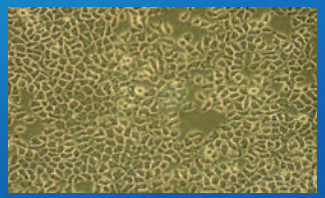
PFAS – toxische Profile im Wasser






Dr. Peter Behnisch (BDS)

BioDetection Systems BV

Science Park 406

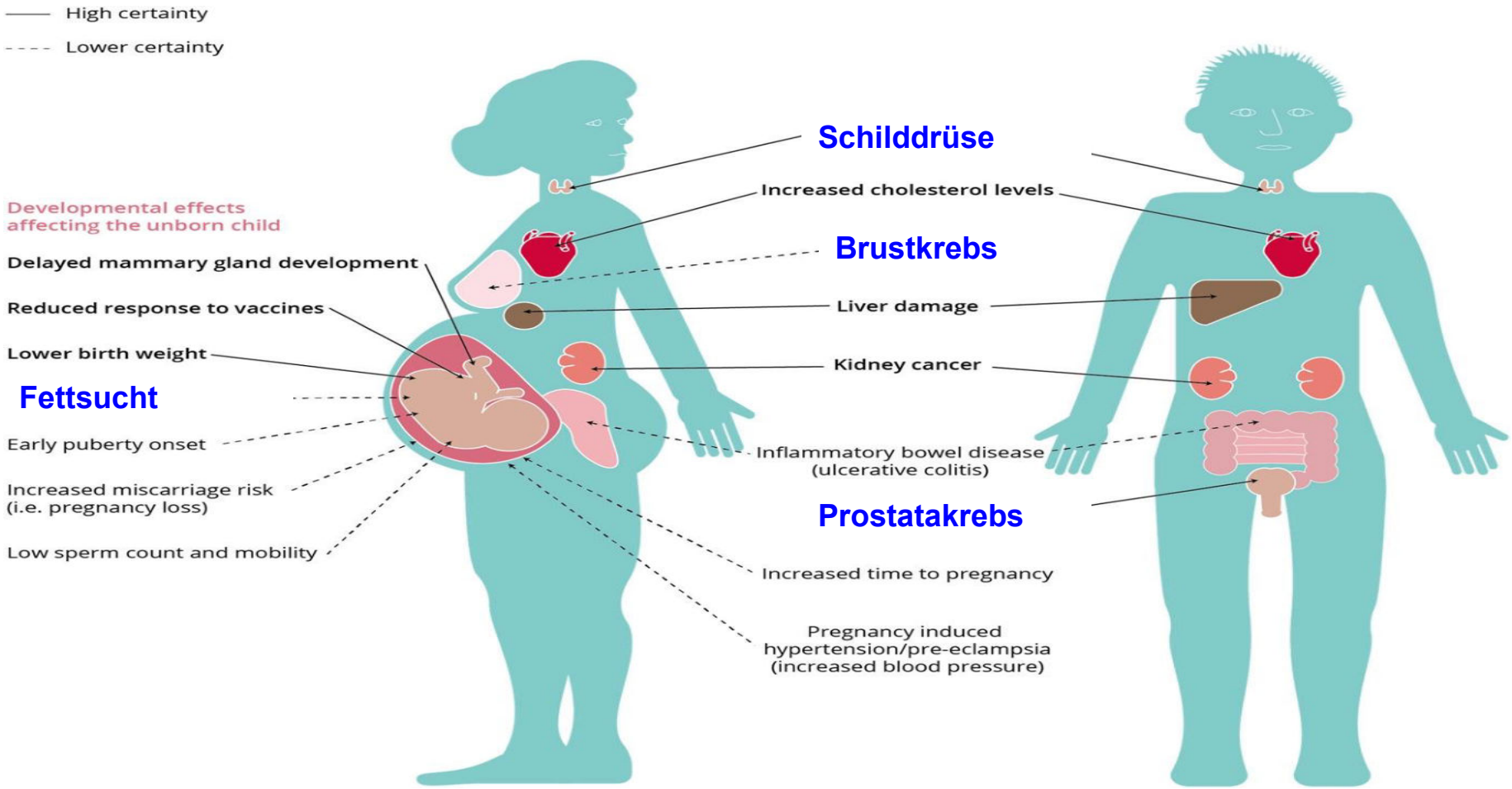
1098 XH Amsterdam

The Netherlands

Übersicht

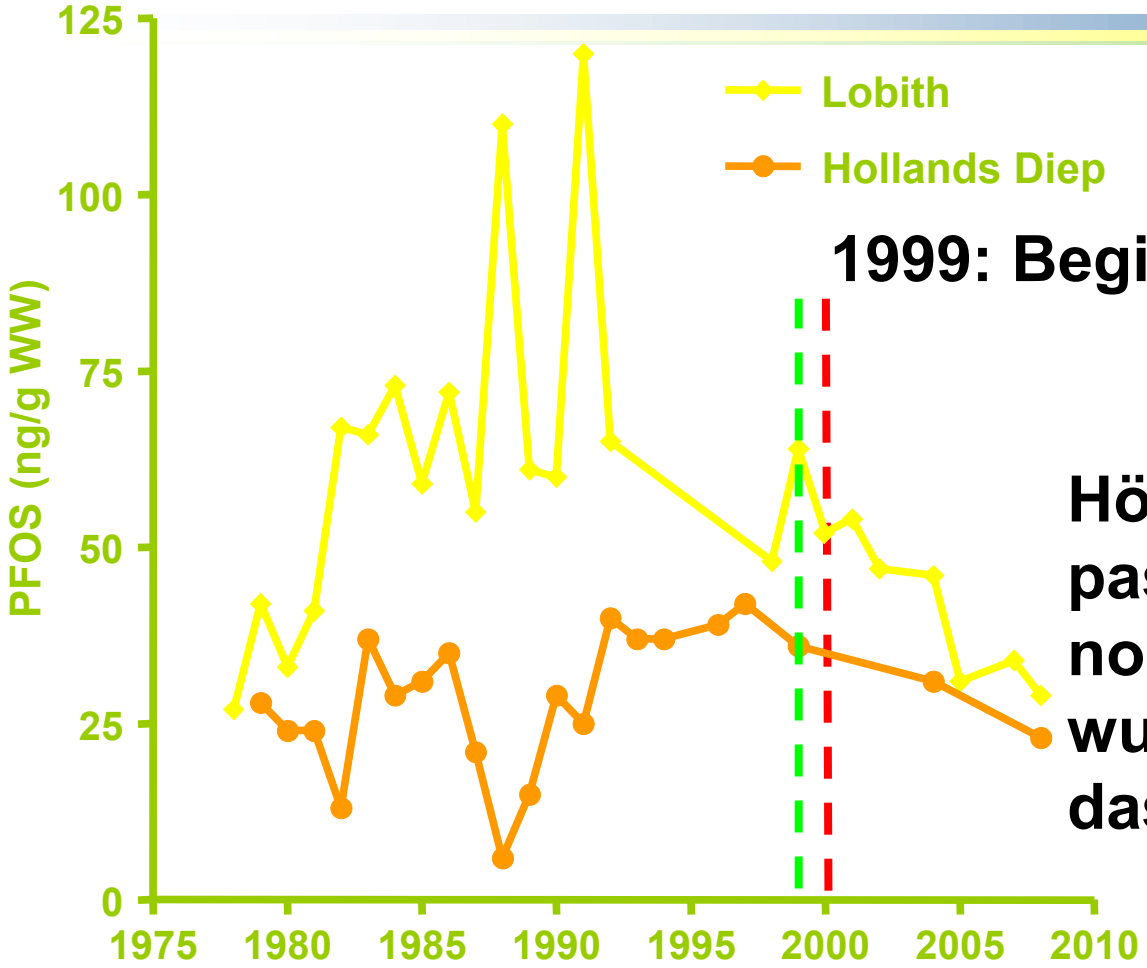
- Einführung zu PFAS
- Einführung über BIO-Analytik
- In vitro toxische Profile der PFAS
- Komplexe Mischungen von PFAS (in PFOA-Equivalenten)
- Erste Ergebnisse des PFAS CALUX in Wasser
- Zusammenfassung

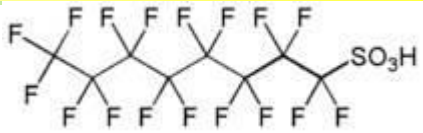
PFAS – bekannte toxische Wirkungen im Mensch



Fenton et al (2021). Environmental Toxicology and Chemistry, 40, 606ff.

PFOS in Aal (historische Probenbank)



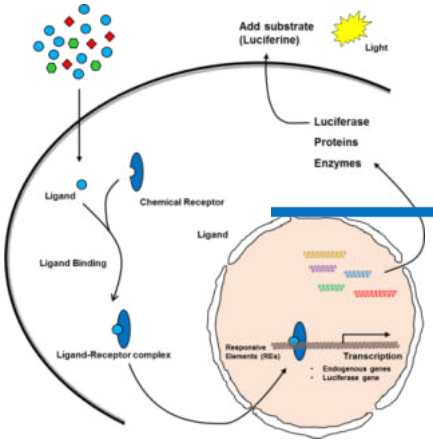


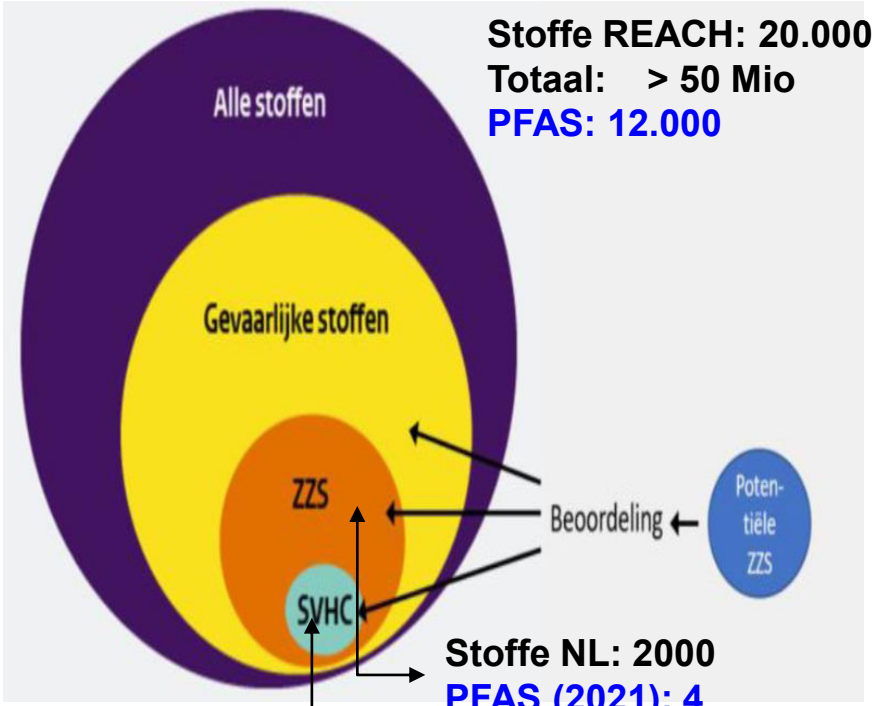
1999: Beginn Routine Analyse

Höchstes Risiko passiert als der Stoff noch nicht gemessen wurde..! (PCBs dasselbe)

Kwadijk et al., 2010

Mischung aus Bekannten vs. Unbekannten Stoffe im Wasser





Welche toxische PROFILE?

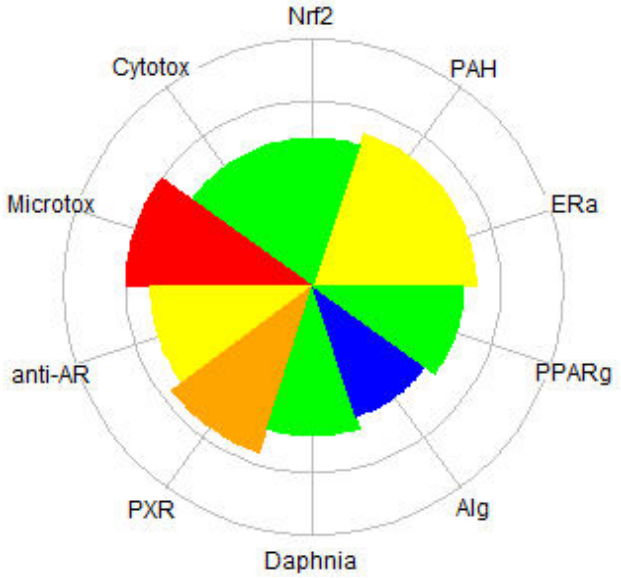
Basis-Set: Wasser-Qualität in 5 Farben

Keine Aktion ← → Aktion

- geen risico verwacht: excellent
- geen risico verwacht: goed
- risico mogelijk: klein
- risico mogelijk: medium
- risico mogelijk: groot

Plek: test
Datum: 2021-12-03

Oppervlaktewater		Geringe TOX Risiko	Kleine TOX Risiko	Möglich TOX Risiko	Erhöht TOX Risiko	Hohes TOX Risiko
ER CALUX	ng EEQ/L	0	0,13	**0,52**	3,2	32
PAH CALUX	ng BaPEQ/L	0	20	**41**	160	565
Oppervlaktewater		**0-0,2 ESW**	**>0,2 ESW**	**ESW klassen**	**>5 ESW**	**>10 ESW**
Nrf2 CALUX	µg CEQ/L	0	2	**10**	50	100
PXR CALUX	µg NEQ/L	0	0,6	**3**	15	30
PPARγ CALUX	ng RosEQ/L	0	2	**10**	50	100
Anti-AR CALUX	µg FEQ/L	0	5	**25**	125	250
Microtox*	TU	0	0,01	**0,05**	0,25	0,5
Cytotox	TU	0	0,01	**0,05**	0,25	0,5
Algen	TU	0	0,01	**0,05**	0,25	0,5
Daphnia	TU	0	0,01	**0,05**	0,25	0,5



Effekt-Signal Wert (ESW) = Wirkungs-bezogener Richtwert (EBT)

https://kiwk-tox.netlify.app/nl/interpretatie-tox/

Was können diese TOXISCHE Profile bedeuten?

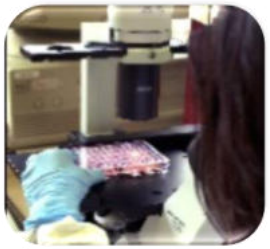
Krankheit	Mechanismus	Chemikalien	CALUX Tests
Chlorakne	AhR Rezeptor	Dioxine, dl-PCBs	DR CALUX
Fettsucht	PPAR Rezeptoren	TBT, PFOA/PFOS	PPAR CALUX
Brustkrebs, Menopause	Estrogen sensitive Zellen	E2, EE2, E3, BPA, Phthalate, Pesticide	ER CALUX
Prostatakrebs	Androgen sensitive Zellen	BPA, Anabolic steroide	AR CALUX
Unfruchtbarkeit	endocrine dependent sex organ function/development	Phthalate, BPA, NP, OP,	ER, AR, TR, PR CALUX
Hypersensitivitaet	Oxidativer Stress	Pestizide	Nrf2 CALUX
Krebs Allgemein	Genotoxizitaet, DNA Schaedigung	BaP, Dioxins, PCBs	P53, PAH CALUX, Dioxin CALUX
Asthma, Allergie	Glucocorticoid sensitiv	Dexamethason, Pharmakas	GR CALUX
Thyroid gland	TTR-TR	PFAS	PFAS CALUX
Metabolisches Syndrom	complex	Dioxine, dl-PCBs, Hormone	DR und ER CALUX
Leukemie	Estrogen sensitiv	Dioxine	DR CALUX

Probenbehandlung und Bioassay Messung

Wasser Probennahme

Probenextraktion
- SPE
- WAX-SPE
- Passive sampler

Bioassay Hochdurchsatz-Verfahren
- manual
- automatisiert (Roboter)



Menschliche Zellen

Luminometer-Messung

Daten Interpretation

Übersicht

- Einführung über BIO-Analytik
- **In vitro toxische Profile der PFAS**
- Komplexe Mischungen von PFAS in PFOA-Equivalenten
- Erste Ergebnisse des PFAS CALUX in Wasser
- Zusammenfassung

Sind PFAS Umwelthormone?
PFAS nicht aktiv in (anti)-AR, -ER, -PR and GR-CALUX (2007)

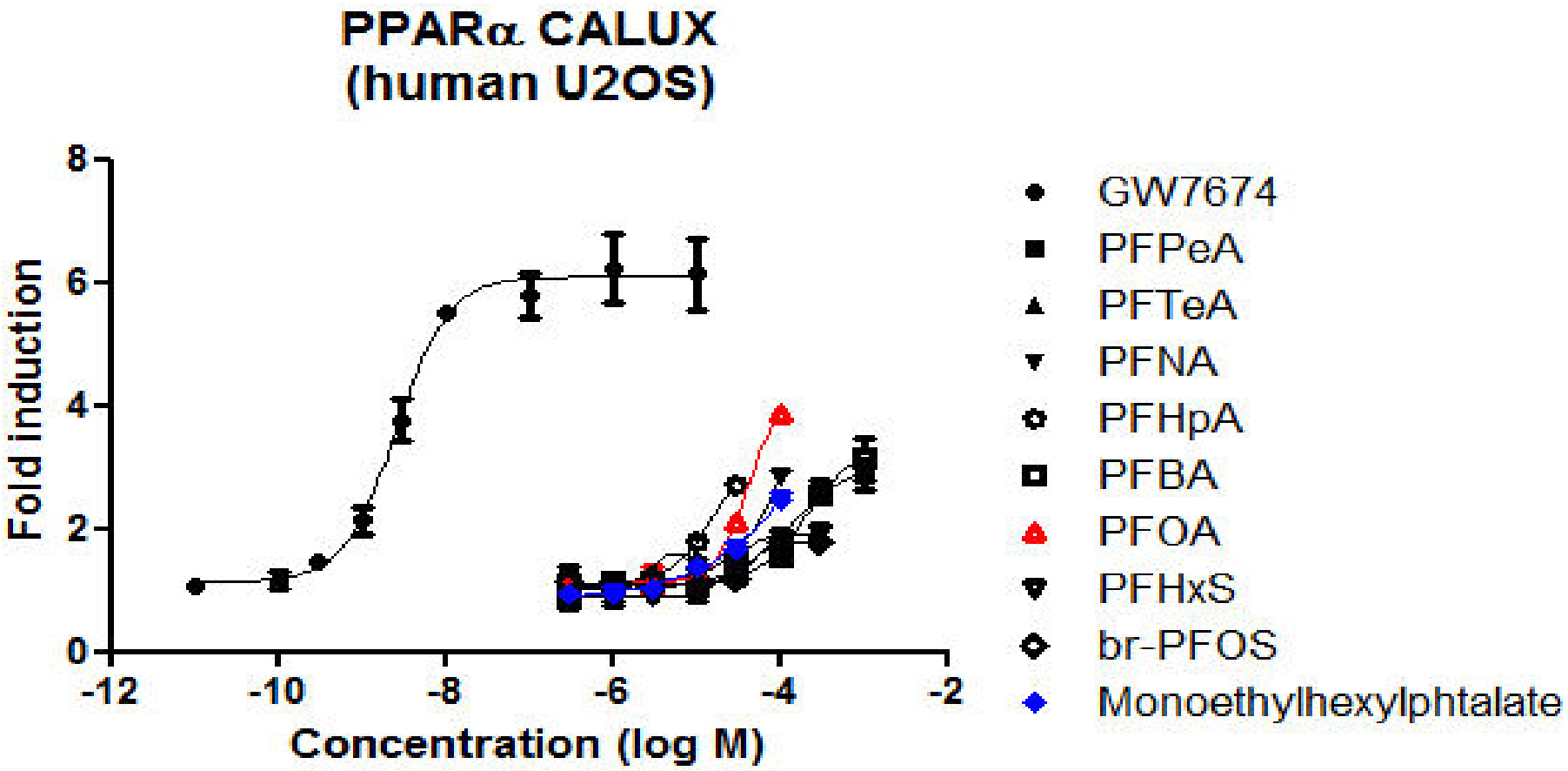
PERFLUOROALKYL ACIDS HAVE NO ENDOCRINE DISRUPTING ACTIVITIES VIA HUMAN STEROID HORMONE RECEPTORS AS DETERMINED BY A PANEL OF CALUX® BIOASSAYS

Sonneveld E[1], Man HY[1], Pieterse B[1], Brouwer A [1], Behnisch P[1], Van der Burg B[1]
[1]BioDetection Systems B.V. (BDS), 1098 SM, Amsterdam, the Netherlands

Compound	AR agonistic logEC50 (M)	ERa agonistic logEC50 (M)	ERb agonistic logEC50 (M)	PR agonistic logEC50 (M)	GR agonistic logEC50 (M)	AR antagonistic logIC50 (M)	ERa antagonistic logIC50 (M)	ERb antagonistic logIC50 (M)	PR antagonistic logIC50 (M)	GR antagonistic logIC50 (M)
PFOS	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5
PFHxA	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5
PFOA	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5
PFNA	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5
PFHpA	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5	>-5

Sonneveld E, Man HY, Pieterse B, Brouwer A 1 , Behnisch P , Van der Burg B. Organohalogen Compounds 69, 2987ff (2007)

Sind PFAS Fettsucht-beeinflussende Stoffe ?
PFAS wenig aktiv in den PPAR CALUX Bioassays (2012)



Behnisch PA, Besselink H , Van der Linden S, DeVoogt P , Brouwer A.
Organohalogen Compounds 74, 186 (2012)

PFAS in vitro Toxizitäts Profile (2021): Literatur-Übersicht

	Exposure levels in dust samples			Bioactivity classification (RPF) [Median percentage contribution to potency-weighted concentration sum of chemical class]				
Chemical	Percentage of samples >MDL	Median [range (ng/g)]	Median percentage of class sum	PPARγ antagonism (Huang et al. 2016)	Thyroid hormone receptor β antagonism (Huang et al. 2016)	Androgen receptor antagonism (Huang et al. 2016)	Estrogen receptor α agonism (Huang et al. 2016)	Thyroid hormone transport interference (Besselink 2020)[a]
Per- and polyfluoroalkyl substances (PFAS)								
PFHxA	97.8	193 (<MDL–2,980)	66	Inactive	Inactive	Inactive	Inactive	Active (0.044) [19]
PFOS	97.8	15.2 (<MDL–296)	5.4	Active (0.55) [51]	Active (0.52) [50]	Inactive	Inactive	Active (0.85) [30]
PFOA	73.9	7.63 (<MDL–1,520)	4.5	Active (0.4) [25]	Inactive	Inactive	Inactive	Active (0.37) [11]
PFHxS	63.0	1.82 (<MDL–23.7)	<1	Unknown	Unknown	Unknown	Unknown	Active (1) [3.5]
FOSA	60.9	3.26 (<MDL–236)	1.5	Inactive	Active (0.59) [14]	Inactive	Active (0.39) [100]	Active (0.33) [3.6]
PFHpA	52.2	0.918 (0–1,760)	<1	Inactive	Inactive	Inactive	Inactive	Active (0.35) [2.0]
PFPeA	32.6	<MDL (<MDL–455)	<1	Unknown	Unknown	Unknown	Unknown	Active (0.013) [<1]
PFNA	30.4	<MDL (<MDL–1,480)	<1	Active (0.76) [2.3]	Active (0.47) [1.2]	Inactive	Inactive	Active (0.13) [<1]
PFBS	30.4	<MDL (<MDL–16.1)	<1	Unknown	Unknown	Unknown	Unknown	Active (0.028) [<1]
PFDS	10.9	<MDL (<MDL–12.5)	<1	Unknown	Unknown	Unknown	Unknown	Unknown
PFBA	4.35	<MDL (<MDL–155)	<1	Unknown	Unknown	Unknown	Unknown	Active (0.0003) [<1]
PFDA	4.35	<MDL (<MDL–35.0)	<1	Inactive	Active (0.29) [<1]	Inactive	Inactive	Active (0.033) [<1]
PFUnDA	0	<MDL (<MDL–<MDL)	<1	Active (1) [4.2]	Inactive	Inactive	Inactive	Active (0.017) [<1]
PFDoDA	0	<MDL (<MDL–<MDL)	<1	Unknown	Unknown	Unknown	Unknown	Active (0.0037) [<1]
N-MeFOSAA	0	<MDL (<MDL–<MDL)	<1	Unknown	Unknown	Unknown	Unknown	Unknown

Young Behnisch et al., Environm. Health Perspect., 2021, 129

In vitro Toxizitäts-Equivalente für PFAS (2020)

Testing of 13 PFAS standard compounds using the PFAS CALUX® bioassay.

Final report

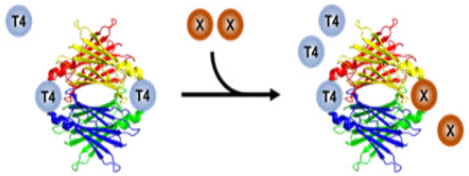
Requested by: Dr. Tamara Grummt

Umweltbundesamt
Bismarckplatz 1
14193 Berlin
Germany

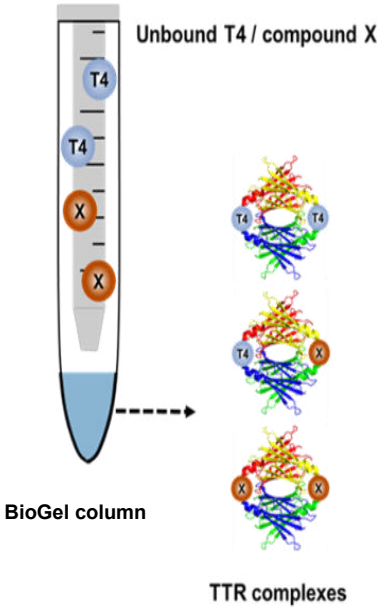
Phone: +49 3743776354
E-mail: Tamara.Grummt@uba.de

Transthyretin Rezeptor (TTR)-TRβ basierter PFAS CALUX Bioassay

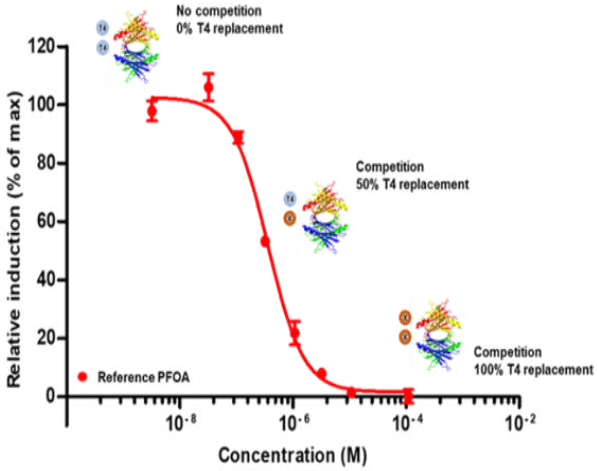
Step 1 Inkubation (TTR Verdringung)



Step 2 Separierung TTR-bound vs. freie T4-Stoffe



Step 3 TRβ-CALUX analysis



In vitro Toxizitäts-Equivalente für PFAS (2023)

Substanz	Abkürzung	CAS Nummer	RPF (EC)	PFAS CALUX
Perfluorooctanoic acid	**PFOA**	**335-67-1**	**1**	**1**
Perfluorooctane sulfonic acid	PFOS	1763-23-1	2	2
Perfluorohexane sulfonic acid	PFHxS	355-46-4	0.6	
Perfluorononanoic acid	PFNA	375-95-1	10	
Perfluorobutanoic acid	PFBA	375-22-4	0.05	0.0018
Perfluoropentanoic acid	PFPeA	2706-90-3	0.03	0.08
Perfluorohexanoic acid	PFHxA	307-24-4	0.01	0.19
Perfluoroheptanoic acid	PFHpA	375-85-9	0.505	1.4
Perfluorodecanoic acid	PFDA	335-76-2	7	0.12
Perfluoroundecanoic acid	PFUnDA	2058-94-8	4	
Perfluorododecanoic acid	PFDoDA	307-55-1	3	
Perfluorotridecanoic acid	PFTrDA	72629-94-8	1,65	
Perfluorotetradecanoic acid	PFTeDA	376-06-7	0.3	
Perfluorohexadecanoic acid	PFHxDA	67905-19-5	0.02	
Perfluorooctadecanoic acid	PFODA	16517-11-6	0.02	
Perfluorobutane sulfonic acid	PFBS	375-73-5	0.001	0.052
Perfluoropentane sulfonic acid	PFPeS	2706-91-4	0.3005	
Perfluorohexane sulfonic acid	PFHxS		Not listed (0.6)	1.6
Perfluoroheptane sulfonic acid	PFHpS	375-92-8	1.3	1.0
Perfluorodecane sulfonic acid	PFDS	335-77-3	2	
Ammonium perfluoro (2-methyl-3-oxahexanoate)	HFPO-DA or Gen X	62037-80-3	0.06	
Propanoic Acid / Ammonium 2,2,3-trifluoro-3-(1,1,2,2,3,3-hexafluoro-3-(trifluoromethoxy)propoxy)propanoate	ADONA	958445-44-8	0.03	
6:2 Fluorotelomer sulfonic acid	6:2 FTS	27619-97-2	Not listed (0.2)	0.019
2- (Perfluorohexyl)ethyl alcohol	6:2 FTOH	647-42-7	0.02	
2-(Perfluorooctyl)ethanol	8:2 FTOH	678-39-7	0.04	
Acetic acid / 2,2-difluoro-2-((2,2,4,5-tetrafluoro-5-(trifluoromethoxy)-1,3-dioxolan-4-yl)oxy)	C6O4	1190931-41-9	0.06	

Relative Potency Factors von 24 PFAS gemäß "Proposal for a Directive of the European Parliament and of the Council amending Directive 2000/60/EC establishing a framework for Community action in the field of water policy, Directive 2006/118/EC on the protection of groundwater against pollution and deterioration and Directive 2008/105/EC on environmental quality standards in the field of water policy" in comparison to in vitro PFAS CALUX (state 01-01-2023)

PFOA Toxizitäts-Equivalente für PFAS: Trinkwasser (DE, 2017) vs Grundwasser (EU, 2023)

Bundesgesundheitsbl 2017 · 60:350–352
DOI 10.1007/s00103-016-2508-3
Online publiziert: 2. Januar 2017

Empfehlung des Umweltbundesamtes

Fortschreibung der vorläufigen Bewertung von per- und polyfluorierten Chemikalien (PFC) im Trinkwasser

PFAS		TW/GOW (µg/L)	PFAS CALUX RPF	PFAS CALUX [µg PFOA-eq/L]	EU RPF	Summe PFAS (EU) [µg PFOA-eq/L]
PFBA	C4	10	0.0018	0.018	0.05	0.5
PFPeA	C5	3	0.08	0.24	0.03	0.09
PFHxA	C6	6	0.19	1.14	0.01	0.06
PFHpA	C7	0.3	1.4	0.42	0.505	0.1515
PFOA	C8	0.1	1	0.1	1	0.1
PFNA	C9	0.06	0.32	0.0192	10	0.6
PFDcA	C10	0.1	0.12	0.012	7	0.7
PFUnDA	C11	0.1	0.052	0.0052	4	0.4
PFDoDA	C12	0.1	0.01	0.00098	3	0.3
PFTrDA	C13	0.1	0.075	0.0075	1.65	0.165
PFTeDA	C14	0.1	0.019	0.0019	0.3	0.03
						0
PFBS	C4	6	0.052	0.31	0.001	0.006
PFPeS	C5	6			0.3005	1.803
PFHxS	C6	0.1	1.6	0.16	0.6	0.06
PFHpS	C7	0.3	1	0.3	1.3	0.39
PFOS	C8	0.1	2	0.2	2	0.2
PFNS	C9	0.1			2	0.2
PFDS	C10				2	0
Summe PFAS				**2.9**		**5.8**

Brussels, 26.10.2022
COM(2022) 540 final

ANNEXES 1 to 6

ANNEXES

to the

Proposal for a Directive of the European Parliament and of the Council

amending Directive 2000/60/EC establishing a framework for Community action in the field of water policy, Directive 2006/118/EC on the protection of groundwater against pollution and deterioration and Directive 2008/105/EC on environmental quality standards in the field of water policy

{SEC(2022) 540 final} - {SWD(2022) 540 final} - {SWD(2022) 543 final}

(1)	(2)	(3)	(4)	(5)	(6)
[Entry] N°	Name of substance	Category of substances	CAS number (1)	EU number (2)	Quality Standard (3) [µg/l unless otherwise indicated]
3	Per- and poly-fluorinated alkyl substances (PFAS) - sum of 24 (6)	Industrial substances	See table note 6	See table note 6	0,0044 (7)

Faktor 1000 Differenz !

In vitro toxische Profile der PFAS (2022-2023)

PROMISCES

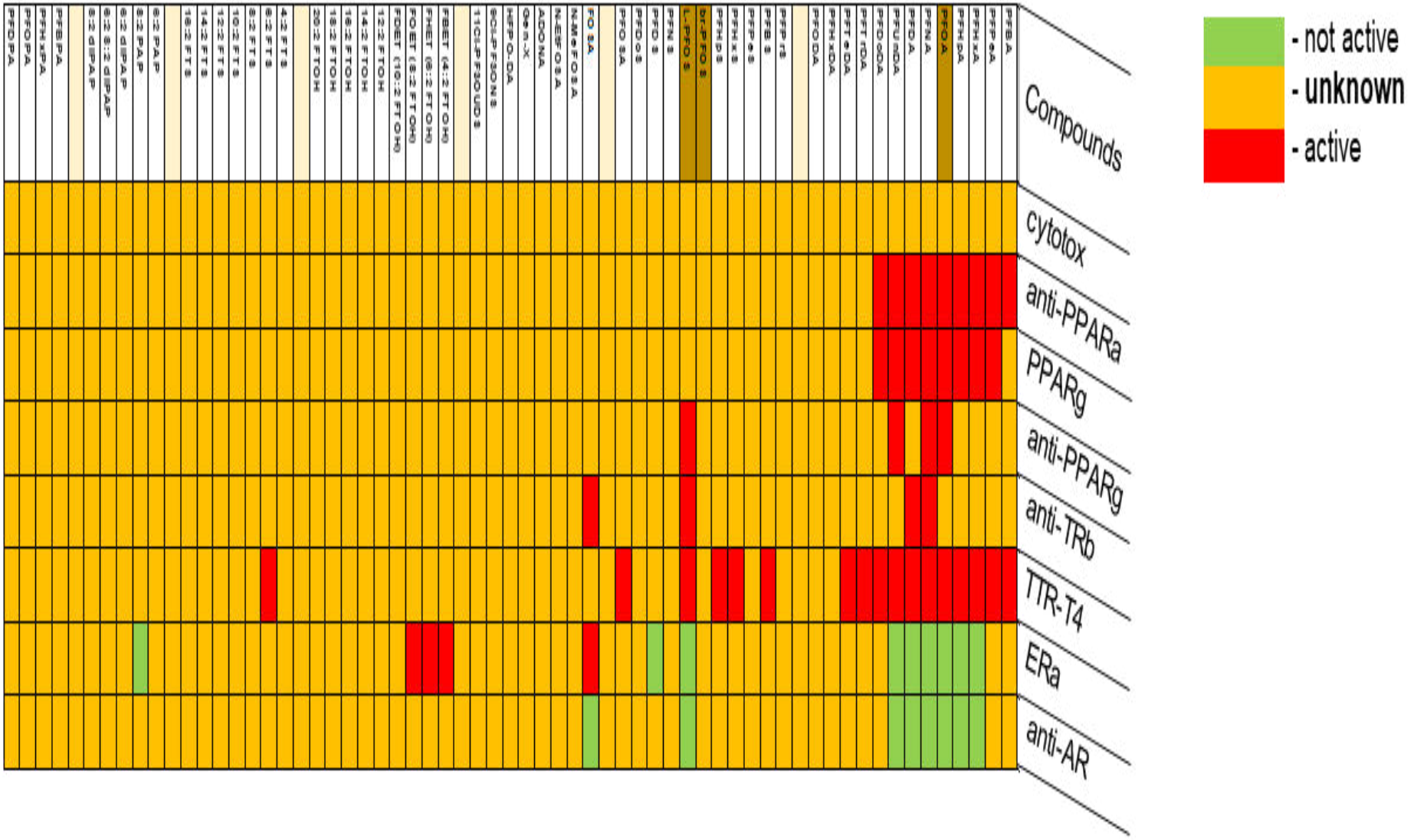
PROMISCES

Preventing Recalcitrant Organic Mobile Industrial chemicalS for Circular Economy in the Soil-sediment-water system

- **20 PFAS wurden auf 13 CALUX Bioassays getested von BDS.**
- **Weitere 25 PFAS werden auf die 7 meist verdächtigen CALUX Bioassay getestet (Cytotox, oxidative stress Nrf2, early warning PXR, anti-TR, anti-PPARγ, PPARα und PFAS CALUX) von BDS**
- **Verschieden industriellen Produkte (GenX, ADONA, ScotchGuard), werden mit demselben CALUX Panel getestet.**
- **UBA testet 45 PFAS auf die biologischen Endpunkte wie z. Bsp. Zelltod, Genotoxizität (z. Bsp. Ames, Micronuclei), oxidative Stress (ROS), Hormone (ER, AR, TR) und Neurotoxizität (MEA).**
- **Z. Zt. werden die besten Konzentrations-Wirkungs-Kurven der meisten PFAS auf die sensitivste Manier im PFAS CALUX erfasst**

The PROMISCES project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 101036449

PFAS-45: In vitro Toxizitäts Profile (2022-2023)



Feuerlöschschäume in PFOA-eq/l

Environment International 157 (2021) 106791

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Developing potency factors for thyroid hormone disruption by PFASs using TTR-TRβ CALUX® bioassay and assessment of PFASs mixtures in technical products

Peter A. Behnisch [a], Harrie Besselink [a], Roland Weber [b], Wolfram Willand [c], Jun Huang [d], Abraham Brouwer [a,e,*]

Feuerlöschschäume in PFOA-eq/l

ENVIRONMENTAL Science & Technology LETTERS

Letter

Cite This: *Environ. Sci. Technol. Lett.* 2019, 6, 259−264

pubs.acs.org/journal/estlcu

Per- and Polyfluoroalkyl Substances in Representative Fluorocarbon Surfactants Used in Chinese Film-Forming Foams: Levels, Profile Shift, and Environmental Implications

Mehvish Mumtaz, Yixiang Bao, Liquan Liu, Jun Huang,* Giovanni Cagnetta,* and Gang Yu

State Key Joint Laboratory of Environment Simulation and Pollution Control (SKJLESPC), Beijing Key Laboratory for Emerging Organic Contaminants Control (BKLEOC), School of Environment, Tsinghua University, Beijing 100084, China

Untreated FFF																			UHPCL-MS/MS			PFAS-CALUX
[g/l]	4A	5A	6A	7A	8A	9A	10A	4S	5S	6S	7S	8S	9S	10S	PFOSA	4:2FTS	6:2FTS	8:2FTS	g PFOA-TEQ/l	Dominant	Impact 6:2 FTS	g PFOA-BEQ/l
VF-368 (2013)	0.29	0.17	0.10	0.09	0.30	0.00	0.00	0.01	0.03	0.53	0.55	22.0	0.08	0.58	na	0.00	0.00	0.00	41	96 % PFOS		45
VF-570 (2013)	1.62	0.93	0.49	0.30	0.95	0.00	0.00	0.20	0.38	7.64	5.45	87.3	0.52	0.00	na	0.00	0.00	0.00	174	90 % PFOS		57
VF-9128 (2019)	0.26	0.09	1.40	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.0	0.00	0.00	na	0.00	22.4	0.00	0,70		67% 6:2 FTS	1,6
FUMETROL 21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.0	0.00	0.00	na	0.07	1.16	0.01	0,04		61% 6:2 FTS	1,4

TEF-factors PFAS CALUX	0.0019	0.0350	0.16	1.2	1.0	0.33	0.11	0.05	na	2.0	0.0013	1.8		0.71	na	0.021	na

na = not yet analysed

Heat-Top Assay treated																			UHPCL-MS/MS			PFAS-CALUX
[g/l]	4A	5A	6A	7A	8A	9A	10A	4S	5S	6S	7S	8S	9S	10S	PFOSA	4:2FTS	6:2FTS	8:2FTS	g PFOA-TEQ/l	Dominant	Impact 6:2 FTS	g PFOA-BEQ/l
VF-368 (2013)	2.1	1.6	2.2	2.8	12	0.29	0.00	0.009	0.027	0.53	0.55	22	0.08	0.58	na				57	70 % PFOS		270
VF-570 (2013)	2.1	3.4	2.2	2.7	6.4	0.23	0.00	0.20	0.38	7.6	5.5	87	0.52	0.00	na				183	86 % PFOS		180
VF-9128 (2019)	1.6	2.8	0.82	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	na				0,4	42% PFHpA		<LOQ
FUMETROL 21	4.9	12	3.4	0.63	0.02	0.00	0.00	0.00	0.00	0.01	0.00	0.01	0.00	0.00	na	0.00	0.00	0.00	1,8	39% PFHpA	0% 6:2 FTS	<LOQ

Behnisch et al 2021. Environmental International

Oberflächen- und Abfall-Wasser in PFOA-eq/l (SETAC, IWA und DIOXIN 2022)

Evaluation of thyroid hormone disruption by PFAS in WWTP influent/effluent and surface waters in the Netherlands

Peter A. Behnisch[1], Harrie Besselink[1], Dorien ten Hulscher[2], Anne Jans[2], Carmen Hogendoorn[2], John Hin[2], Carolien van der Wielen[1], Abraham Brouwer[1]

[1]BioDetection Systems BV, Science Park 406, 1098 XH, Amsterdam, the Netherlands,
[2]Rijkswaterstaat Water, Verkeer en Leefomgeving (RWS-WVL), Griffioenlaan 2, 3526 LA, Utrecht, the Netherlands.

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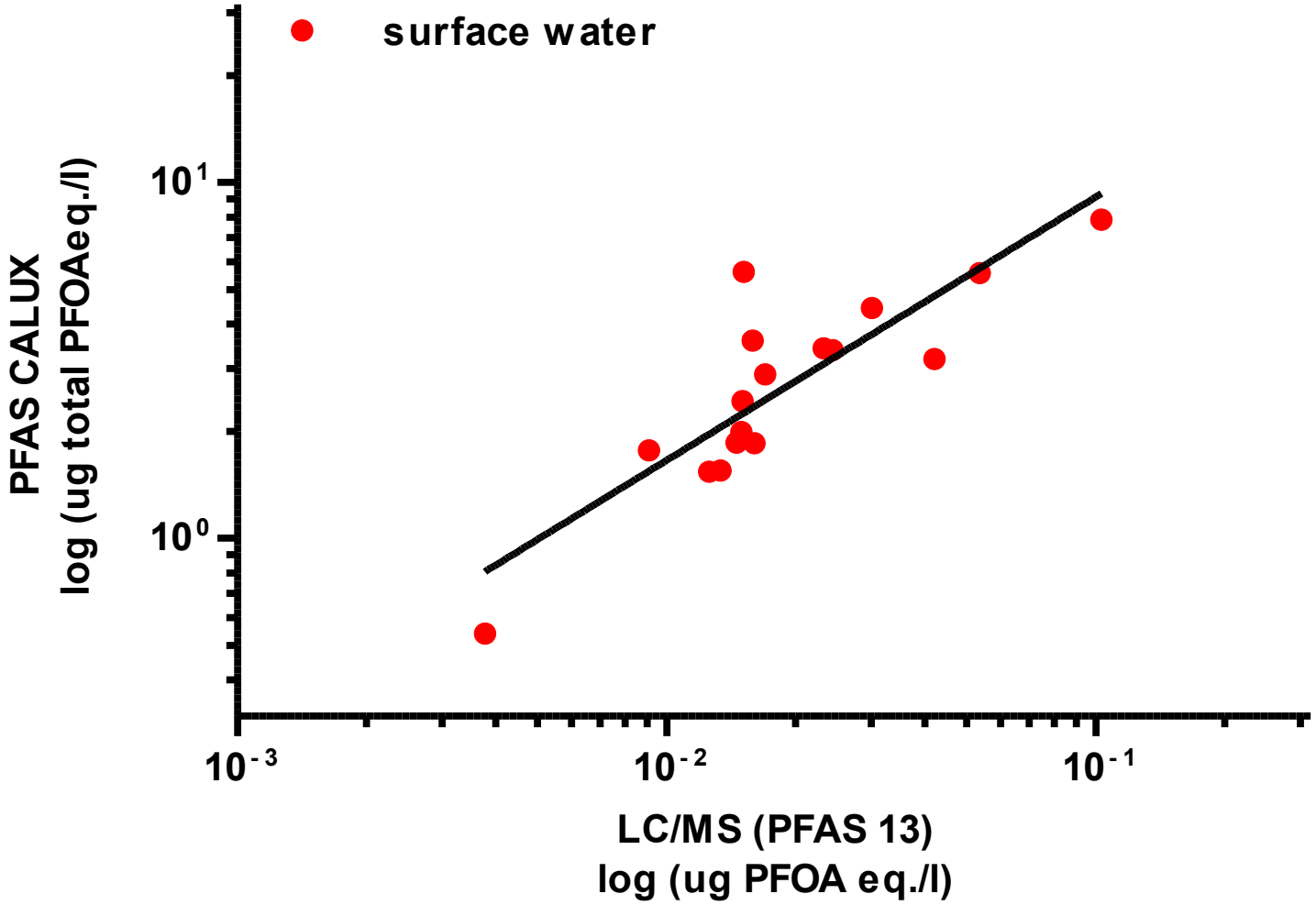
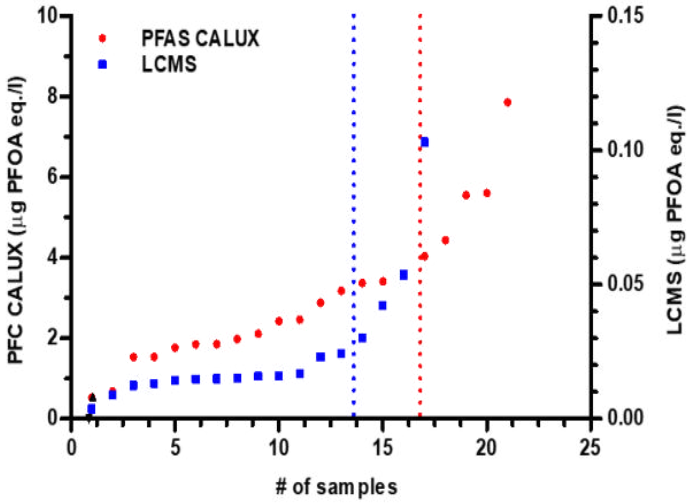


Oberflächenwasser (NL): PFAS CALUX (Sum in vitro PFAS) vs LC/MS (13 PFAS)



	PFAS CALUX (ug total PFOA eq./l)	LC/MS (PFAS 13) (ug PFOA eq./l)
5% Percentile	0.56	0.0038
80% Percentile	4.3	0.035

Scientific Committee on Health, Environmental and Emerging Risks
SCHEER

Scientific Opinion on "Draft Environmental Quality Standards for Priority Substances under the Water Framework Directive"

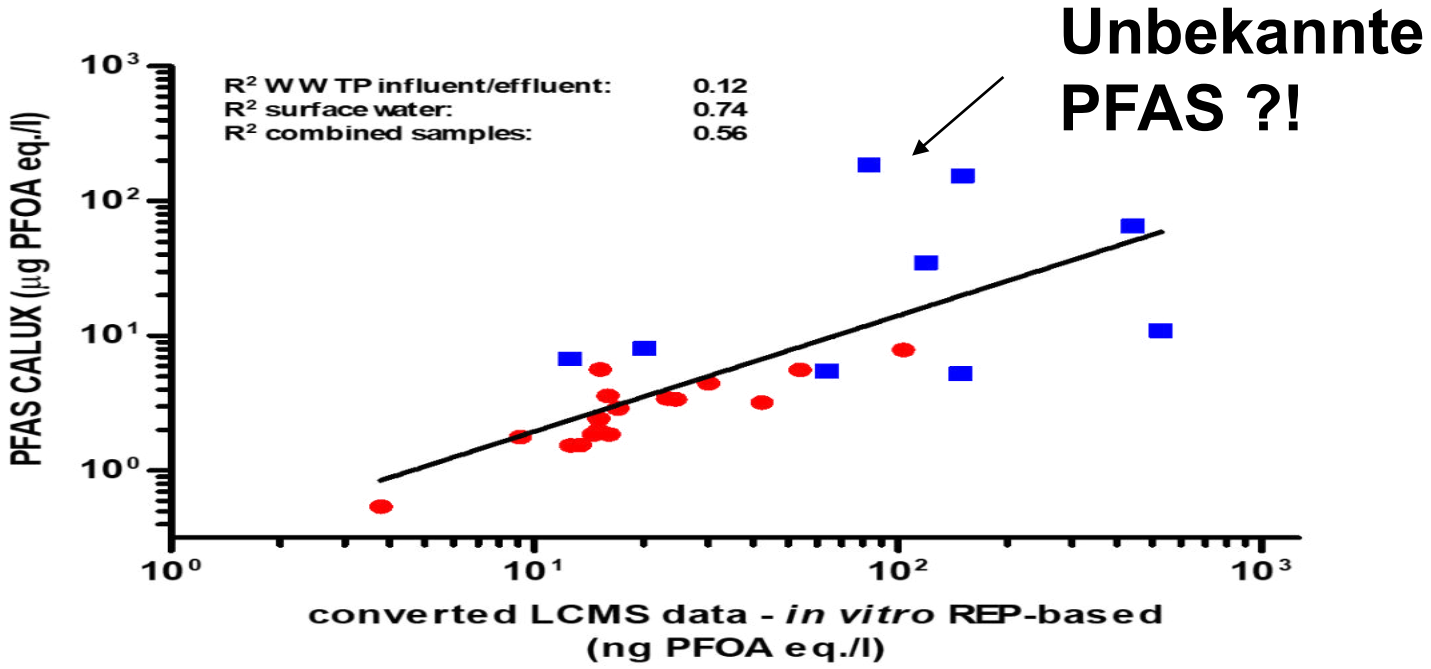
PFAS

Scientific Committees

The SCHEER adopted this document via written procedure on 18 August 2022

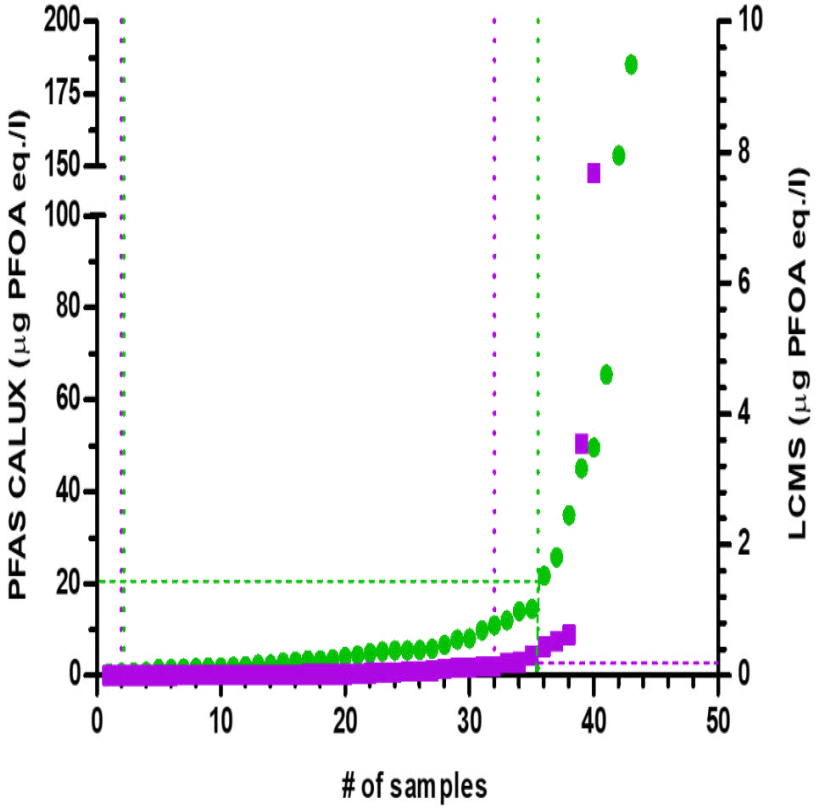
Oberflächen und Abfall-Wasser
PFAS CALUX (Summe in vitro PFAS) vs LCMS (13 PFAS)

Rot =Oberflächenwasser
Blau = Kläranlagenabwasser



Oberflächen und Abfall-Wasser
PFAS CALUX (Sum in vitro PFAS) vs LCMS (13 PFAS)

Summe PFOA equivalente
Lila = LC/MS/MS
Grün = PFAS CALUX



Percentile (%)	PFAS CALUX (ug PFOA eq./l water)	LCMS (PFAS 13; upperbound) (ug PFOA eq./l water)
5	0.71	0.0094
80	22	0.19

PFOA-Äquivalente für Oberflächenwasser und Abwasser:

Um diese PFAS-EQ-Gesamtlücken zu füllen, müssen mehr PFAS durch chemische Analyse analysiert und mehr In-vitro-Potenzfaktoren für diese PFAS-Verbindungen ermittelt werden.

In der Kürze liegt die Würze
…warum toxische Profile in Wasser ?

- **Wirkungs- und Summen-bezogen**
- **Ethisch (kein Tierversuch, NAM)**
- **Relevant für Mensch (Menschliche Zellen)**
- **Luminometer-basiert**
- **Relevant für Green Deal & Zero-Pollution & Toxic-freien Strategien**

Herzlichen Dank für Ihr freundliches Interesse!

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