PFAS CONFERENCE BERLIN 2025

EFSA 2020: RISK ASSESSMENT AND RELATED CHALLENGES

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HEALTH BASED GUIDANCE VALUES IN EFSA 2008

- TDI for PFOS of 150 ng/kg bw per day
  - Subchronic study on cynomolgus monkeys:
  - decrease in serum total cholesterol and effects on thyroid hormone levels in monkeys
  - NOAEL of 30 µg/kg bw per day (UF 200)
- TDI for PFOA of 1500 ng/kg bw per day
  - increased liver weight in mice and rats
  - BMDL10 of 300 µg/kg bw per day (UF 200)
- Estimated exposure to PFOA and PFOS far below these TDIs, so no concern for a human health risk

INCREASED NUMBER OF HUMAN DATA

- Looking for associations with human serum levels
  - Relatively easy to analyse PFASs in blood
  - Including studies in water districts Ohio river
- Many studies on possible effects in humans based on effects observed in animals, including
  - Increased serum cholesterol
  - Liver damage base on ALT
  - Decreased birth weight
  - Immune effects (decreased vaccination response)

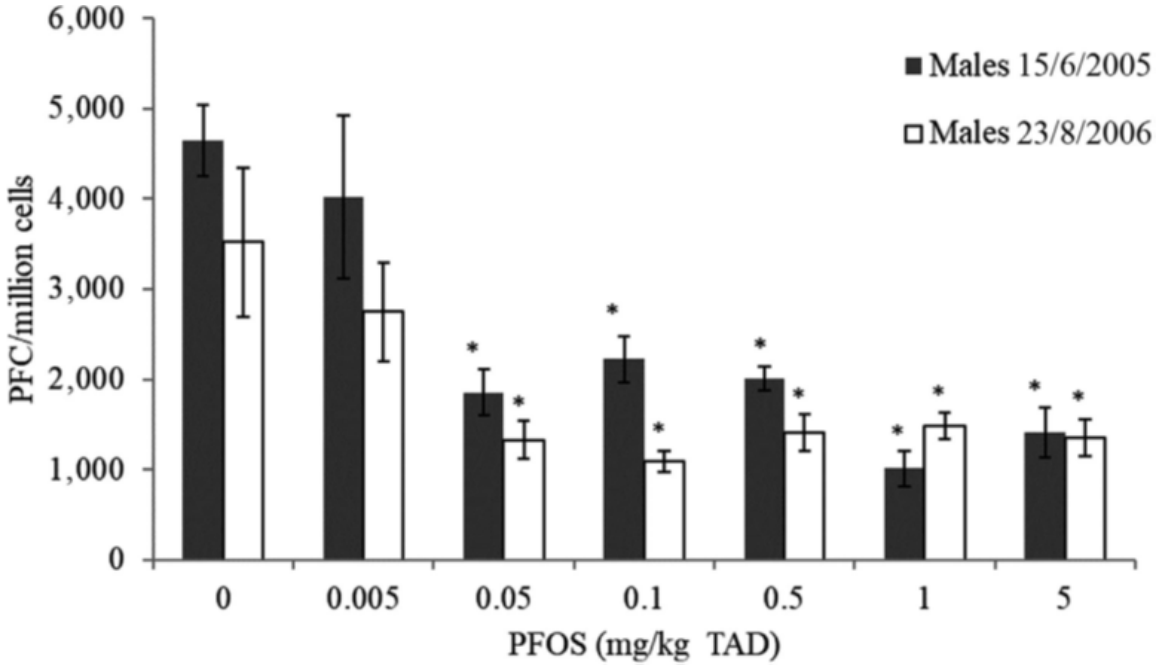
NEW ASSESSMENT BY EFSA (2018)

- Request for risk assessment for 28 PFASs
  - First PFOS/PFOA (published in December 2018)
- Opinion 2018
  - Based on human data, rather than animals
  - Critical endpoint: increase in serum cholesterol
- Separate HBGVs for PFOS and PFOA
  - 13 and 6 ng/kg bw per week, respectively
  - Much lower than the 150 and 1500 ng/kg bw per day from 2008, and no UFs applied
- Estimated exposure exceeds TWIs

UPDATED RISK ASSESSMENT BY EFSA 2020

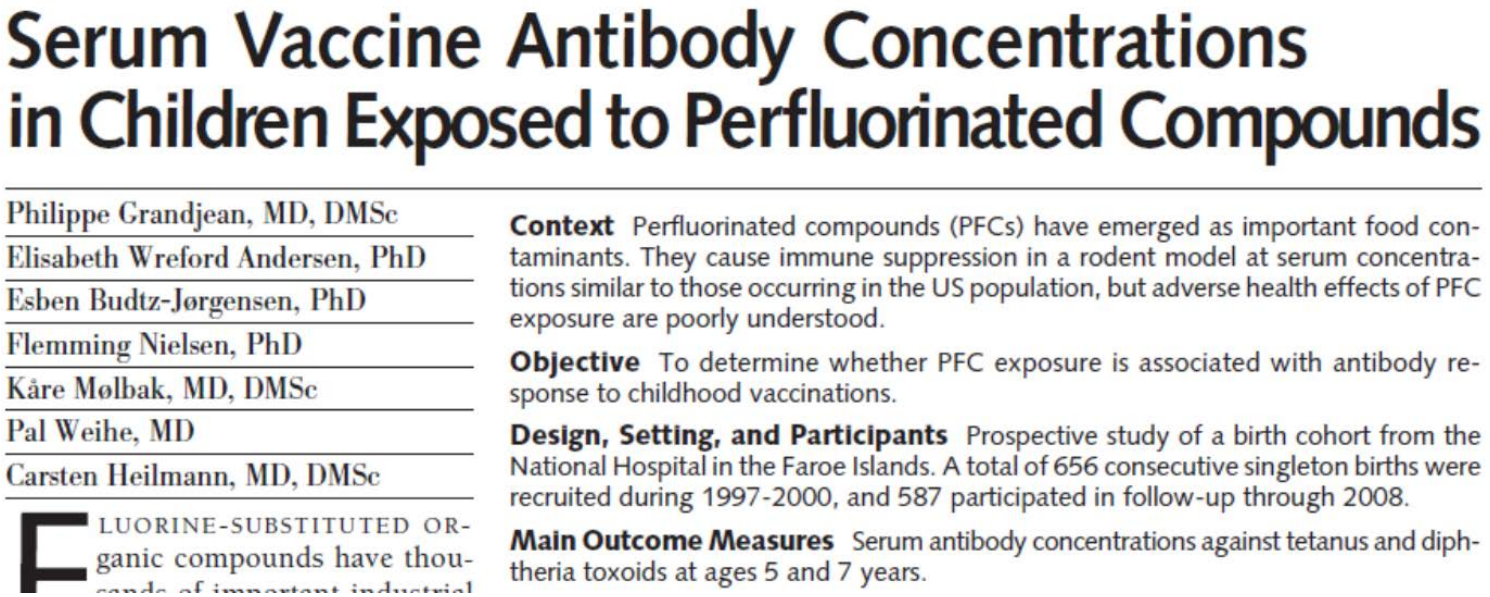
- Inclusion of other PFASs, including mixture approach
- Too much uncertainty on cholesterol increase
  - In animals decrease rather than increase
  - Possibly not a causal relationship: “bile acid hypothesis”
  - More research required
- Effects on immune system selected as critical endpoint
  - Observed in animals and humans

EFFECTS IN MICE (PEDEN-ADAMS ET AL., 2008)



- Effect PFOS on plaque forming colonies spleen
- NOAEL at Total Applied Dose (TAD) of 0.005 mg/kg bw (28 days)
- Serum level at NOAEL of 0.005 mg/kg: 18 ng/ml
- Would result in very low TWI when using UFs of 10 x 2.5

VACCINATION RESPONSE IN CHILDREN (GRAND-JEAN ET AL., 2012)



Serum Vaccine Antibody Concentrations in Children Exposed to Perfluorinated Compounds

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FLUORINE-SUBSTITUTED ORganic compounds have thou-

Context Perfluorinated compounds (PFCs) have emerged as important food contaminants. They cause immune suppression in a rodent model at serum concentrations similar to those occurring in the US population, but adverse health effects of PFC exposure are poorly understood.

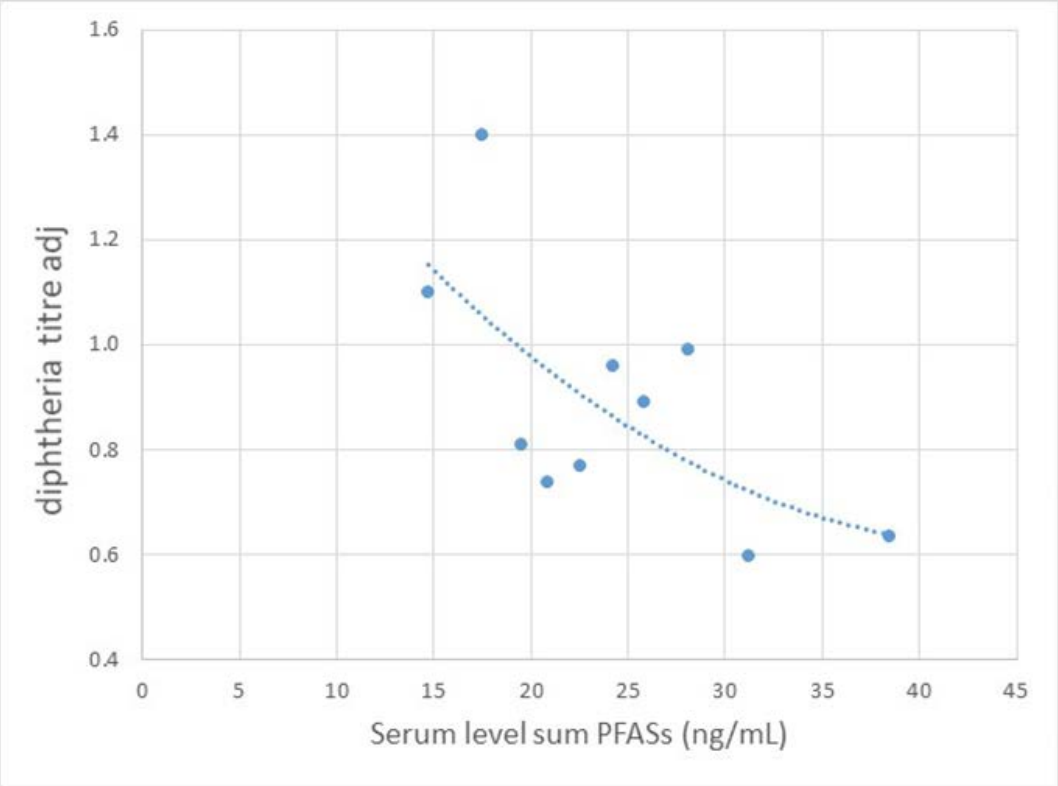
Objective To determine whether PFC exposure is associated with antibody response to childhood vaccinations.

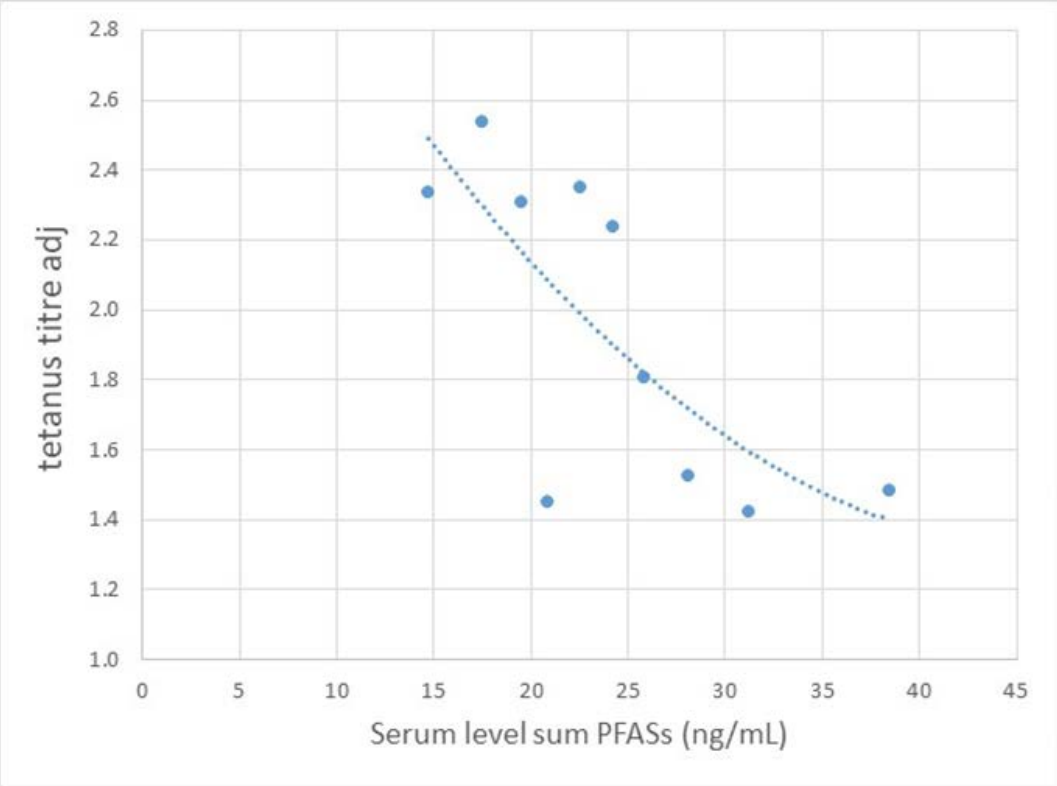
Design, Setting, and Participants Prospective study of a birth cohort from the National Hospital in the Faroe Islands. A total of 656 consecutive singleton births were recruited during 1997-2000, and 587 participated in follow-up through 2008.

Main Outcome Measures Serum antibody concentrations against tetanus and diphtheria toxoids at ages 5 and 7 years.

- Associations for individual PFASs detected in serum
- Additional data on sum provided to EFSA upon request

ASSOCIATIONS FOR SUM OF PFOA, PFNA, PFHxS AND PFOS





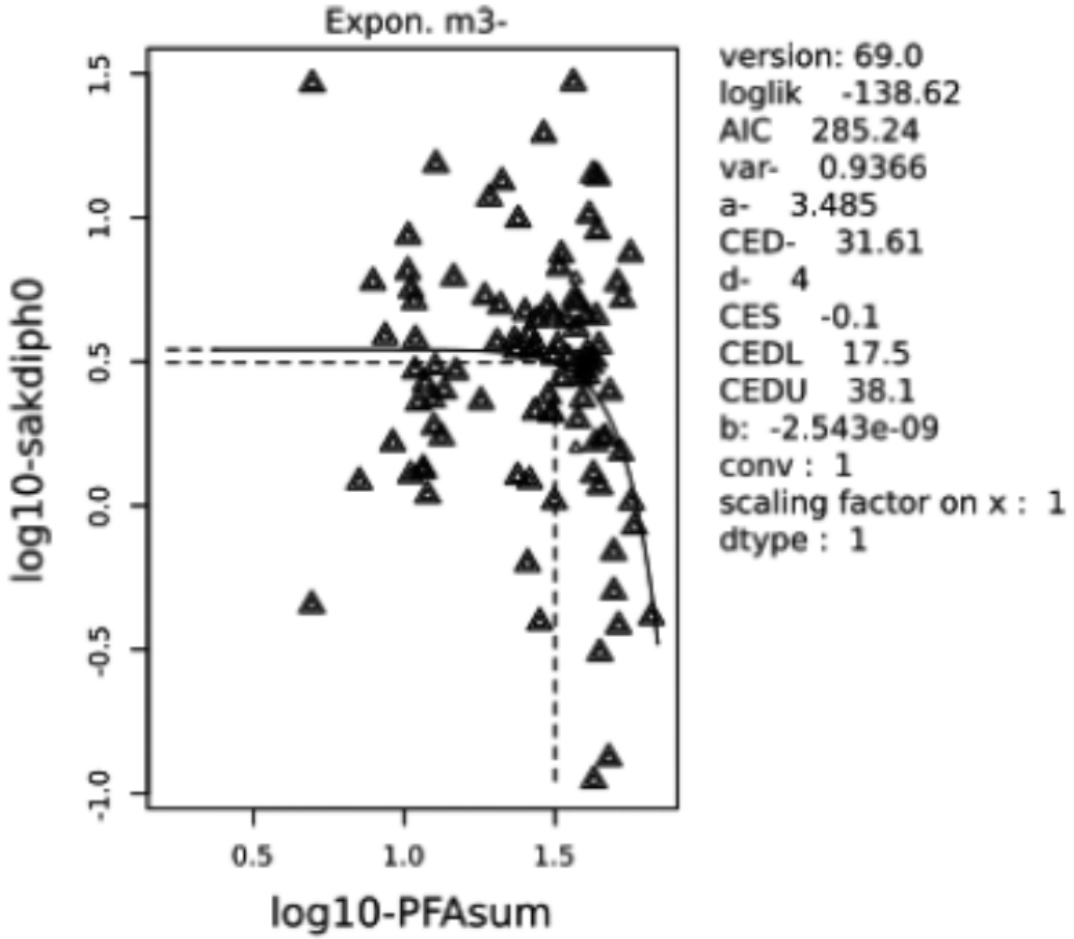
- NOAEC: 27 ng/mL (based on quintiles)
- At LOAEC 50% decrease in titre

NEW STUDY WITH INFANTS (ABRAHAM ET AL., 2020)

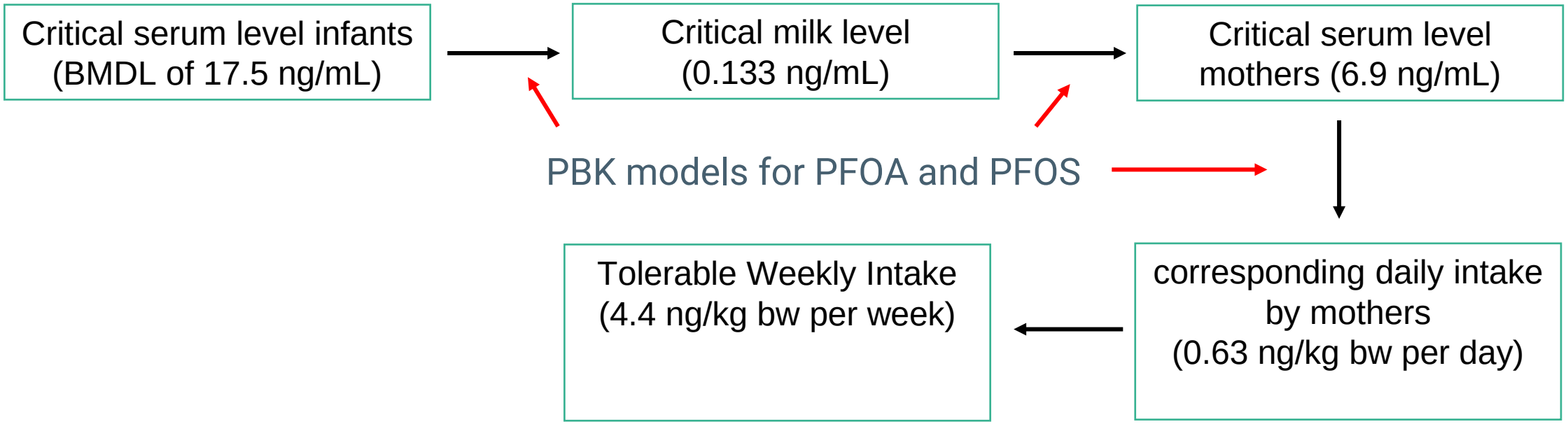
- Carried out end of nineties, focus on OCPs and dioxins
  - Most infants breastfed, 20% formula fed (total n=101)
- Serum samples mothers and infants at child's age 1 year
  - Samples analysed for PFASs
  - And titres against Hib, tetanus and diphtheria
  - Possible confounding by other contaminants excluded
- Reverse association between PFOA serum levels and antibodies against all 3 vaccines
  - NOAECs of 12.2, 16.9 and 16.2 ng/mL for PFOA
- No significant association for PFOS, PFNA and PFHxS

BMD MODELLING DIPHTHERIA FOR SUM OF 4 PFASs

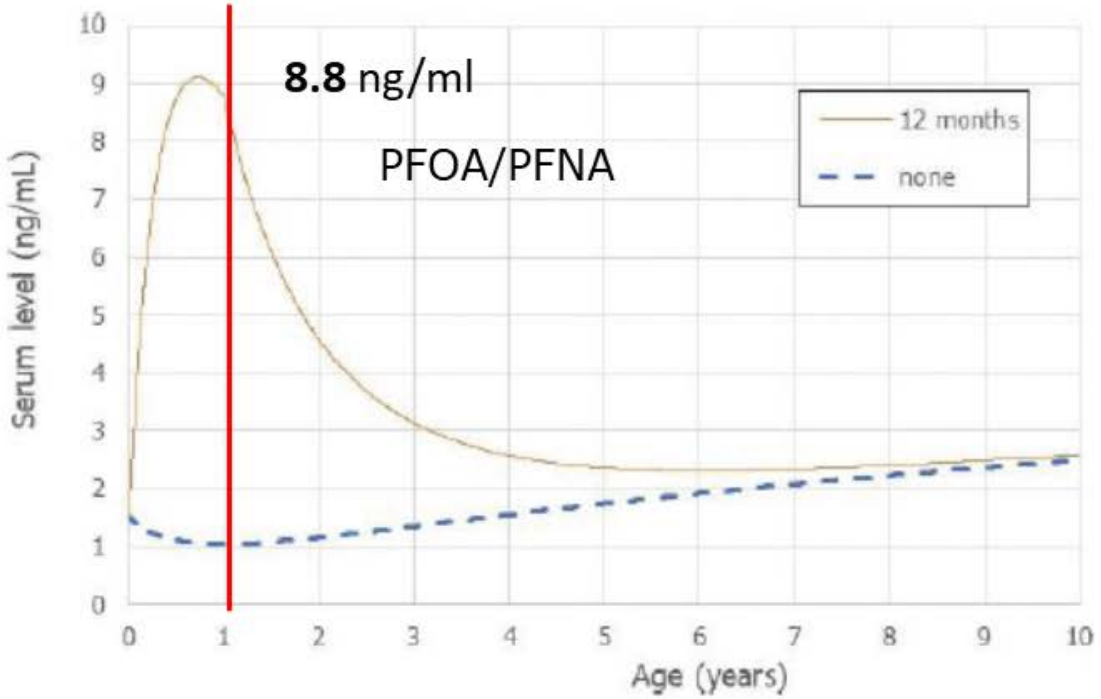
- Data on the sum of the 4 PFASs detected in serum provided to EFSA
- NOAEC of 31.9 ng/mL for the sum of 4 PFASs
- Data modelled with PROAST software
- BMDL10 of 17.5 ng/mL for the sum of 4 PFASs

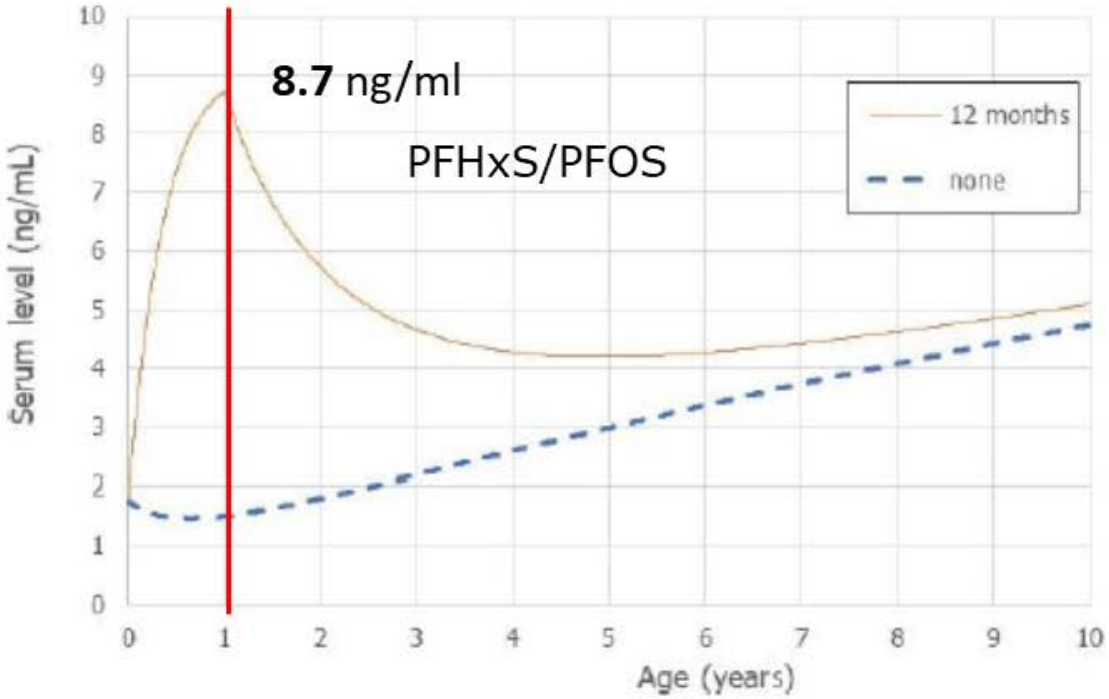


DERIVATION OF THE TWI BASED ON BMDL IN SERUM INFANTS



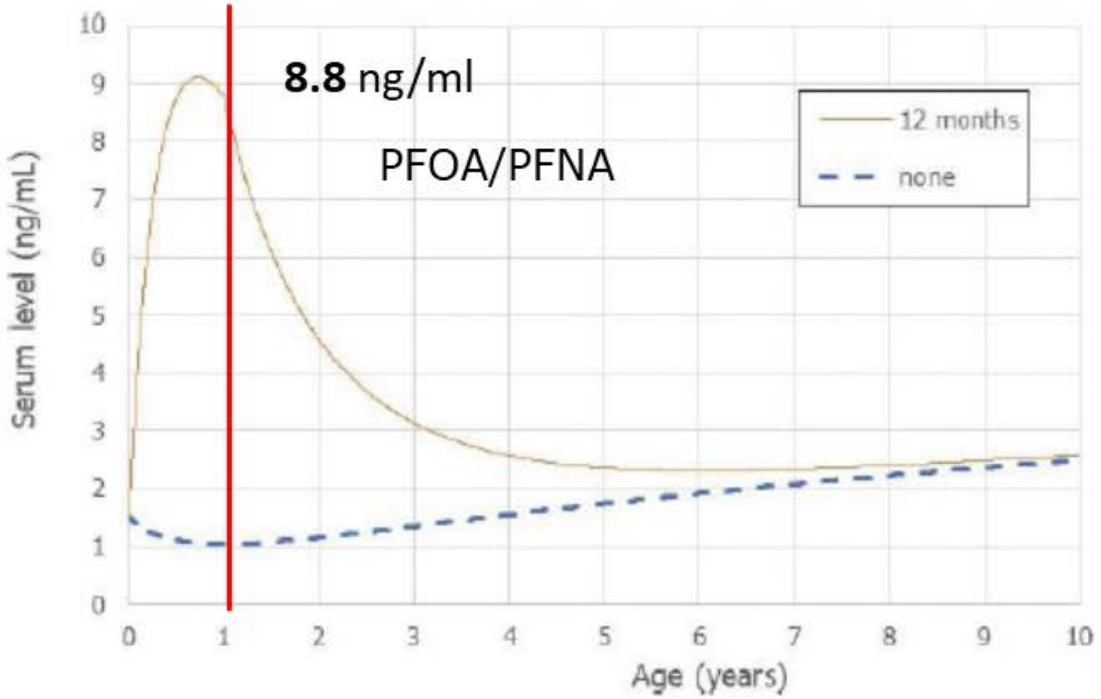
PBK MODELLING SERUM LEVELS CHILDREN

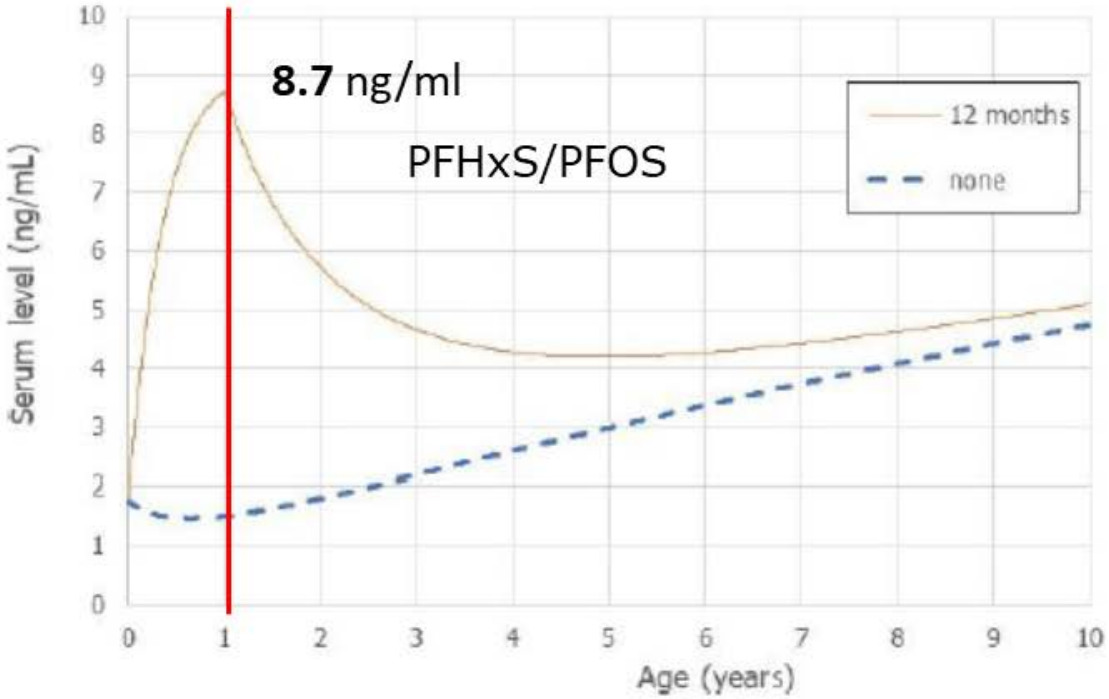




- Required human milk levels:
  - PFOA/PFNA: 0.060 ng/ml
  - PFHxS/PFOS: 0.073 ng/ml
  - Sum 4 PFASs 0.133 ng/ml

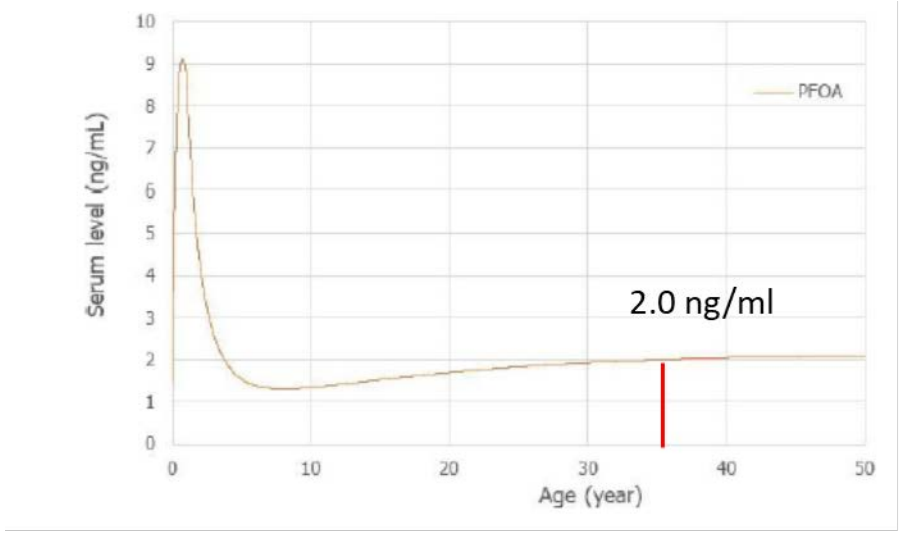
CRITICAL SERUM LEVELS MOTHERS BASED ON RATIOS MILK/SERUM

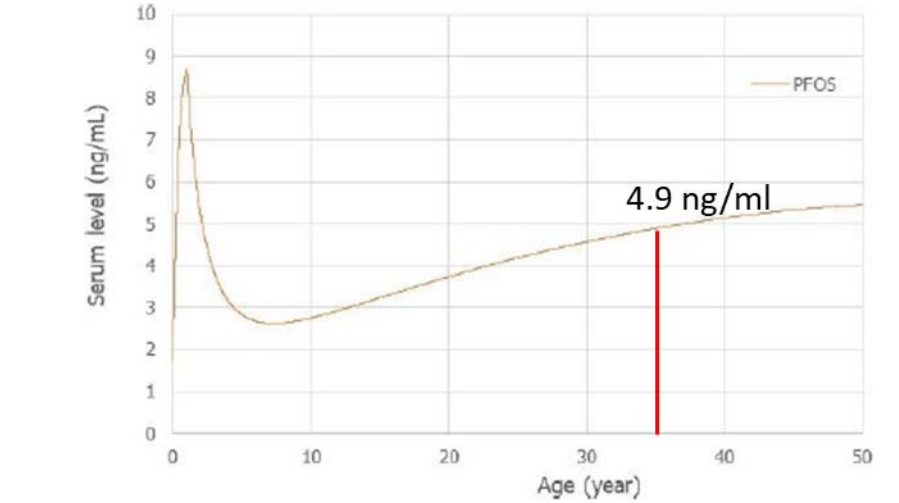




- Corresponding milk and serum levels mothers:
  - PFOA/PFNA: 0.060 ng/ml, serum level 2.0 ng/ml
  - PFHxS/PFOS: 0.073 ng/ml, serum level 4.9 ng/ml
  - Sum 4 PFASs **0.133** ng/ml, serum level **6.9** ng/ml

INTAKE MOTHERS RESULTING IN CRITICAL SERUM LEVEL





- Required intake mothers:
  - 0.19 ng/kg bw per day PFOA/PFNA
  - 0.44 ng/kg bw per day PFHxS/PFOS
  - **0.63** ng/kg bw per day for sum4

TWI (TOLERABLE WEEKLY INTAKE)

- Reference Point: 0.63 ng/kg bw per day
- TWI: 7 x 0.63 = 4.4 ng/kg bw per week
  - For the sum of PFOA, PFNA, PFHxS and PFOS
  - Lower than TWIs from EFSA 2018
- Should protect against immune effects at higher age,
  - and against potential other effects used in first Opinion
- Similar potencies assumed for 4 PFASs (default when lack of data)
- Effects may also occur with other PFASs, but no data
  - Only for effects occurring at higher doses; would suggest lower toxicity
  - TWI would only apply for PFASs accumulating and transferred to infants

EXPOSURE ASSESSMENT

- Many data <LOQ, left censored (>90%)
  - Creates large uncertainty in assessment
- Exposure calculations based on consumption surveys from many European countries
- Estimated for various age groups

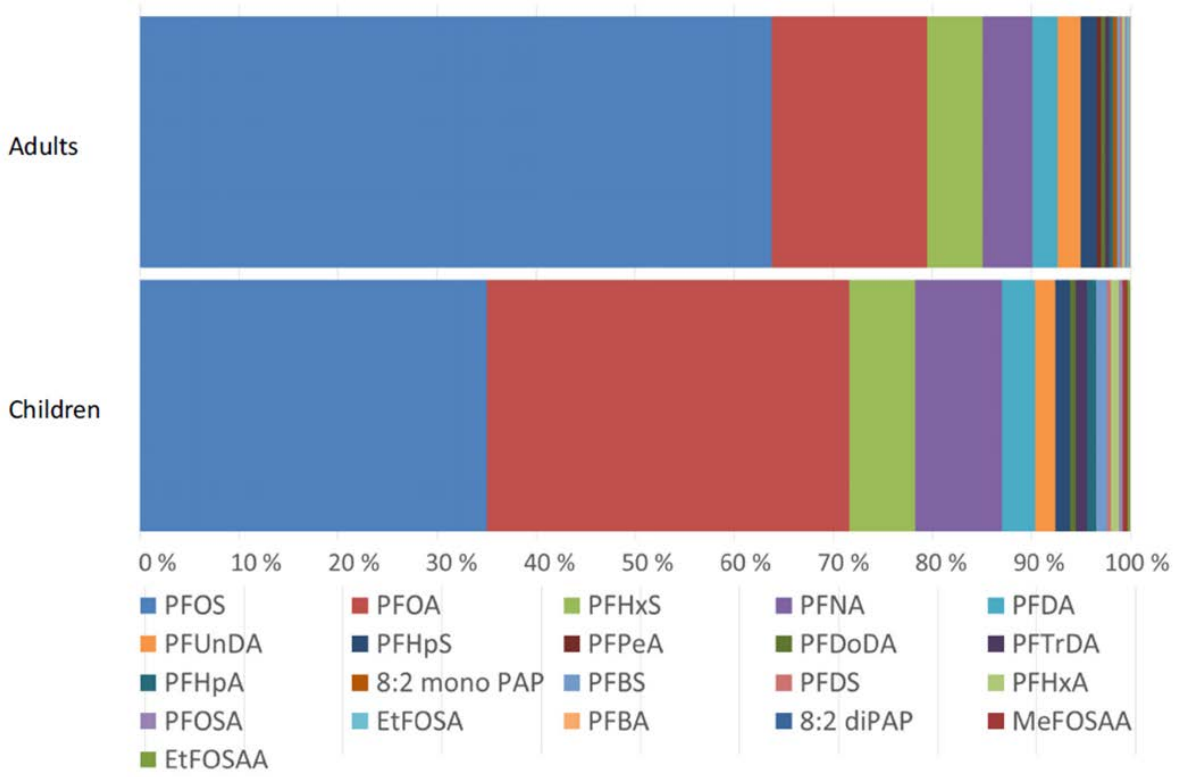
EXPOSURE TO 4 PFASs

Age group	Mean lower bound dietary exposure			95th percentile lower bound dietary exposure		
	Minimum	Median	Maximum	Minimum	Median	Maximum
Toddlers	10	21	46	23	53	96
Other children	6	11	21	19	29	68
Adolescents	3	6	11	9	15	37
Adults	4	6	9	9	16	35
Elderly	5	6	15	12	17	39
Very elderly	3	6	22	9	16	70

- Lower bound estimates (ng/kg bw per week)
- Upperbound estimates much higher but considered to present larger uncertainty
- Most estimates exceed TWI of 4.4 ng/kg bw/week, implying a health concern

BIOMONITORING DATA IN 2020 OPINION

- Extensive review of human biomonitoring data
- Levels of the 4 selected PFASs contribute most to the levels
- Shift PFOS/PFOA in children due to higher transfer PFOA to human milk
- Short-chain PFASs contribute to the exposure but seem not to accumulate
- Levels in blood support the lowerbound exposure estimates rather than the upperbound ones



CONCLUSIONS

- New TWI of 4.4 ng/kg bw per week
  - for sum of 4 PFASs that are most consistently detected in human blood
  - In particular PFOS and to lesser extent PFOA, PFNA and PFHxS
- Lack of data on mode of action behind decreased vaccination response
  - and to derive relative potency factors based on this endpoint
- TWI exceeded by European population


QUESTIONS?