



Rijksinstituut voor Volksgezondheid  
en Milieu  
*Ministerie van Volksgezondheid,  
Welzijn en Sport*

## **Voedselveiligheid:**

**“Health Based Guidance  
Values” en Epidemiologie**

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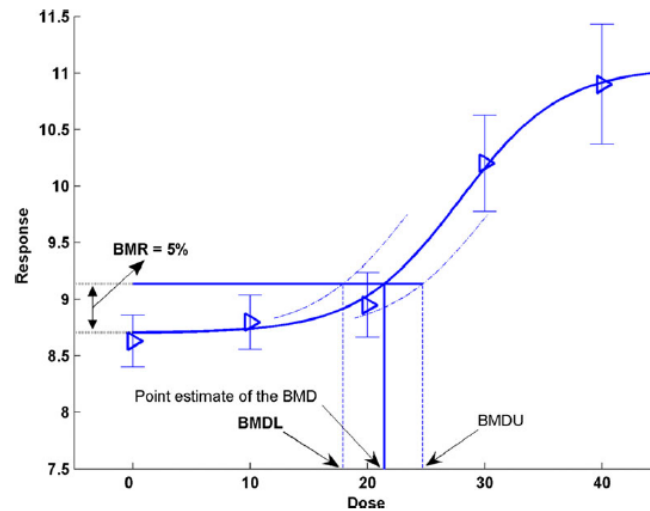
## **Health Based Guidance Value (HBGV): Traditioneel**



## PoD: BMD analyse

Let op: "0"-blootstelling gegeven!

Epi-data: "0"-blootstelling schatten!





# Lood



EFSA Journal 2010; 8(4):1570

## SCIENTIFIC OPINION

### Scientific Opinion on Lead in Food<sup>1</sup>

EFSA Panel on Contaminants in the Food Chain (CONTAM)<sup>2, 3</sup>

European Food Safety Authority (EFSA), Parma, Italy

This Scientific Opinion, published on 22 March 2013, replaces the earlier version published on 20 April 2010<sup>4</sup>.



## Kritische studie lood: Epi

Kritisch effect: Ontwikkeling van het Centraal Zenuwstelsel

Studie: Lanphear (2005)

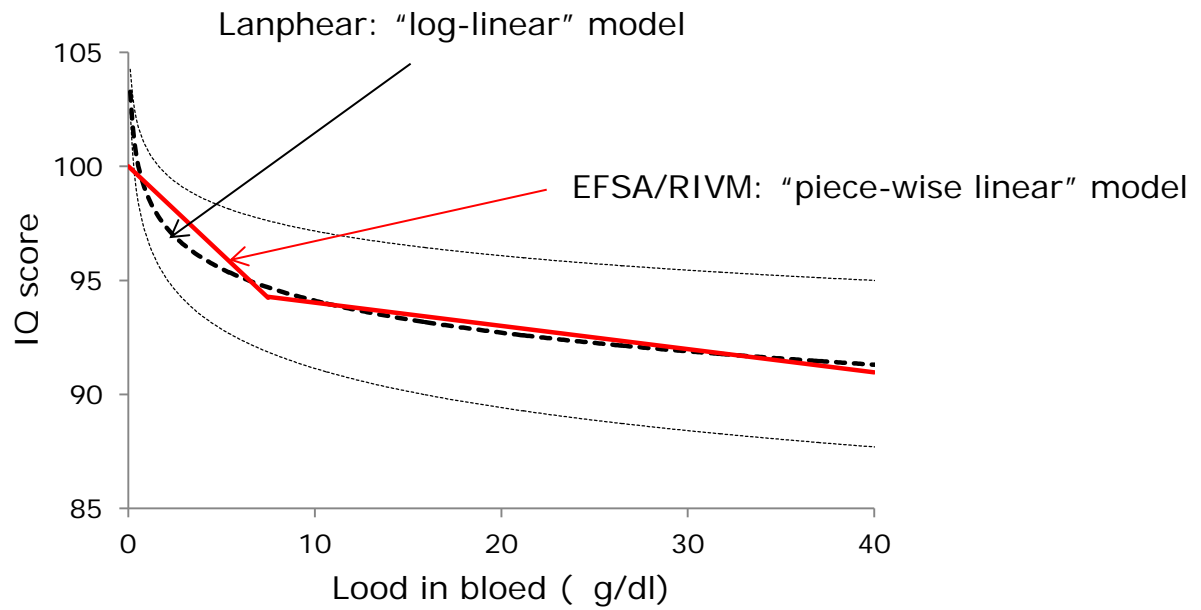
Meta-analyse

- 7/8 longitudinale studies in kinderen (n=1333)
- Blootstelling: lood-in-bloed (4 tijdmetingen: biomonitoring!)
- Effect: IQ meting (4-10 jaar)

EFSA (2010): Her-analyse van **oorspronkelijke** data.



# Dosis-respons lood





## Acceptabele blootstelling lood

PoD: IQ = 1 (sociaal-economisch criterium!)

0.50  $\mu\text{g}$  lood/kg lg/dag

12  $\mu\text{g}/\text{L}$

IQ = 1



# PCDD/F en DL-PCB

## SCIENTIFIC OPINION



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**

EFSA Panel on Contaminants in the Food Chain (CONTAM),  
Helle Katrine Knutsen, Jan Alexander, Lars Barregård, Margherita Bignami, Beat Brüscheweiler,  
Sandra Ceccatelli, Bruce Cottrill, Michael Dinovi, Lutz Edler, Bettina Grasl-Kraupp,  
Christer Hogstrand, Carlo Stefano Nebbia, Isabelle P Oswald, Annette Petersen, Martin Rose,  
Alain-Claude Roudot, Tanja Schwerdtle, Christiane Vleminckx, Günter Vollmer,  
Heather Wallace, Peter Fürst, Helen Håkansson, Thorhallur Halldorsson,  
Anne-Katrine Lundebye, Raimo Pohjanvirta, Lars Rylander, Andrew Smith, Henk van Loveren,  
Ine Waalkens-Berendsen, Marco Zeilmaker, Marco Binaglia, José Ángel Gómez Ruiz,  
Zsuzsanna Horváth, Eugen Christoph, Laura Ciccolallo, Luisa Ramos Bordajandi,  
Hans Steinkellner and Laurentius (Ron) Hoogenboom





## Kritische studie PCDD/F en DL-PCB: Epi

Mengselblootstelling: Geaggregeerde blootstellingsmaat (TEQ)

Kritisch effect: Repro-tox (effect op spermakwaliteit; ook in proefdieren!)

Gevoelige periode: Prenataal, postnataal (0-6 maanden), puberteit

Studie: Mínguez-Alarcón (2017)

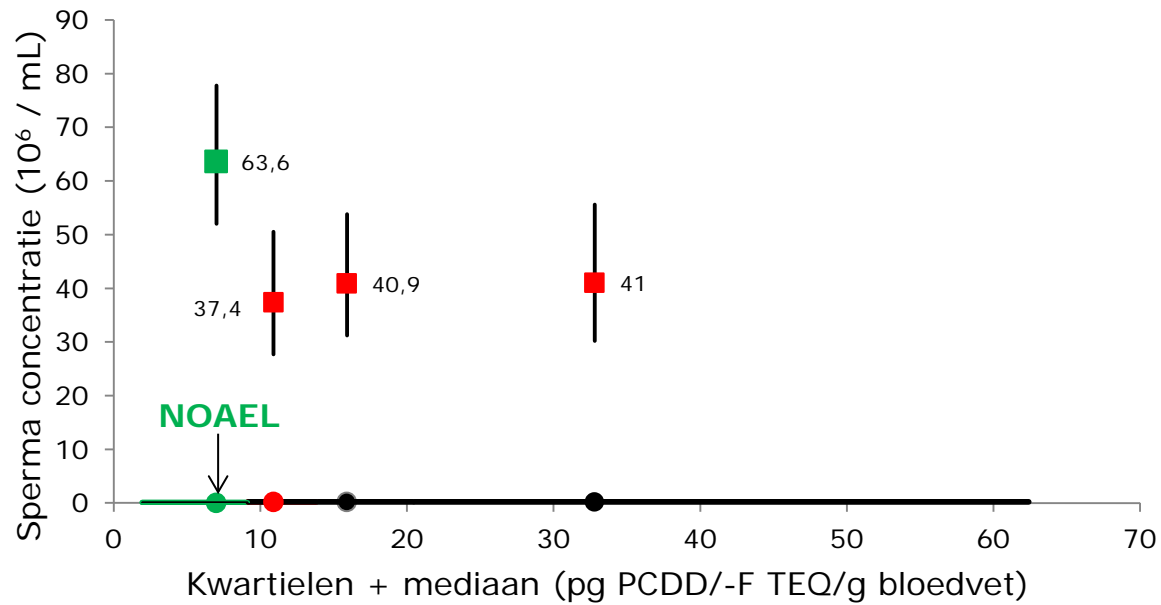
- Longitudinale studie in jonge jongens
- Blootstelling: Dioxine/Furaan TEQ/g bloedvet (8-9 jaar)
- Effect: Kwaliteit sperma (18-19 jaar)

EFSA (2018): Her-analyse **gepubliceerde** data (samen met auteurs)



## Dosis-respons PCDD/F en DL-PCB : "Condensed data"

Waarom zo?





## HBGV PCDD/F en DL-PCB (voeding)

PoD: "NOAEC" = 7 pg TEQ/g bloedvet

Kinetisch

0.25 pg TEQ/kg lg/dag    7 pg TEQ/g bloedvet in borstgevoede jongens



## Toets aanname zaadparameters

Aangenomen normaalwaarde: 63.6

WHO referentiewaarden: "0"-blootstelling?

WHO reference values for human semen

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**Table II** Distribution of values, lower reference limits and their 95% CI for semen parameters from fertile men whose partners had a time-to-pregnancy of 12 months or less

	N	Centiles										
		2.5	(95% CI)	5	(95% CI)	10	25	50	75	90	95	97.5
Semen volume (ml)	1941	1.2	(1.0–1.3)	1.5	(1.4–1.7)	2	2.7	3.7	4.8	6	6.8	7.6
Sperm concentration ( $10^6$ /ml)	1859	9	(8–11)	15	(12–16)	22	41	73	116	169	213	259
Total number ( $10^6$ /Ejaculate)	1859	23	(18–29)	39	(33–46)	69	142	255	422	647	802	928
Total motility (PR + NP, %)*	1781	34	(33–37)	40	(38–42)	45	53	61	69	75	78	81
Progressive motility (PR, %)*	1780	28	(25–29)	32	(31–34)	39	47	55	62	69	72	75
Normal forms (%)	1851	3	(2.0–3.0)	4	(3.0–4.0)	5.5	9	15	24.5	36	44	48
Vitality (%)	428	53	(48–56)	58	(55–63)	64	72	79	84	88	91	92

\*PR, progressive motility (WHO, 1999 grades a + b); NP, non-progressive motility (WHO, 1999 grade c).

The values are from unweighted raw data. For a two-sided distribution the 2.5th and 97.5th centiles provide the reference limits; for a one-sided distribution the fifth centile provides the lower reference limit.



## Perfluors (PFASs)

Mengselblootstelling: **Geen** geaggregeerde blootstellingsmaat!  
Dus iedere PFAS apart (PFOA, PFOS, ....)

EFSA (2018): Her-analyse van al **geanalyseerde, gepubliceerde** data

Studie: Steenland (2009)

- C8-cohort (drinkwatervergiftiging met PFOA)
- Blootstelling: Individuele congenen in bloed
- Effect: Totaal serum Cholesterol (niet in proefdieren!)

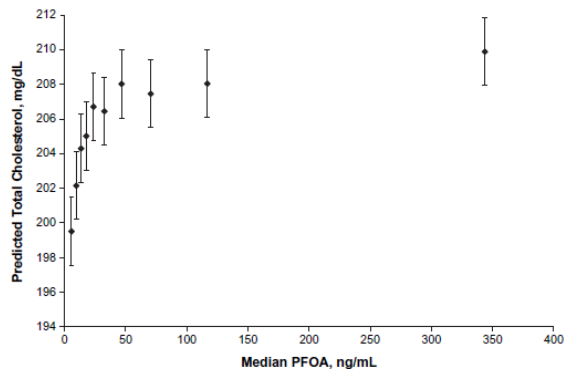


## Dosis-respons PFAS: “Condensed data of analysed data”

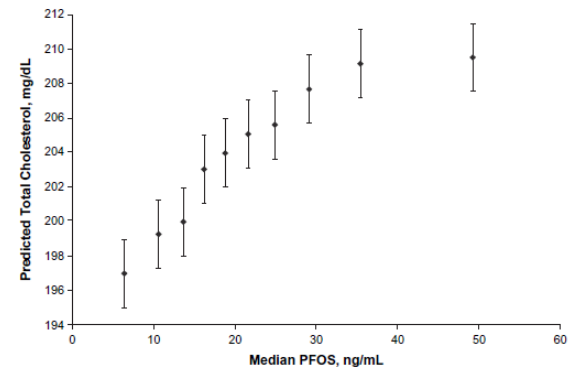
Subpopulatie!

Totaal mengseleffect toegekend aan PFOA of PFOS

Impasse die alleen opgelost kan worden door aanname over “Relative Potency” van congeneren te doen. Primaire data nodig!



**Figure 2.** Total cholesterol by decile of perfluorooctanoic acid (PFOA), with 95% confidence intervals, Ohio and West Virginia, 2005–2006. The model was adjusted for covariates. The x-axis uses medians of PFOA deciles. Predicted cholesterol levels are based on an “average” subject with the following characteristics: age 60–69 years, male gender, not taking cholesterol-lowering medication, never smoked, high school diploma, does not participate in regular exercise, does not drink alcohol, and body mass index between 24 and 27 kg/m<sup>2</sup>. Confidence intervals are based on the predicted population mean given those covariate levels.



**Figure 3.** Total cholesterol by decile of perfluorooctane sulfonate (PFOS), with 95% confidence intervals, Ohio and West Virginia, 2005–2006. The model was adjusted for covariates. The x-axis uses medians of PFOS deciles. Predicted cholesterol levels are based on an “average” subject with the following characteristics: age 60–69 years, male gender, not taking cholesterol-lowering medication, never smoked, high school diploma, does not participate in regular exercise, does not drink alcohol, and body mass index between 24 and 27 kg/m<sup>2</sup>. Confidence intervals are based on the predicted population mean given those covariate levels.

*Am J Epidemiol* 2009;170:1268–1278



## Toekomstige ontwikkelingen

“Public consultation” voor alle concept EFSA CONTAM panel beoordelingen

EFSA SC/WG Epidemiologie en Toxicologie (2019-2020; RIVM: Hearing expert)

RIVM: WG Epidemiologie en Toxicologie (onderlinge kruisbestuiving)



## Stellingen

Voor het afleiden van HBGVs blijft dierexperimenteel onderzoek nodig

Bij het afleiden van HBGVs op basis van epi onderzoek zou ziektelast uitgangspunt moeten zijn (Lanphear *et al.*, 2018, *Lancet* (3): e177-184).

Biomonitoring van stoffen moet een vast onderdeel worden van longitudinaal epi gezondheidsonderzoek (Chiao *et al.*, 2016, *JAMA*: 73(7): 803-811; Goutman *et al.*, 2019, *J. Neurol. Neurosurg Psychiatry*, 0: 1-6).