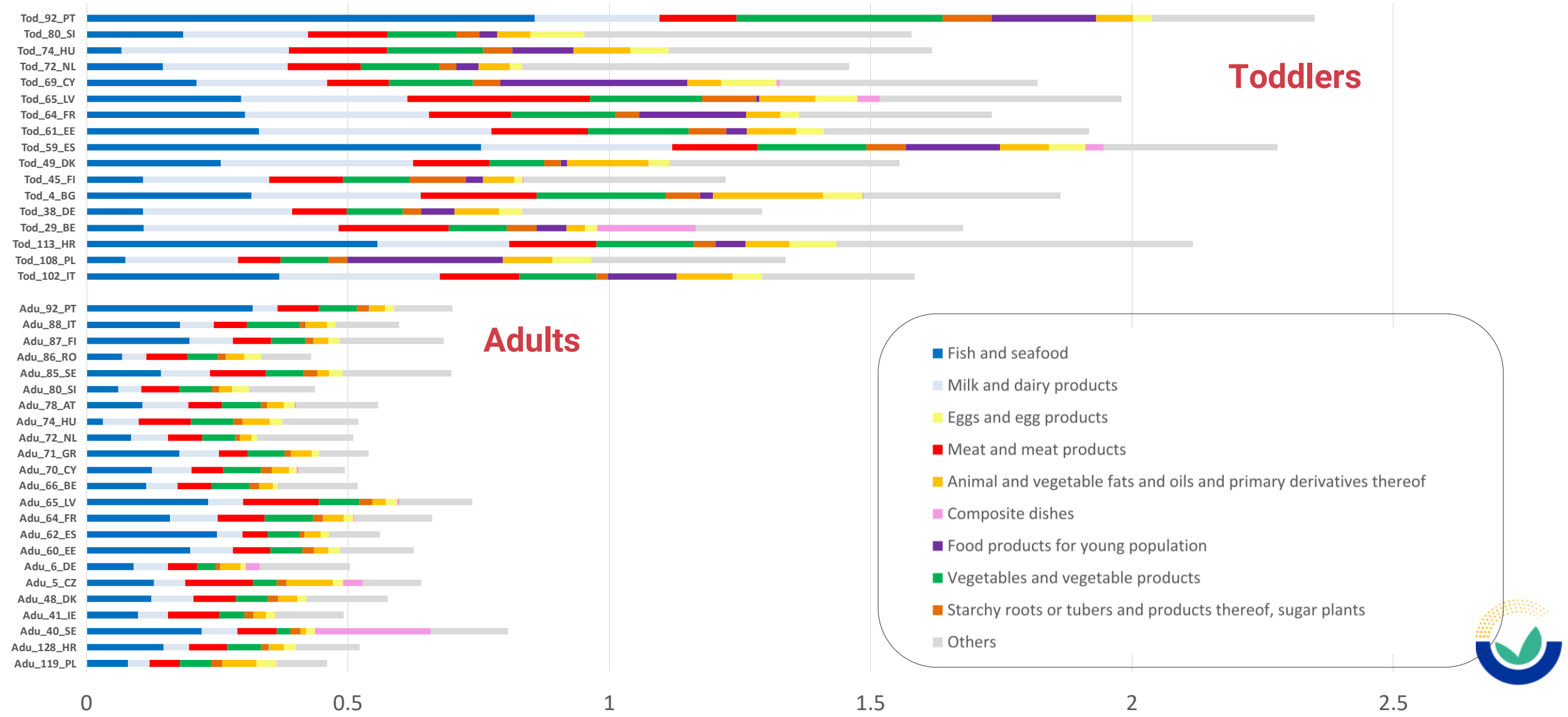
- The **% contribution** was calculated considering the exposure estimated at the Lower Bound (to avoid that the contribution of certain food groups is artificially driven by left-censored results):


Milk and dairy products and **Fish and fish products** were the food categories contributing most to the dietary exposure

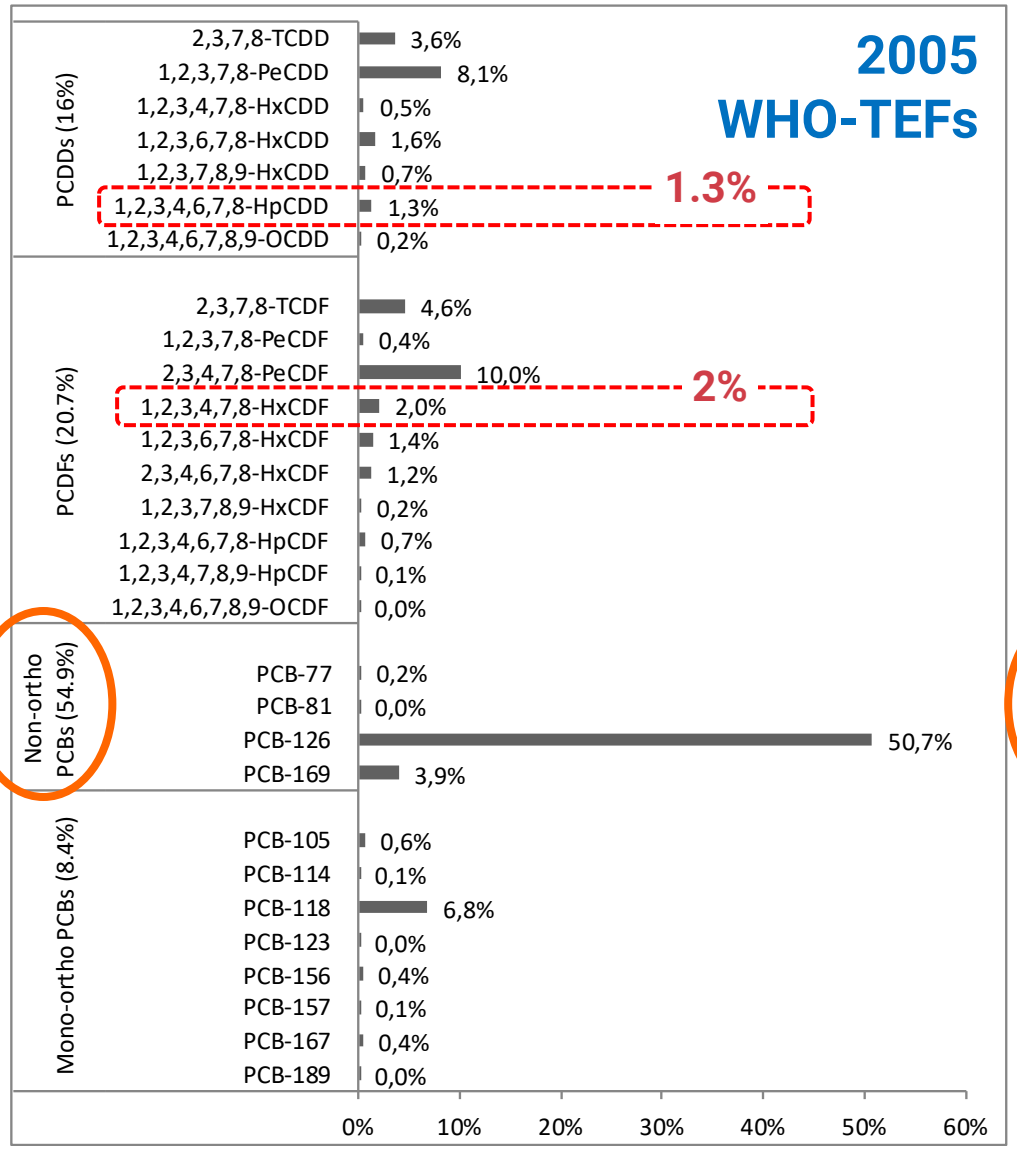
- 'Milk and milk products', up to 43% to the exposure in Other children
- 'Fish and fish products', up to 67% to the exposure in Elderly

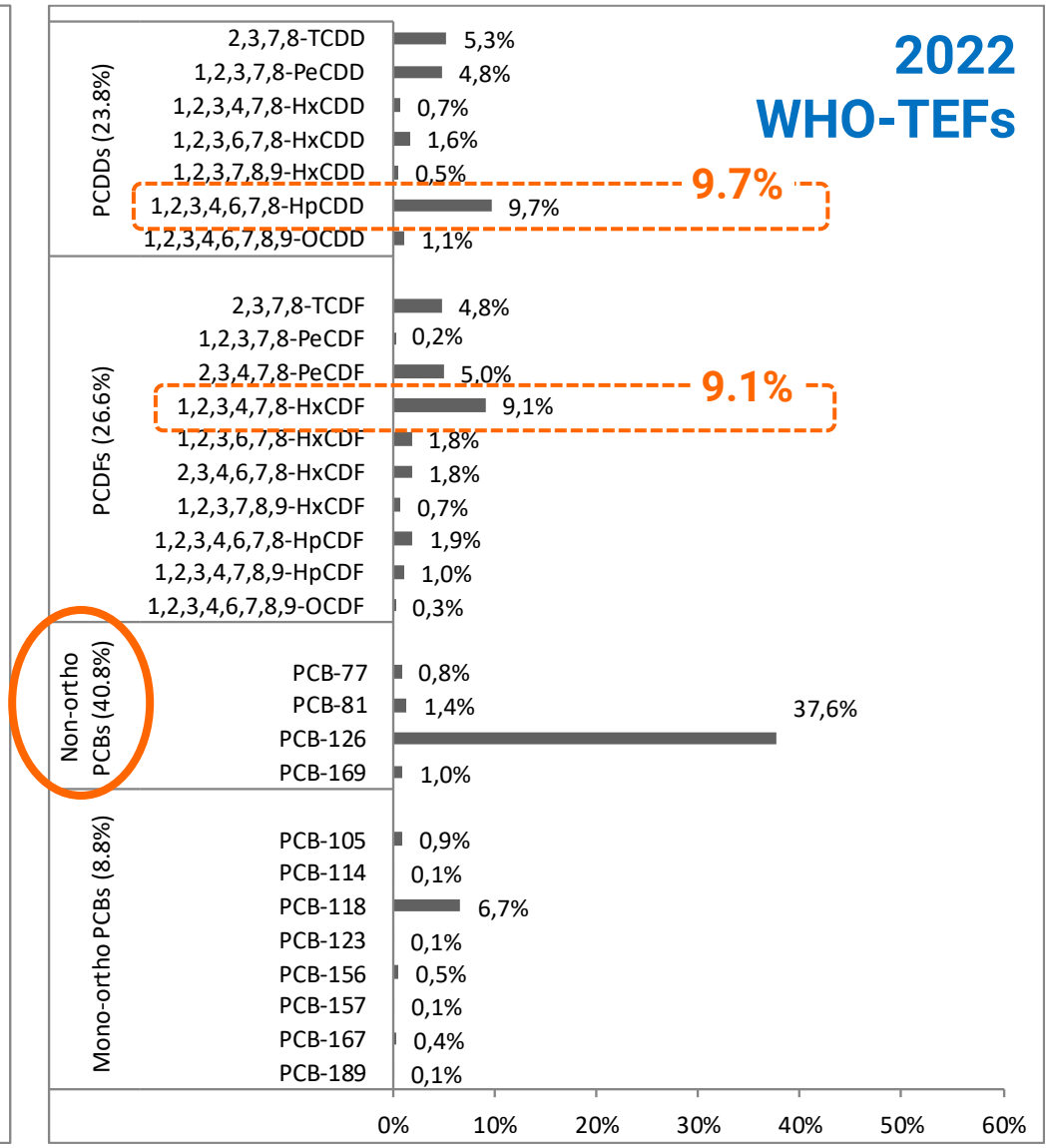

Vegetables and vegetable products and **Meat and meat products** were important contributors in a large number of surveys.

CURRENT DIETARY EXPOSURE - CONTRIBUTION DIFFERENT FOOD GROUPS

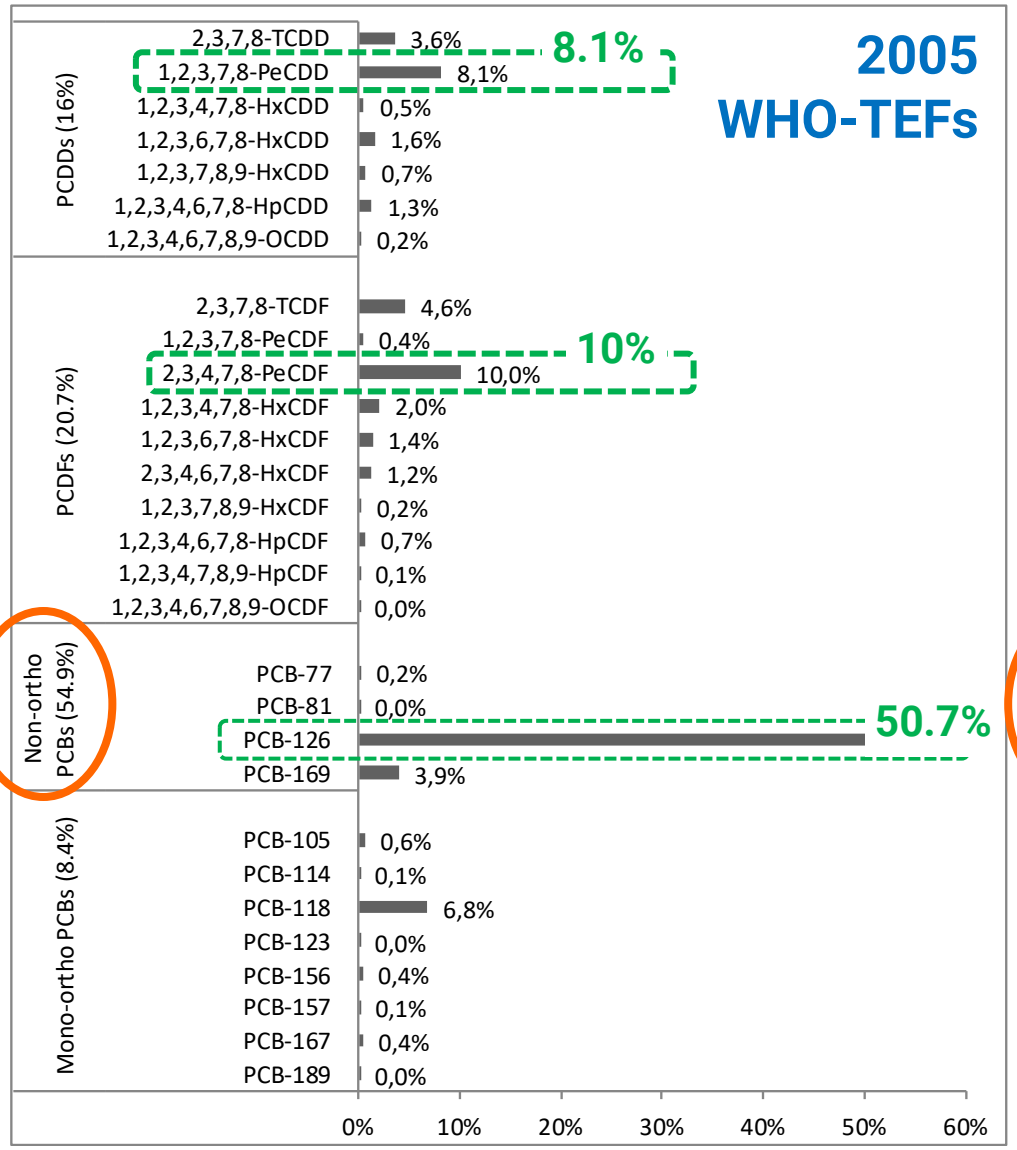


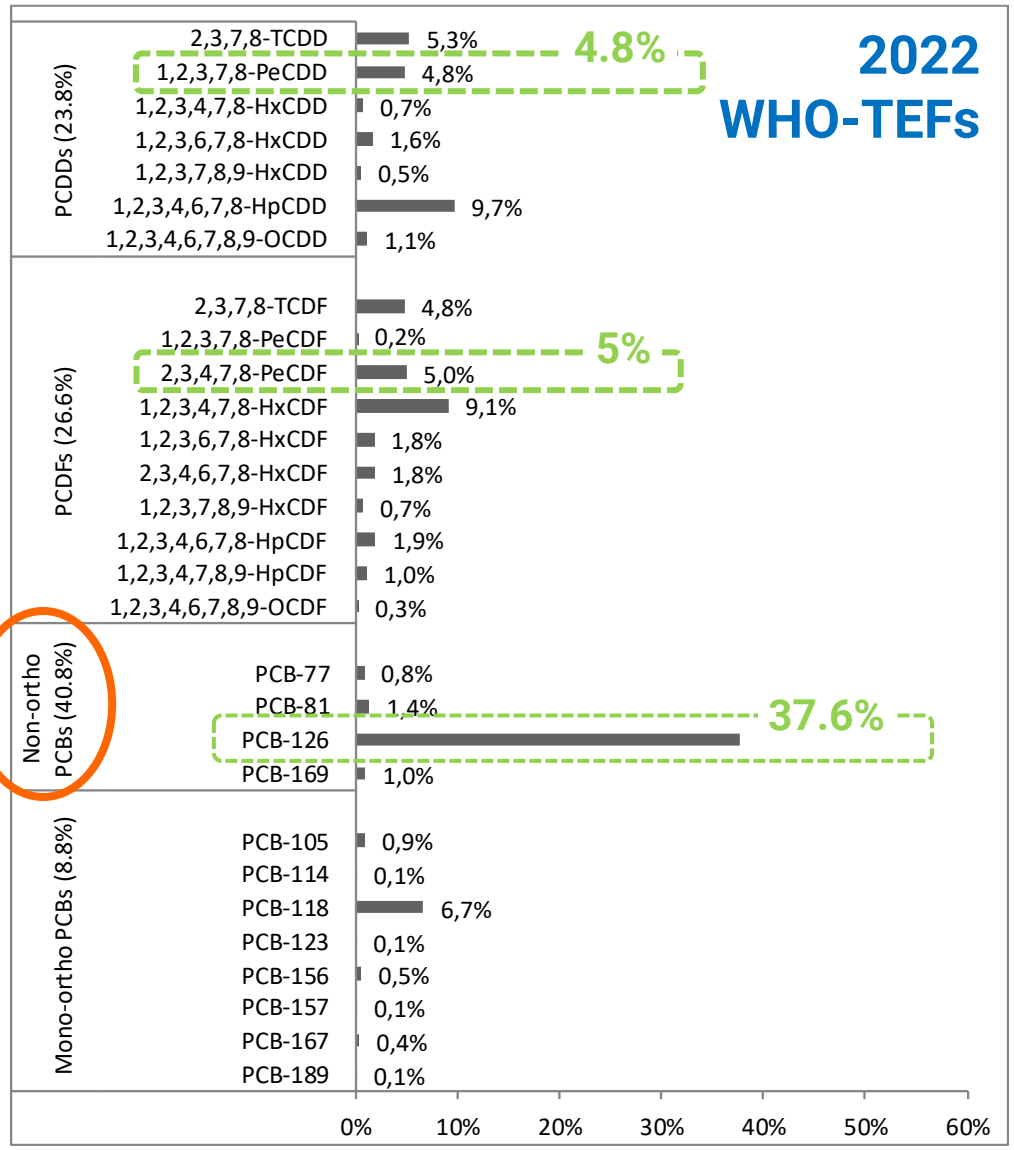
CURRENT DIETARY EXPOSURE - CONTRIBUTION CONGENERS





CURRENT DIETARY EXPOSURE - CONTRIBUTION CONGENERS





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How EFSA approached the update of the tolerable weekly intake (TWI)

Ron Hoogenboom (WG Chair Dioxins update)

TWI DERIVED BY SCF (2001)

- The former Scientific Committee on Food (SCF) derived a Tolerable Weekly Intake (TWI) of **14 pg TEQ/kg bw per week**:

  – Based on a **rat study** in which a decrease in sperm production was observed in offspring of dams treated with TCDD (Faqi et al. 1998).

  – Using a **body burden approach**, based on the levels in the dams.

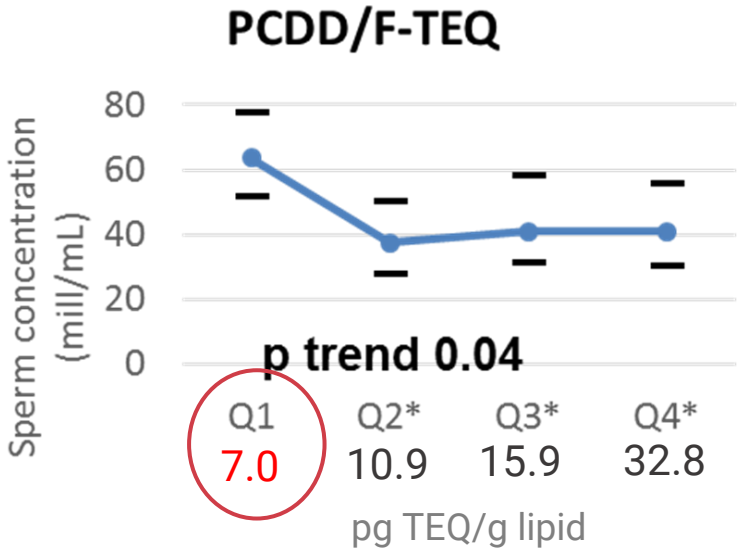
  – Translated to an estimated daily intake of future mothers of 14 pg TEQ/kg bw per week, using a **one-compartment model**.

  – Applying only an **uncertainty factor of 3.16 for intraspecies differences in toxicokinetics** in humans (no UFs for inter- and intraspecies differences in toxicodynamics).

TWI DERIVED BY EFSA (2018)

- Lower sperm concentrations observed in boys in the critical study (Russian Children's Study, Mínguez-Alarcón et al. 2017):
  - Effect also observed in animal studies
  - Effect also observed in other human studies (Seveso cohort)

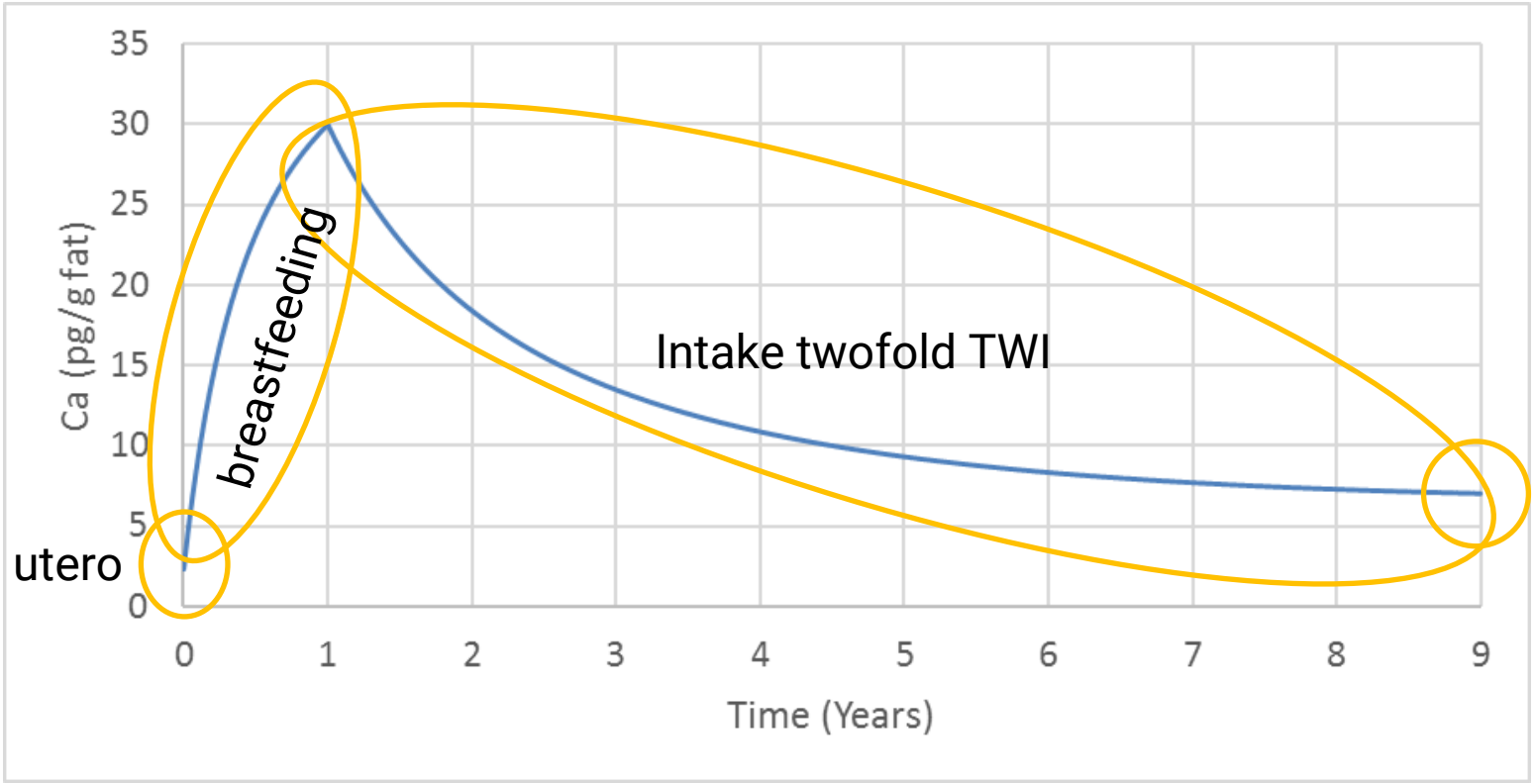
- NOAEC for serum PCDD/F-TEQ level of 7.0 pg TEQ/g lipid (WHO_{2005}-TEFs)
  - Levels measured at the age of 8-9 years



- No significant association for DL-PCBs, and also not for Total-TEQ.

- In agreement with much lower relative potency of DL-PCBs in human cells.

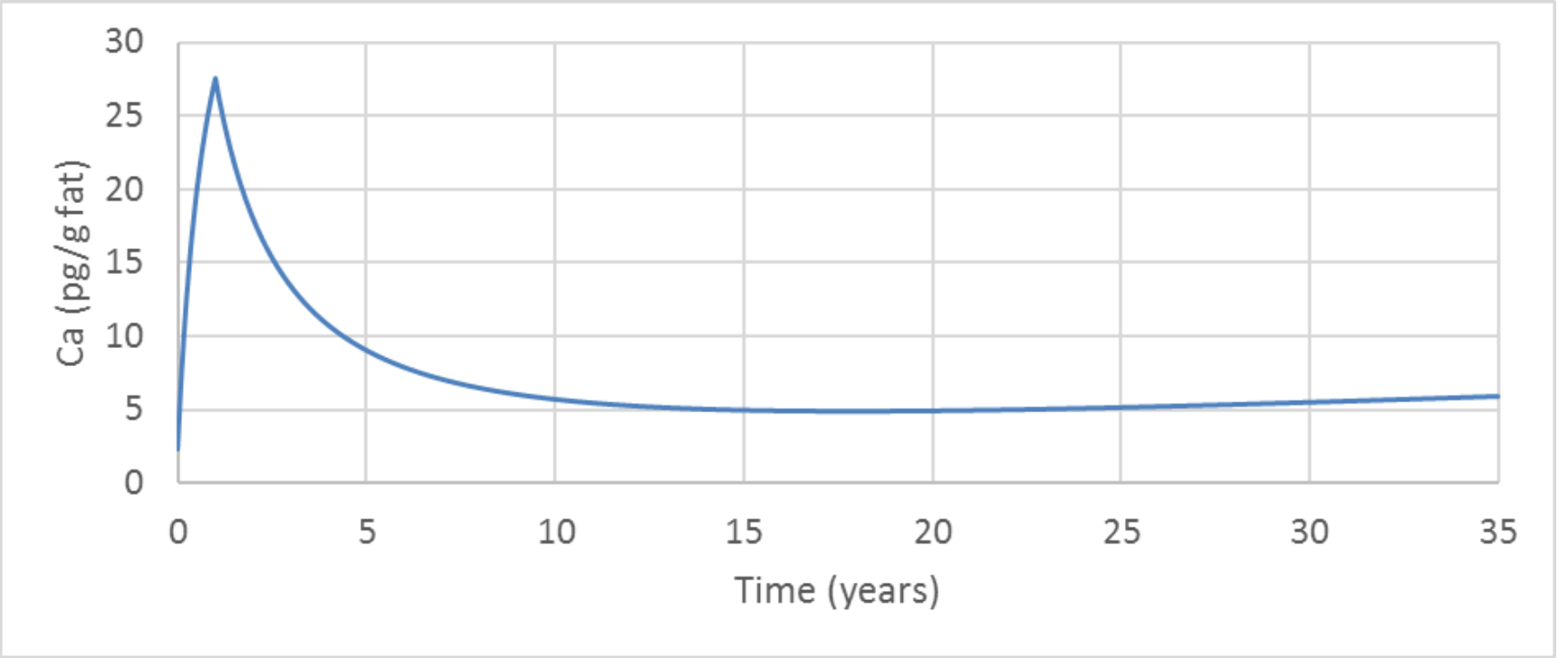
EFSA 2018 - PBK MODELLING BOYS (CADM)



NOAEC serum level of
7.0 pg WHO_{2005}-TEQ/g lipid

Serum level (Ca) in **boys**, breastfed for 12 months with human milk containing **5.9** pg/g fat (800 mL per day, 3.5% fat), followed by an intake of **0.5** pg/kg bw per day for an additional 8 years, resulting in a serum level of 7 pg/g fat (NOAEL).

EFSA 2018 - PBK MODELLING MOTHERS (CADM) TO DERIVE EDI



Serum levels (Ca) in a **woman**, breastfed for 12 months in infancy with human milk containing **5.9** pg/g fat, and then being exposed to **0.25** pg/kg bw per day for 34 years

EFSA 2018 - DERIVATION OF THE TWI

- No Uncertainty Factors applied
- Estimated Daily Intake (EDI) of 0.25 pg WHO-TEQ/kg bw per day translated to a TWI of 2 pg WHO-TEQ/kg bw per week (using 2005 WHO-TEFs)
- TWI applies for PCDD/Fs and DL-PCBs, but:
  - Recommendation to update the 2005 WHO-TEFs, based on data showing that DL-PCBs are less potent in humans
  - Expectation that association for total-TEQ would improve with new TEFs in the critical study (Russian Children's Study)

CURRENT DRAFT UPDATE - USE OF NEW 2022 WHO-TEFs

- The authors of the 2018 critical study (the Russian Children's Study – epidemiological study) recalculated the serum levels using the new 2022 WHO-TEFs:
  - Recalculation for the levels of PCDD/Fs, of DL-PCBs and of Total-TEQ
  - For **PCDD/F-TEQ**: a significant decrease of sperm concentrations at higher serum levels is observed
  - No significant association observed for **DL-PCB-TEQ** and **Total-TEQ**
- The application of the new 2022 WHO-TEFs is a prerequisite for the updated assessment.
- Hence **this study can no longer be used as the critical study to derive the TWI**.

CURRENT DRAFT UPDATE - USE OF NEW 2022 WHO-TEFs

Multivariable adjusted mean semen parameters by quartiles (Q) of serum PCDD/Fs and Total-TEQ from the **Russian Children's Study** (133 young men contributing 256 semen samples) (Table provided by authors)

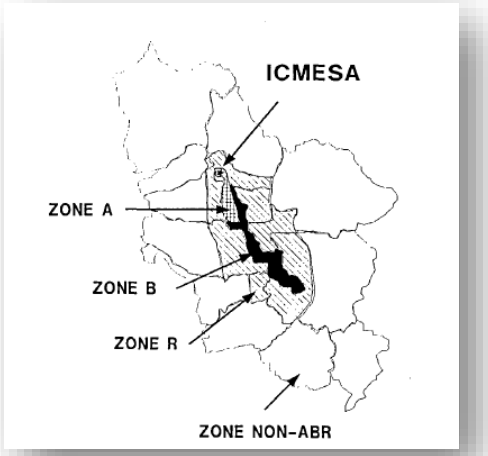
	Median	Sperm concentration (million/mL)	Total sperm count (million)	Motile sperm (%)	Total motile sperm count (million)
		WHO_{2022}-TEQ (ng TEQ/kg lipid)			
PCDD/F-TEQ					
Q1 [2.08-8.08]	6.65	63.6 (52.0, 77.8)	145 (110, 190)	54.9 (52.3, 57.4)	78.5 (58.2, 106)
Q2 [8.11-12.0]	9.63	37.4 (27.7, 50.5)*	89.6 (62.6, 128)*	53.3 (49.9, 56.7)	46.3 (30.7, 70.0)*
Q3 [12.2-16.4]	13.7	40.9 (31.2, 53.8)*	90.7 (65.3, 126)*	52.6 (49.5, 55.7)	46.8 (32.1, 68.2)*
Q4 [16.5-78.4]	23.9	41.0 (30.2, 55.6)*	117 (85.8, 160)	54.6 (50.7, 58.4)	62.0 (43.1, 89.2)
p, trend		0.04	0.36	0.84	0.38
Total-TEQ					
Q1 [3.55-12.1]	9.56	56.9 (42.1, 76.9)	131 (94.9, 183)	53.9 (50.9, 57.0)	69.8 (48.1, 101)
Q2 [12.7-16.9]	14.5	39.3 (28.9, 53.5)	81.1 (55.2, 119)*	53.5 (50.4, 56.6)	42.5 (27.8, 65.2)
Q3 [17.1-24.1]	20.0	38.4 (30.8, 47.8)	109 (81.7, 144)	53.2 (50.3, 56.1)	56.7 (40.8, 78.7)
Q4 [25.1-83.5]	34.7	44.7 (32.7, 61.1)	110 (80.3, 151)	54.1 (49.9, 58.3)	57.7 (39.7, 83.7)
p, trend		0.61	0.75	0.99	0.76

*: $p \leq 0.05$

Data are presented as predicted estimates (95% CI) adjusted for BMI, smoking status, alcohol drinker, season, and abstinence time at the mean level of continuous covariates and adjusted for frequency of categorical measures. Motile sperm and total motile sperm count models were further adjusted for time to start semen analysis.

CURRENT DRAFT UPDATE - SEVESO STUDIES

- Two studies on the **Seveso cohort** were considered pivotal in the 2018 Opinion:



(Mocarelli et al. 1991)

  - **Mocarelli et al. 2008**: on boys exposed at young age during the incident
  - **Mocarelli et al. 2011**: on boys born to mothers exposed during the incident

Both studies show decreased sperm concentrations in men exposed at young age compared to controls, at lowest quantiles.

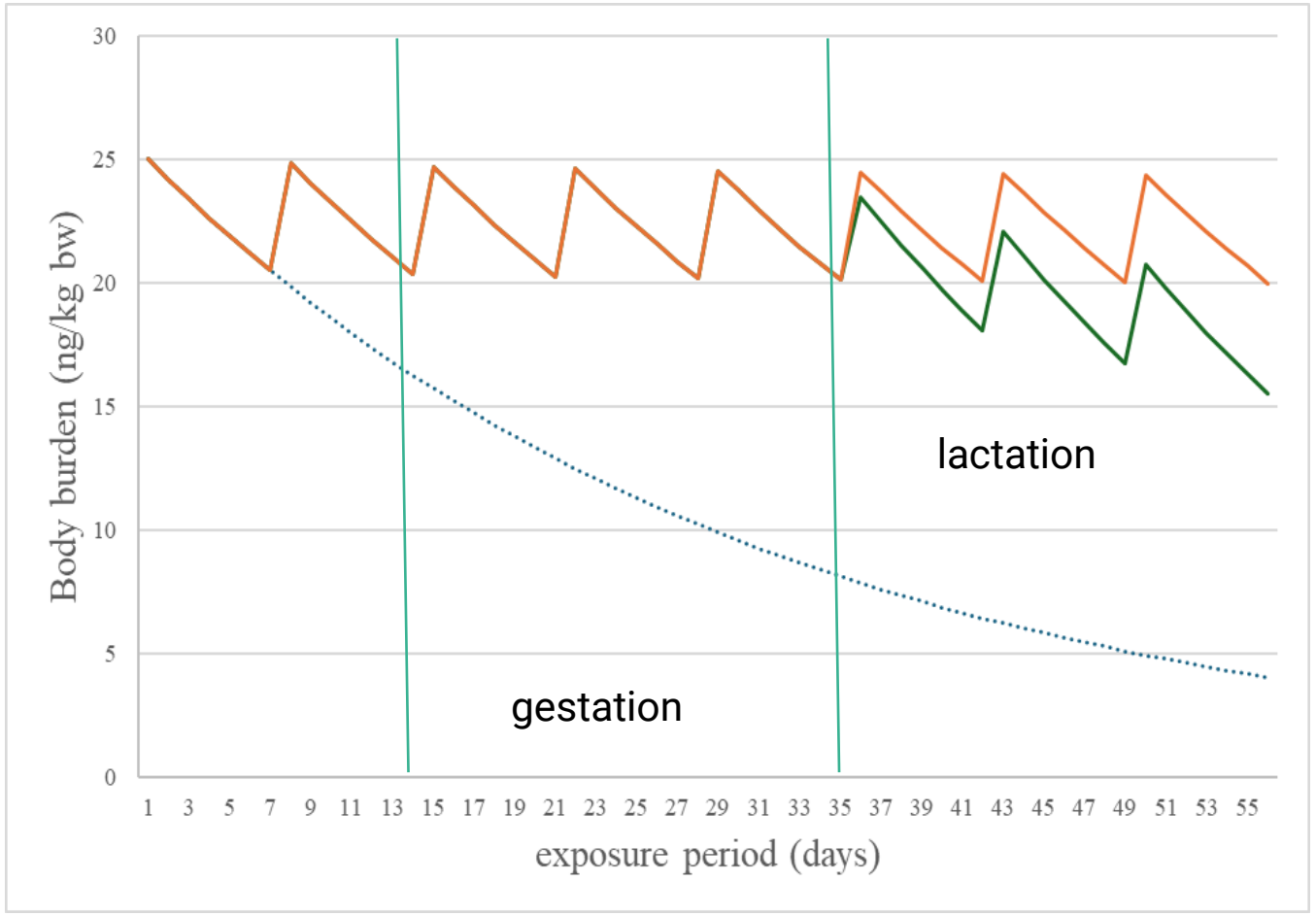
- Only TCDD measured in blood, and is the most relevant congener in this cohort,
  - But other congeners may contribute, especially at lower TCDD serum levels
  - No information on serum levels in controls during the incident
- Hence, **human studies used as supporting evidence, not as the sole basis to derive TWI**.

CURRENT DRAFT UPDATE - SELECTION OF CRITICAL ANIMAL STUDY

- Study by Faqi et al. (1998) considered as the critical study.
- Rat dams exposed weekly with 3 dose levels of **TCDD**:
  - from before conception till the end of lactation
  - loading doses and weekly maintenance dose, i.m. application
- Measurement of tissue levels at Gestational Day 21 confirmed the intended body burden.

CURRENT DRAFT UPDATE - SELECTION OF CRITICAL ANIMAL STUDY

- Dosing and estimated body burden of rat dams in the study by **Faqi et al. (1998)**



Dotted line: body burden after a single sc dose of 25 ng/kg bw, based on a half-life of 3 weeks.

Solid orange line: body burden after the weekly sc maintenance doses.

Green solid line: includes the expected effect of lactation, assuming similar lipid-based levels in the body and milk (based on 30 mL milk per day containing 9% fat and 20% body fat in the dams).

FAQI ET AL. (1998)

TABLE 3

Effect of *In Utero* and Lactational TCDD Exposure on Sperm Number/Cauda Epididymis, Daily Sperm Production, Sperm Transit Rate, Sperm Morphology, and Serum Testosterone Concentration Investigated at Days 70 and 170 Postnatally

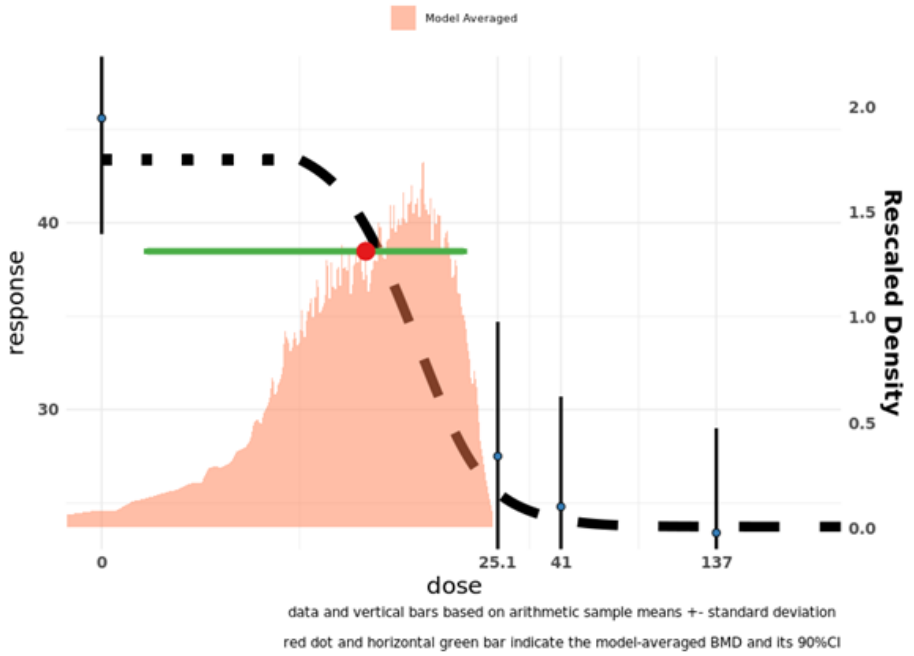
Parameters	Control	TCDD 25/5 *	TCDD 60/12 *	TCDD 300/60 *
PND 70				
Number of animals	20	20	20	20
Sperm number from cauda epididymis ($\times 10^6$)	209 ± 43	176 ± 38*	203 ± 42	172 ± 52*
Daily sperm production ($\times 10^6$)	34.4 ± 4.3	28 ± 5.7*	25.2 ± 5.6*	23.1 ± 4.9*
Sperm transit rate (days)	6.1 ± 1.5	6.5 ± 2.0	8.4 ± 2.7**	7.8 ± 3.0**
Testosterone concentration (ng/ml)	2.08 ± 1.1	2.1 ± 1.0	2.92 ± 1.6	2.7 ± 1.5
PND 170				
Number of animals	20	20	20	20
Sperm number from cauda epididymis ($\times 10^6$)	326 ± 75	270 ± 61*	235 ± 44*	257 ± 86*
Daily sperm production ($\times 10^6$)	45.6 ± 6.2	27.5 ± 7.2*	24.8 ± 5.9*	23.4 ± 5.6*
Sperm transit rate (days)	7.4 ± 2.3	10.6 ± 4.0**	10.0 ± 3.6**	12.1 ± 4.3**
Percent of abnormal sperm	7.3 ± 2.1	10.9 ± 3.3*	14.1 ± 3.5*	12.4 ± 4.2*
Testosterone concentration (ng/ml)	2.2 ± 1.1	2.3 ± 1.6	1.7 ± 1.1	1.2 ± 0.7*

Note. Values are means ± SD. *Values are significantly decreased from control values. **Values are significantly increased from control values.

* Female Wistar rats treated s.c. with a single dose of 0, 25, 60 or 300 ng ^{14}C-labelled TCDD/kg bw two weeks prior to mating (loading dose), followed by weekly injections of 0, 5, 12 and 60 ng/kg bw during mating, pregnancy and lactation as a maintenance dose

CURRENT DRAFT UPDATE - BMD FAQI ET AL. (1998)

- BMD modelling was performed according to the **latest EFSA Guidance on BMD modelling published in 2022**.
- Study not ideal for BMD modelling since the **lowest body burden shows near-maximal effect.**
- No clear view on relevant BMR; therefore, **based on SD of the control group**:
  - BMR of 15% (about 1 SD)
- **$BMDL_{15}$: 1.65 ng/kg bw** (BMD_{15}: 9.01, $BMDU_{15}$: 19.3)
- For body burden of the dams
- The $BMDL_{15}$ obtained is 15-fold lower than the LOAEL body burden of 25.1 ng/kg bw (BMD 2.8-fold)



CURRENT DRAFT UPDATE - UNCERTAINTY FACTORS NOT APPLIED

- Highest body burden not leading to adverse effects in boys of 6.8 ng/kg body fat derived from Faqi et al. (1998), based on 25% body fat
- Regarding the **UF of 100 for inter- and intraspecies differences in kinetics and dynamics**:
  - **Interspecies differences in toxicokinetics (UF = 4): not needed** when applying a body burden approach.
  - **Inter-** and **Intraspecies differences in toxicodynamics (UF = 2.5** and **3.16): not applied** since there is evidence that humans are not more sensitive than rats:
    - Based on studies with human cells and humanised mice
    - Supported by the 3 human studies on sperm effects:

CURRENT DRAFT UPDATE – COMPARISON OF BODY BURDENS

Highest body burden not raising a health concern in boys for the three pivotal human studies, for comparison with that of **6.8 ng/kg body fat derived from the critical rat study** (Faqi et al., 1998)

Study	Body burden at LOAEC/NOAEC (ng/kg body fat)	Congeners	Type	UFs	Highest body burden after application of UFs in the human studies (ng/kg body fat)
Mocarelli et al. (2008) Boys	68 (in blood, boys Q1)	**TCDD** (other congeners not analysed)	LOAEC	10 for LOAEC to NOAEC	**6.8**
Mocarelli et al. (2011) Mothers/boys	19 (in blood, mothers)	**TCDD** (other congeners not analysed)	LOAEC	>3 for LOAEC to NOAEC	**<6.8**
Mínguez-Alarcón et al. (2017) Boys	3.3 (in blood, boys at 9 years)	**PCDDs**	NOAEC (Q1) (e)	None	**3.3**
	6.7 (in blood, boys at 9 years)	**PCDD/Fs**	NOAEC (Q1) (e)	None	**6.7**

CURRENT DRAFT UPDATE - UNCERTAINTY FACTOR APPLIED

- Factor for intraspecies differences in toxicokinetics (UF = 3.16): **applied** to the chronic intake leading to the body burden of 6.8 ng/kg fat

NOTE: The **correction factor for single dose regimen in the critical rat study (Faqi et al. 1998)** used by SCF (2001): **not applied** in the current draft update.

CURRENT DRAFT UPDATE - OVERVIEW DERIVATION OF TWI

Body burden at the lowest dose in rat dams:
25 ng TCDD/kg bw (near maximal response)

BMDL body burden in rat dams (BMR = 15%): **1.7 ng TCDD/kg bw**

BMD modelling

UFs not applied:

- Interspecies TK differences (UF = 4) (BB approach)
- Interspecies TD differences (UF = 2.5) and Intraspecies TD differences (UF = 3.16) (humans are not more sensitive than rats)

✓ *Assuming similar kinetics for the other PCDD/Fs and DL-PCBs as for TCDD to convert to TEQ*

Body burden in the mothers:
1.7 ng WHO-TEQ/kg bw or
6.8 ng WHO-TEQ/kg fat (25% body fat)

PBK modelling (CADM model)

Estimated daily intake:
0.29 pg WHO-TEQ/kg bw per day

✓ **UF applied: Intraspecies TK differences (UF = 3.16)**
✓ *Conversion from daily intake (0.09 pg WHO_{2022}-TEQ/kg bw per day) to weekly intake*

TWI = 0.6 pg WHO-TEQ/kg bw per week

PBK modelling (CADM)

Critical level of 2.2 ng WHO-TEQ/kg fat in human milk
(equal to lipid-based critical body burden in mothers)

COMPARISON WITH TWI OF SCF (2001) AND EFSA (2018)

- Reduction from 14 to 0.6 pg TEQ/kg bw per week, based on the same critical study used by **SCF (2001):**
  - Use of **BMD modelling** instead of applying a factor 3 to derive a NOAEL from a LOAEL: 4.9-fold lower.
  - No correction factor applied for single high dose: 1.6-fold lower.
  - Using **PBK CADM** instead of 1-compartment model: 3-fold lower (higher absorption, 'longer half-life')

- Reduction from 2 to 0.6 pg TEQ/kg bw per week compared to **EFSA (2018):**
  - Primarily caused by the use of the **UF of 3.16 for intraspecies differences in toxicokinetics** , which has also been applied in other assessments using animal data, including SCF (2001).
  - This UF was considered not needed in the 2018 Opinion when using as critical the Russian Children's Study (epidemiological study).

5

Draft conclusions of the risk characterisation

Helle Katrine Knutsen (CONTAM Panel Chair)

RISK CHARACTERISATION BASED ON DIETARY EXPOSURE

- The estimated dietary exposure was compared with the **TWI of 0.6 pg TEQ/kg bw per week**.
- The exposure estimated on a daily basis was extrapolated to a **weekly basis**, by multiplication by a factor of 7.

Range of mean dietary exposure (pg WHO-TEQ/kg bw per week) using WHO_{2022}-TEFs

		Minimum		Median		Maximum	
Age group	N surveys	LB	UB	LB	UB	LB	UB
Toddlers	17	4.33	8.56	6.64	11.7	11.0	16.4
Other children	21	3.59	7.15	5.01	8.74	7.77	12.0
Adolescents	23	2.03	3.35	2.68	4.53	4.63	7.16
Adults	23	1.87	3.01	2.50	3.90	3.94	5.64
Elderly	21	1.77	2.95	2.57	3.85	4.79	6.35
Very elderly	16	1.69	2.90	2.47	3.96	4.41	6.10

Range of P95 dietary exposure (pg WHO-TEQ/kg bw per week) using WHO_{2022}-TEFs

		Minimum		Median		Maximum	
Age group	N surveys	LB	UB	LB	UB	LB	UB
Toddlers	16	8.58	13.8	14.3	21.5	23.1	33.1
Other children	21	6.77	12.2	10.7	16.2	16.8	22.9
Adolescents	22	4.29	7.55	6.06	9.32	14.7	17.8
Adults	23	4.15	6.30	6.47	8.72	11.5	14.6
Elderly	21	3.96	6.04	7.22	8.98	13.4	14.8
Very elderly	12	3.98	6.27	6.16	8.18	9.77	12.0

RISK CHARACTERISATION BASED ON DIETARY EXPOSURE

The **estimated weekly exposure estimates** were compared with the **TWI of 0.6 pg TEQ/kg bw per week:**

- **Adolescents, Adults, Elderly and Very Elderly:**

  Mean exposure estimates: 3- to 12-fold exceedance (lowest LB-highest UB)

  P95 exposure estimates: 6- to 30-fold exceedance (lowest LB-highest UB)

- **Toddlers and Other Children:**

  Mean exposure estimates: 6- to 27-fold exceedance (lowest LB-highest UB)

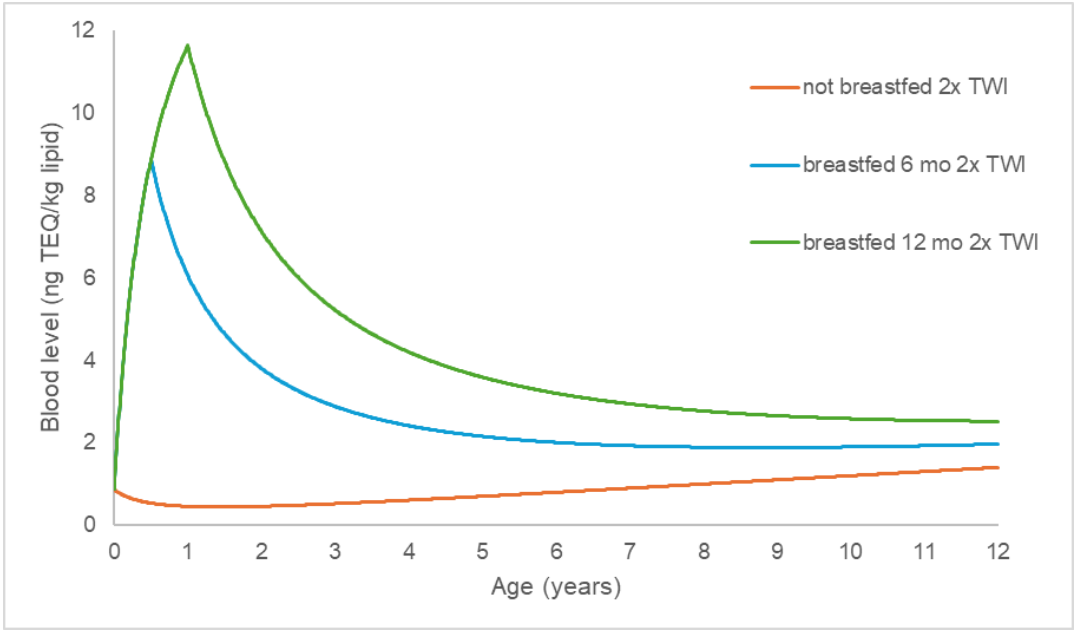
  P95 exposure estimates: 11- to 55-fold exceedance (lowest LB-highest UB)

- **Infants**: Not included in the Risk Characterisation

  The TWI should prevent that the body burden in women of childbearing age will result in exposure of the offspring in utero and during breastfeeding that could increase the risk of adverse effects. Thus, the exposure of infants was taken into account when setting the TWI.

INTERPRETATION OF THE EXCEEDANCE FOR DIFFERENT AGE GROUPS

- Sensitive period for critical effect: perinatal and until puberty.
- An intake higher than the TWI slows down the decrease in the blood levels of PCDD/F- and DL-PCB-TEQ in previously breastfed infants. In non-breastfed infants it would increase the rate of building up the body burden.
- Besides Toddlers and Other children, **women of childbearing age** is the most relevant part of the population, in order to protect their future infants.
- **Adolescents**, **Adults**, and **older age groups**, appear to be less sensitive. At the current exceedance of the TWI there is no evidence of effects in these age groups.



Lipid-based blood levels (reflecting the body burden) of PCDD/Fs and DL-PCBs in children. Breastfed for 6 or 12 months with 800 mL milk per day containing 3.5% fat and a level of 2.2 ng WHO_{2022}-TEQ/kg fat. After the breast-feeding, the children were exposed via food at two-fold the TWI, in accordance with the exposure assessment. The non-breastfed children were exposed via food at two-fold the TWI from birth.

RISK CHARACTERISATION BASED ON LEVELS IN HUMAN MILK

- Based on the PBK modelling, a TWI of 0.6 pg WHO2022-TEQ/kg bw per week would lead to a Body Burden in the mothers of **2.2 ng WHO2022-TEQ/kg fat**. This is also the **critical human milk level** and **can thus be compared with reported human milk levels.**

- Data on measured human milk levels from:

WHO/UNEP studies - pooled samples	**CVUA-MEL - individual samples**
Period 2019: CZ, DE, IRE, SK, SE: • Average: 2.7 ng WHO_{2022}-TEQ/kg fat • Range 2.4-3.0 ng WHO_{2022}-TEQ/kg fat	Period 2021-2024, DE • Mean: 2.3 ng WHO_{2022}-TEQ/kg fat • Range 0.5–6.0 ng WHO_{2022}-TEQ/kg fat

→ Average levels in human milk are **close to the critical human milk level**.

→ At the higher end, based on individual data, **exceedance by a factor of 2.6**.

RISK CHARACTERISATION - UNCERTAINTIES

The exceedance of the critical milk level is lower than the exceedance of the TWI based on the dietary estimated exposure

Possible reasons:

(i) **toxicokinetic model** applied to link the critical body burden to a long-term exposure, including the assumption that other PCDD/F and DL-PCB congeners behave similar to TCDD,

(ii) **overestimation of the current dietary exposure -** in a "best case scenario" the dietary exposure was maximally 34% lower,

(iii) **human milk samples covering only a few countries**.

ADDITIONAL UNCERTAINTY IN THE TEF OF PCB-126

- Uncertainties in TEFs for DL-PCBs were not included in the overall uncertainty assessment (as in ToR):
  - **PCB-126-TEF** was reduced from 0.1 to 0.05, but still it contributes 38% to the dietary exposure.
  - **PCB-126** has more than 10-fold lower potency in human cells than in rat cells.
  - **2022 WHO-TEFs** give **more weight to in vivo studies with toxicological endpoints, most in rats.**
- Extreme exposure scenario: without PCB-126 → exposure would be reduced by a factor of 2.
- The lowest Lower Bound exposure in Adults (best-case: 1.29 pg WHO-TEQ/kg bw per week) would still be above the TWI based on dietary exposure estimates.

CONTAM PANEL DRAFT CONCLUSION

- Exposure for European women of childbearing age raises a health concern for their sons at the mean (80–90% certainty*) and P95 (95–99% certainty) exposure.

- Including uncertainties regarding the TEFs for DL-PCBs decreased this certainty at the mean exposure to 33-66% (about as likely as not) and at the P95 exposure to 70-80%.

** % probability expressed as % certainty, assessed by expert judgment.*

CONTAM PANEL DRAFT RECOMMENDATIONS

To reduce the uncertainties in the human risk assessment:

- **Further development of approaches to compare animal- and human-based data is needed to derive TEFs for PCDD/Fs and DL-PCBs that are more relevant for humans**. This is also important for evaluating associations between TEQ levels and specific effects in human studies.
- To **better estimate the actual contribution of plant-derived products to the dietary exposure**, more data on occurrence levels in such foods are needed.
- **Further improvement of toxicokinetic models** is needed, including parameters related to pregnancy, breastfeeding and day-to-day variation in exposure levels. Inclusion of congeners other than TCDD is required. The use of in vitro models for further refinement should be considered.
- **Biomonitoring data**, especially individual data on occurrence of PCDD/Fs and DL-PCBs in human milk and covering more European populations, are needed.

6

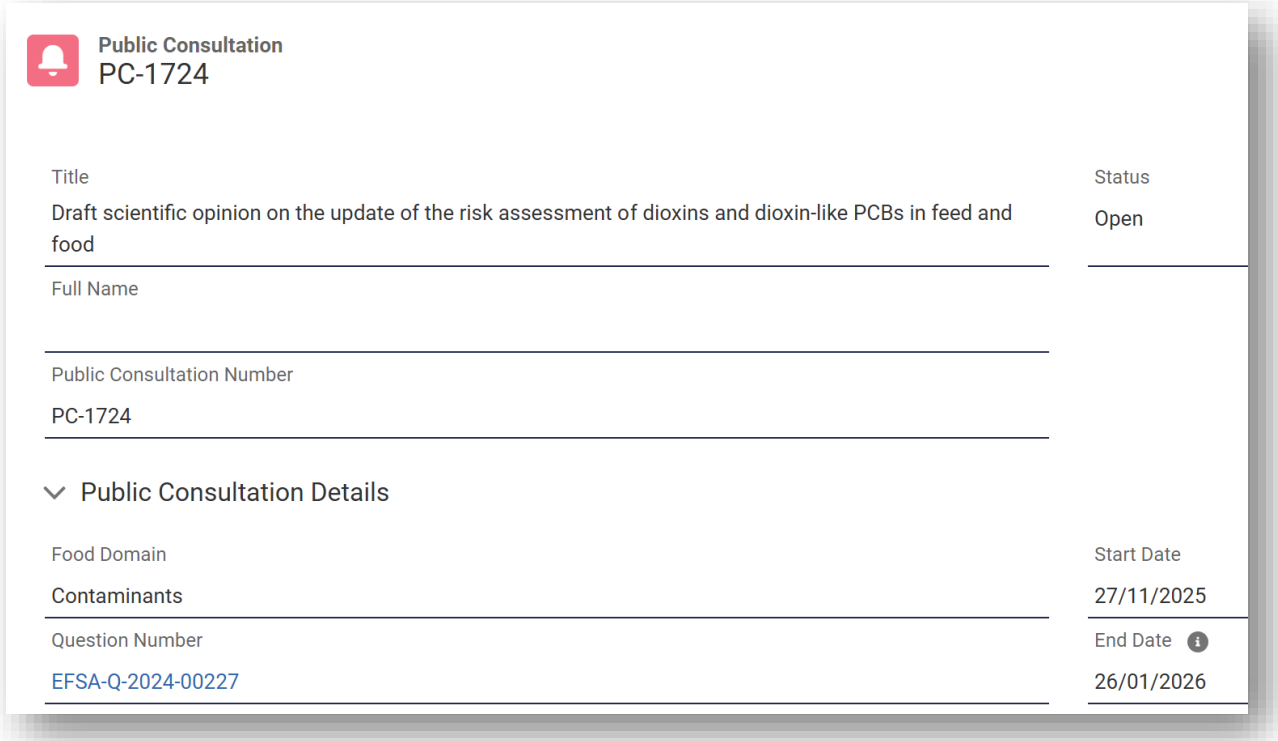
Questions and answers

7

Closing remarks

Mary Gilsenan (Head of Unit FEEDCO, EFSA)

PUBLIC CONSULTATION



How to submit comments

- Access the Open EFSA page
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- Comments should be **finalised** (comments in 'draft' status will not be accepted).
- Deadline for comments **26 January**

https://connect.efsa.europa.eu/RM/s/consultations/publicconsultation2/a0lTk000006Nv0X/pc1724

CONSIDERATION OF THE PUBLIC CONSULTATION COMMENTS

Discussion by the **EFSA WG Dioxins update** and **CONTAM Panel**

Based on their merit, input received may be incorporated in the Opinion

Annex with all original comments will become available

The Annex will provide replies to the comments and explanation of the actions taken and the rationale

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