Introduction:

the need to monitor dioxins in foods

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Exposure and risk assessment

Parecelcus

nichts ohn' Gift; allein die Dosis macht, das ein Ding kein Gift ist.

"All things are poison and nothing is without poison, only the dose permits something not to be poisonous."

“The dose makes the poison.”

Just because it is measurable does not mean it is toxic

An innocuous substance may be toxic at the wrong dose!

Theophrastus Philippus Aureolus Bombastus von Hohenheim (Parecelsus)

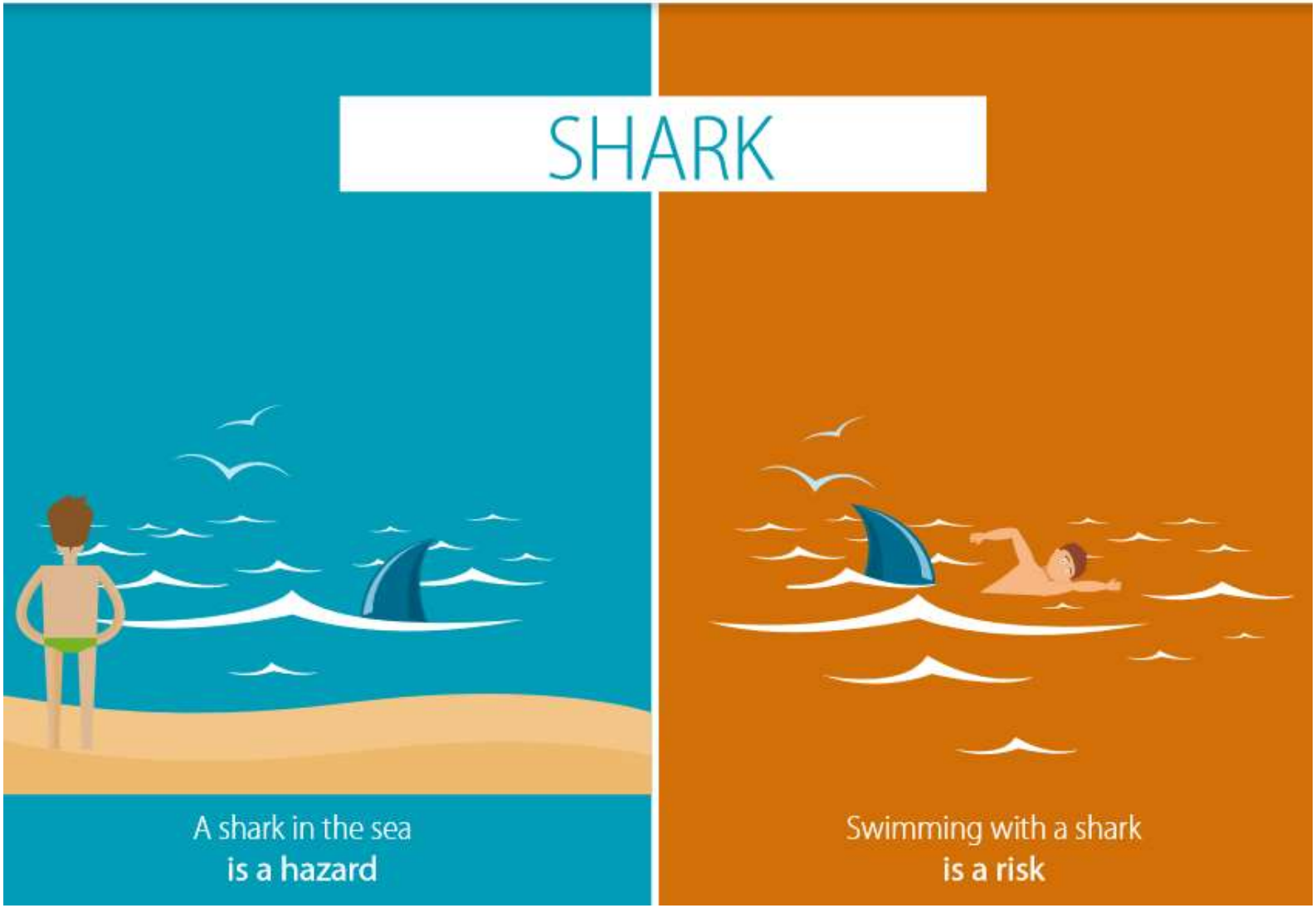
Born 11 Nov or 17 Dec 1493 Finsiedeln, Switzerland; Died 24 Sep 1541

Hazard vs. Risk

A Hazard is something that has the **potential to harm you**

Risk is the **likelihood** of a hazard **causing harm**

SHARK



A shark in the sea **is a hazard**

Swimming with a shark **is a risk**

Risk assessment and risk management

Risk Assessment is a scientific evidence based process that relies on:

- Reliable estimate of **occurrence** and consumption (exposure)
- Hazard characterisation (toxicity)

Risk management takes into account economic and political factors and covers:

- Incident management
- Implementation of regulations and control systems

Division of Responsibilities

scientific risk assessment of food in Europe

DG SANTE is responsible for risk management (setting limits, authorisations, incident response etc)

UK – Food Standards Agency is responsible for both risk assessment and risk management

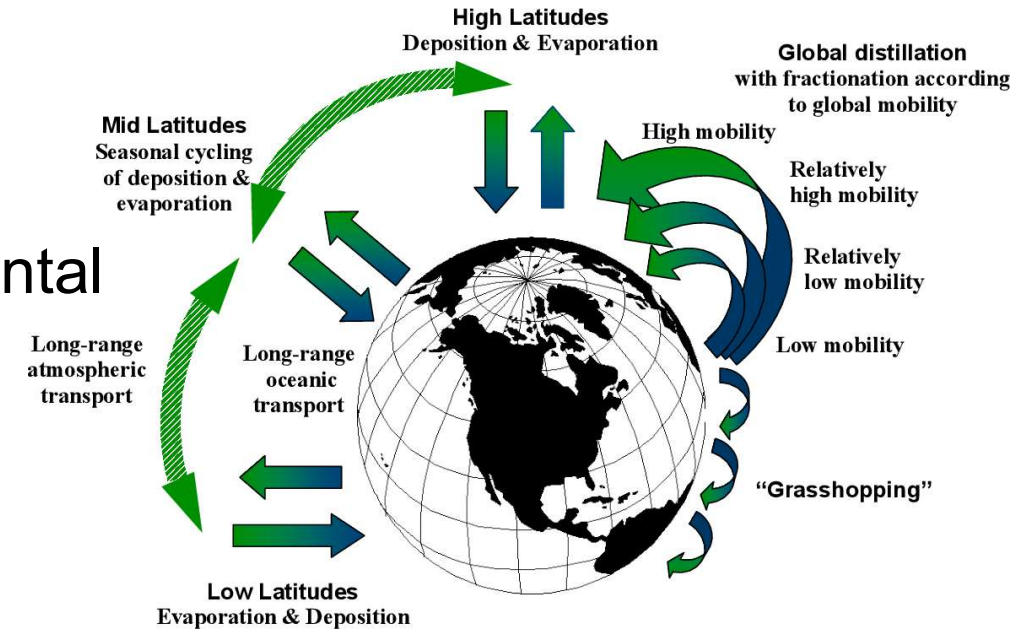
What are ‘Dioxins’

Environmental contaminants

‘Stockholm’ POPs

Persistent; Bioaccumulative; Toxic

- Concentrate at higher trophic levels
- Food can be a useful indicator of environmental contamination – an ‘integrative matrix’



Persistent organic pollutants (POPs)

Identified by Stockholm convention www.pops.int

The Stockholm Convention on POPs was adopted on 22 May 2001 in Stockholm, Sweden. The Convention entered into force on 17 May 2004.

Global treaty to protect human health and the environment from chemicals that remain intact in the environment for long periods, become widely distributed geographically, accumulate in the fatty tissue of humans and wildlife, and have harmful impacts on human health or on the environment.

Exposure to POPs can lead to serious health effects including certain cancers, birth defects, dysfunctional immune and reproductive systems, greater susceptibility to disease and damages to the central and peripheral nervous systems.

Given their long range transport, no one government acting alone can protect its citizens or its environment from POPs.

Parties required to take measures to eliminate or reduce the release of POPs into the environment.

Environmental (industrial) contaminants

Persistent organic pollutants e.g. dioxins produced from non-optimal incineration or as by-products from orgno-chlorine chemicals

Heavy metals – lead, arsenic cadmium etc (not organic compounds)

Radionuclides from nuclear power plants etc (not organic compounds)

The ‘dirty dozen’

Initially, covered twelve POPs recognized as causing adverse effects on humans and the ecosystem:

Pesticides: aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, toxaphene;

Industrial chemicals: hexachlorobenzene, polychlorinated biphenyls (PCBs); and

By-products: hexachlorobenzene; polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/PCDF), and PCBs.

New POPs

16 newly chemicals added to the Stockholm Convention. Include Dicofol, PFOA, PFOS, DecaBDE, SCCP, HCBD. Chemicals under review include PFHxS, Dechloran Plus and methoxychlor.

Formation of dioxins

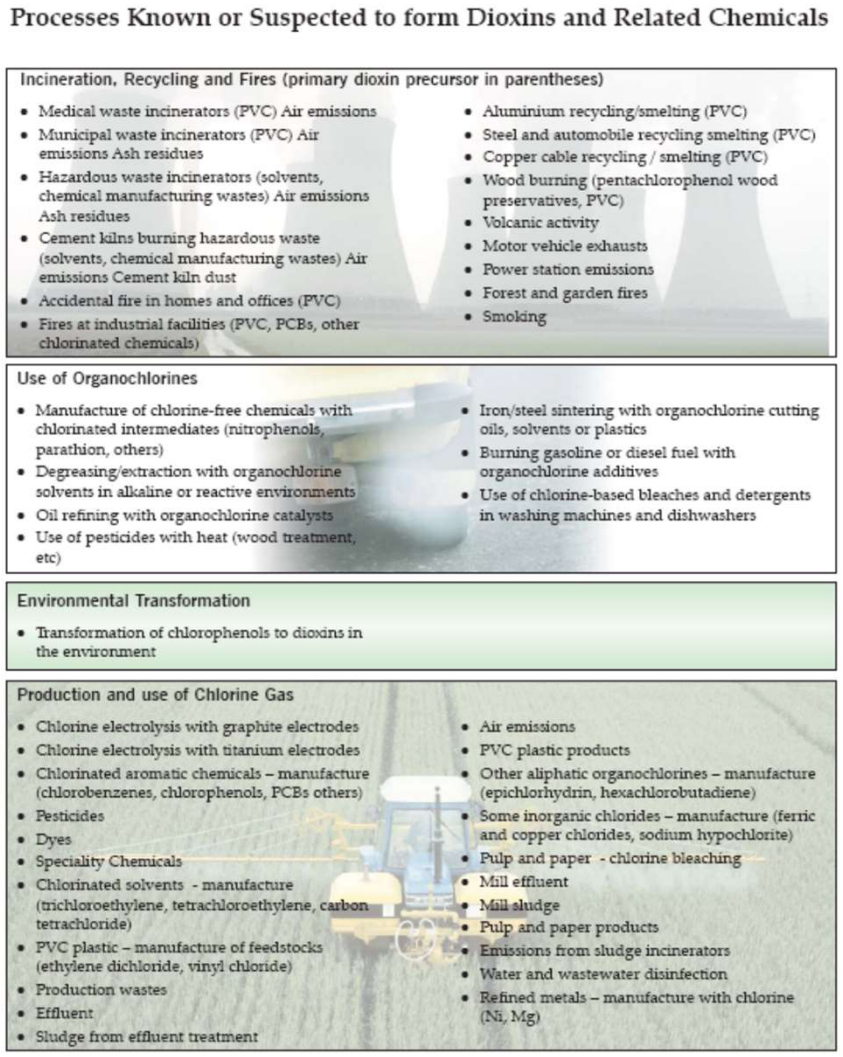
Incineration, recycling and fires
- Incomplete combustion
- PVC etc fires
- Metal reclamation / steel production

Use of organochlorines
- By-products in chlorinated herbicides
- Pentachlorophenol

Environmental transformation
- Chlorophenols

Production and use of chlorine
- Bleaching

Present in some inorganic clays



Dioxins

[Polychlorinated dibenzo-p-dioxins (PCDD) and Polychlorinated dibenzofurans (PCDF)]

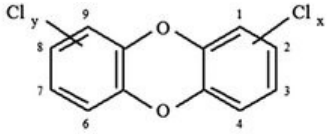
Produced unintentionally due to incomplete combustion, as well during the manufacture of pesticides and other chlorinated substances.

emitted mostly from the burning of waste, and hazardous waste, and also from automobile emissions, peat, coal, and wood.

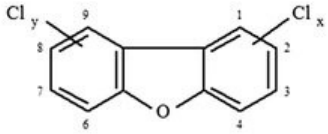
There are 75 different PCDDs, and 135 different PCDFs, of which 12 are considered to be of most concern. Dioxins have been associated with a number of adverse effects in humans, including immune and enzyme disorders and chloracne, and they are classified as possible human carcinogens. Laboratory animals given dioxins suffered a variety of effects, including an increase in birth defects and stillbirths. Fish exposed to these substances died shortly after the exposure ended.

Food (particularly from animals) is the major source of exposure for humans.

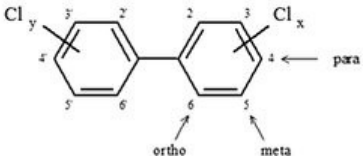
PCDD



PCDF



PCB



Polychlorinated biphenyls (PCBs)

Were used in industry as heat exchange fluids, in electric transformers and capacitors, and as additives in paint, carbonless copy paper, and plastics.

Of the 209 different PCBs, 13 exhibit a dioxin-like toxicity. Their persistence in the environment corresponds to the degree of chlorination, and half-lives can vary from 10 days to one-and-a-half years.

PCBs are toxic to fish, killing them at higher doses and causing spawning failures at lower doses. Associated with reproductive failure and suppression of the immune system in various wild animals, such as seals and mink.

Large numbers of people have been exposed to PCBs through food contamination.

Consumption of PCB-contaminated rice oil in Japan in 1968 and in Taiwan in 1979 caused pigmentation of nails and mucous membranes and swelling of the eyelids, along with fatigue, nausea, and vomiting.

Due to the persistence of PCBs in their mothers' bodies, children born up to seven years after the Taiwan incident showed developmental delays and behavioural problems.

Similarly, children of mothers who ate large amounts of contaminated fish from Lake Michigan showed poorer short-term memory function. PCBs also suppress the human immune system and are listed as probable human carcinogens.

Toxicology

Still not fully defined or understood

- Carcinogen
- Teratogen
- Fetotoxic
- Cognitive effects
- Immune system effects
- Reproductive effects
- Endocrine disrupter

Other compounds with similar ‘additive’ toxic effects, e.g. brominated compounds?

Dioxin’ incidents

- Agent Orange (Viet Nam)
- Seveso (Italy)
- Yusho (Japan)
- Yucheng (Taiwan)
- Times beach (USA)
- Binghampton (USA)

Incidents with PCDD/Fs and dl-PCBs in the feed and food chain, the sources and an indication of the highest levels reported. Also the discovery and the labora indicated.

Country	Year	Source	Highest levels[a] (food in pg TEQ/g fat, feed (ingredients) in ng TEQ/kg)	Discovered by	Reference
US	1957	Feed fat, cow hides, chlorophenols		Effects, authorities	Schmittle et al., 1958 et al., 1958, Higgenb et al., 1968, Firestone
US	1969	Water, chlorophenols		Effects	Firestone, 1973
Japan	1968	Rice oil; PCB-oil		Effects	Kuratsune et al., 197
Taiwan	1979	Rice oil; PCB-oil		Effects	Hsu et al., 1985
Netherlands	1989	Waste incinerators	Grass; milk 14	Authorities	Liem et al., 1991
US	1996	Ball clay, feed, chickens, cat fish	Feed 61, cat fish 43 (lw), eggs	Authorities	Cooper et al. 1995, H et al., 1999, Ferrario 2000
Germany	1997	Brazilian citrus pulp, lime, PVC	Pulp 10; milk 4.9; beef 4.3	Authorities	Malisch, 2000, Carval 2002, Malisch & Kotz
Belgium	1999	Feed fat, PCB-oil	Feed 2000; eggs 2000; chicken meat 3000; pork	Effects, private	Bernard et al., 1999, et al., 2001, De Bont Traag et al., 2006
Austria	1999	Kaolinic clay	Clay 1132	Authorities	Jobst & Aldag, 2000
Germany, Spain	2000	Choline chloride, sawdust, PCP	Choline chloride 122, feed 0.34	Authorities	Llerena et al., 2003
Italy	2001–2004	Mozzarella, waste incineration	Mozzarella (buffalo) 21, sheep milk 30	Authorities	Diletti et al., 2008
Germany	2003	Dried bakery waste, waste wood	Bakery waste 12, pork 2.2	Private	Hoogenboom et al., 2
Italy	2004	Wood shavings, PCP	Wood shavings 51, eggs 88	Authorities	Diletti et al., 2005, Bi 2009
Netherlands	2004	Potato peels, kaolinic clay	Peels 44, Milk 20	Private	Hoogenboom et al., 2
Netherlands	2006	Feed fat, gelatine, HCl	Feed fat 440, feed 8, pork 3	Authorities	Hoogenboom et al., 2
Switzerland	2007	Guar gum	Guar gum 480	Private	Wahl et al., 2008
Chile	2008	Feed, zinc oxide	Zinc oxide 17,148; feed 14, pork 37	Authorities	Kim et al., 2011
Ireland	2008	Dried bakery waste, PCBs in fuel	Bakery waste 8500; Pork 600, Beef, 1000 pig liver 16,000	Private, authorities	Heres et al., 2010, Th 2012, Marnane, 2012
Netherlands, Germany	2010	Organic corn, unknown	Corn 2.7; eggs 11	Private, authorities	RASFF 2010.0519
Germany	2010	Industrial fatty acids, chlorophenols	Feed 1.5; eggs, meat	Private	Abraham et al., 2011

Fera ‘dioxins’ History

Laboratory established 1985 – 1st in UK (MAFF FSL)

Human milk – background exposure (WHO)

UK environmental background – herbage survey (with HMIP) – soil survey from same locations (UEA)

Cows’ milk

Bolsover – milk, herbage, human blood (multi-departmental response)

UK Food surveys and applied research projects

Brazilian citrus pellet problem – animal feed / production issue

Belgium – animal feed / food production crisis

FMD ‘pyres’

‘Emerging contaminants

Toxic Equivalence (TEQ)

- 29 ‘toxic’ congeners assigned toxic equivalency factor related to 2,3,7,8-TCDD (TEF)
- TEFs given to nearest half order of magnitude - 1, 0.3, 0.1, 0.03…….0.00001

$$TEQ = \sum_{n_1} [PCDD_i \times TEF_i] + \sum_{n_2} [PCDF_i \times TEF_i] + \sum_{n_3} [PCB_i \times TEF_i]$$

TEFs for PCDD/Fs and PCBs

Congener	TEF value	Congener	TEF value
Dibenzo-p-dioxins („PCDDs“)		Dioxin-like“ PCBs: **Non-ortho-PCBs + Monoortho-PCBs**	
2,3,7,8-TCDD	1		
1,2,3,7,8-PeCDD	1		
1,2,3,4,7,8-HxCDD	0.1	**Non-ortho PCBs**	
1,2,3,6,7,8-HxCDD	0.1	PCB 77	0.0001
1,2,3,7,8,9-HxCDD	0.1	PCB 81	0.0003
1,2,3,4,6,7,8-HpCDD	0.01	PCB 126	0.1
OCDD	0.0003	PCB 169	0.03
Dibenzofurans („PCDFs“)		***Mono-ortho PCBs***	
2,3,7,8-TCDF	0.1	PCB 105	0.00003
1,2,3,7,8-PeCDF	0.03	PCB 114	0.00003
2,3,4,7,8-PeCDF	0.3	PCB 118	0.00003
1,2,3,4,7,8-HxCDF	0.1	PCB 123	0.00003
1,2,3,6,7,8-HxCDF	0.1	PCB 156	0.00003
1,2,3,7,8,9-HxCDF	0.1	PCB 157	0.00003
2,3,4,6,7,8-HxCDF	0.1	PCB 167	0.00003
1,2,3,4,6,7,8-HpCDF	0.01	PCB 189	0.00003
1,2,3,4,7,8,9-HpCDF	0.01		
OCDF	0.0003		

Abbreviations used: “T“ = tetra; “Pe“ = penta; ”Hx” = hexa; “Hp” = hepta; “O” = octa; “CDD” = chlorodibenzodioxin; “CDF” = chlorodibenzofuran; “CB“ = chlorobiphenyl.

Health based guidance values

Exposure level at which there is no appreciable health risk, such as a tolerable daily intake (TDI)

Takes into account all toxicological information available, including studies on humans, experimental animals, cell- and other systems

UK:	2 pg/kg bw/day
EU (SCF):	14 pg/kg bw/week
WHO/JECFA:	70 pg/kg bw/month
EFSA (2018):	**2 pg/kg bw / week**.

Risk characterisation

Exposure levels for different population groups are compared with the TWI or ARfD

If exposure is lower, there is no appreciable risk

Exceedance does not imply health risks are present, since the TWI etc is not a threshold for toxic effect, but aims to be protective even for the most sensitive groups.

The risk assessment should take into account the nature of adverse effects, at lowest doses, and the magnitude and duration of the exceedance

Limits and enforcement

Maximum levels for various food matrices are laid down in Regulation (EC) No 1881/2006.

Additional action levels are defined (Recommendation 2013/711/EU) to serve as early warning tool in order to identify possible contamination sources.

Analysis using HRMS

Time consuming (2-3 weeks minimum)

High capital (HRGC-HRMS cost £ 300 000) and infrastructure requirements

High analytical skill requirement

Labour intensive

Analysis using MSMS

Greater versatility and flexibility

Less infrastructure required

Less sensitive but sufficient for compliance testing

Quality control

Chlorine containing - Molecular cluster

13C internal standards

Further post extraction internal standards for recovery estimate

Use of reference materials

Over 2000 measurements or calculations to obtain TEQ for a sample!

5000 if measurement uncertainty included!

‘legacy’ vs ‘current use’ POPs

Legacy	Current use
PCBs	BFRs
Toxaphene	PFOS and organo-fluorine compounds
OC pesticides	OC pesticides
PCNs	
Dioxins	nanoparticles
	????????????

‘Emerging’ contaminants

Established	Emerging
PCBs	Some BFRs
Toxaphene	Brominated dioxins
(PAHs)	PFOS and other organo-fluorines
Dioxins	Breakdown products
PBDEs	nanoparticles
PCNs	

Brominated Flame Retardants

Used in furniture and electronics to prevent fires

Five main classes of BFRs:

- Polybrominated diphenyl ethers (PBDEs) – plastics, textiles, electronic castings, circuitry.
- Hexabromocyclododecanes (HBCDDs) – thermal insulation in the building industry.
- Tetrabromobisphenol A (TBBPA) and other phenols – printed circuit boards, thermoplastics (mainly in TVs).
- Polybrominated biphenyls (PBBs) – consumer appliances, textiles, plastic foams.
- Other brominated flame retardants.

The use of certain BFRs is banned or restricted in some countries

due to their persistence in the environment there are still concerns about the risks these chemicals pose to public health.

BFR-treated products, whether in use or waste, leach BFRs into the environment and contaminate the air, soil and water. These contaminants may then enter the food chain where they mainly occur in food of animal origin, such as fish, meat, milk and derived products.

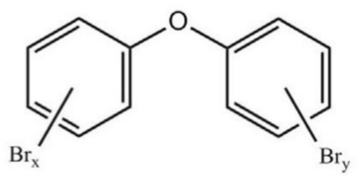
Types of BFRs

Reactive BFRs – Covalently bonded to polymer

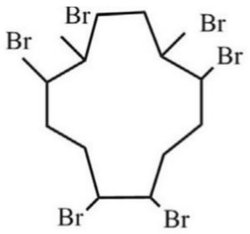
- Tetrabromobisphenol-A
- Tetrabromophthalic Anhydride

Additive Flame Retardants – polymer

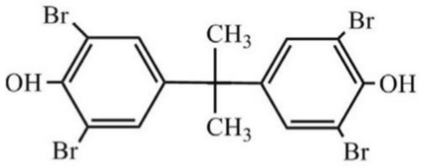
- Polybrominated diphenyl ethers
- Polybrominated biphenyls
- Hexabromocyclododecane



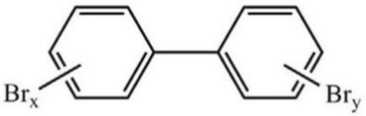
PBDE



HBCD



TBBPA



PBB

Terminology

Legacy or Established FRs (BFRs/CFRs/PFRs) are chemicals which are extensively documented regarding production and use as FRs, chemistry, fate, exposures, environment and health issues (i.e. (eco-) toxicity and/or human health effects).

Emerging FRs (BFRs/CFRs/PFRs) are chemicals which are documented regarding production and use as FRs that have been shown to occur/ distribute to the environment and/or wildlife, humans or other biological matrices.

Novel FRs (BFRs/CFRs/PFRs) are chemicals which are documented as potential FRs that have been shown to be present in materials or products.

Potential FRs (BFRs/CFRs/PFRs) are chemicals reported to have applications as FRs (e.g. in patents).

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Review

A novel abbreviation standard for organobromine, organochlorine and organophosphorus flame retardants and some characteristics of the chemicals

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ABSTRACT

Ever since the interest in organic environmental contaminants first emerged 50 years ago, there has been a need to present discussion of such chemicals and their transformation products using simple abbreviations so as to avoid the repetitive use of long chemical names. As the number of chemicals of concern has increased, the number of abbreviations has also increased dramatically, sometimes resulting in the use of different abbreviations for the same chemical. In this article, we propose abbreviations for flame retardants (FRs) substituted with bromine or chlorine atoms or including a functional group containing phosphorus, i.e. BFRs, CFRs and PFRs, respectively. Due to the large number of halogenated and organophosphorus FRs, it has become increasingly important to develop a strategy for abbreviating the chemical names of FRs. In this paper, a two step procedure is proposed for deriving *practical abbreviations* (PRABs) for the chemicals discussed. In the first step, *structural abbreviations* (STABs) are developed using specific STAB criteria based on the FR structure. However, since several of the derived STABs are complicated and long, we propose instead the use of PRABs. These are, commonly, an extract

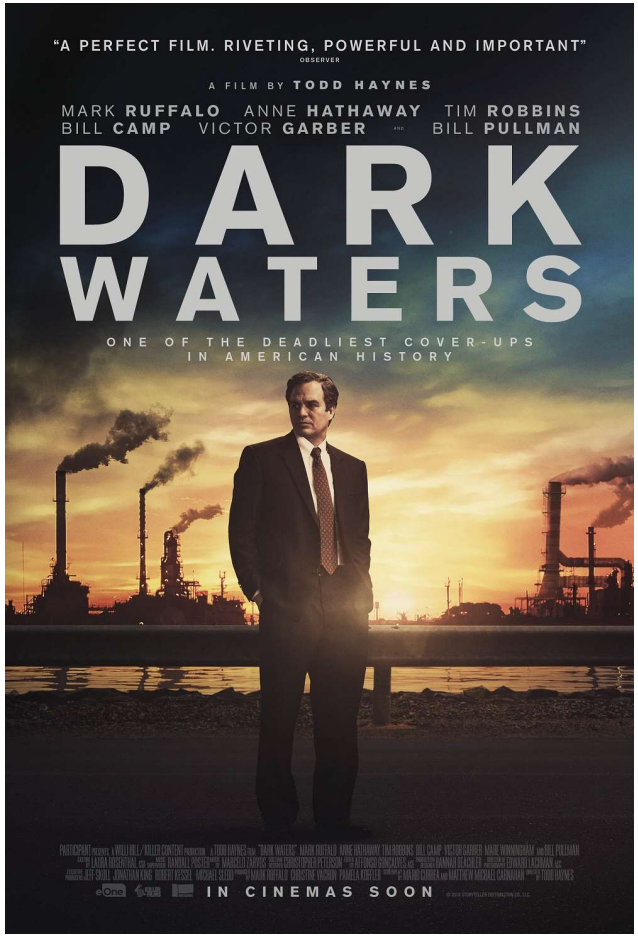
- Many potential BFRs, CFRs and PFRs have been registered (many 100s when congeners and enantiomers are considered)
- Current production volume of BFRs exceeds 200,000 tonnes/year

PFASs – per(/poly)-fluorinated alkyl substances (PFOS and PFOA)

PFAS are a group of man-made chemicals that are manufactured and used in a variety of industries around the world (e.g. textiles, household products, fire-fighting, automotive, food processing, construction, electronics).

Exposure to these chemicals may lead to adverse health effects. People can be exposed to PFAS in different ways, including food, where these substances are most often found in drinking water, fish, fruit, eggs, and egg products.

Subject of the film ‘Dark Waters’.



PFASs

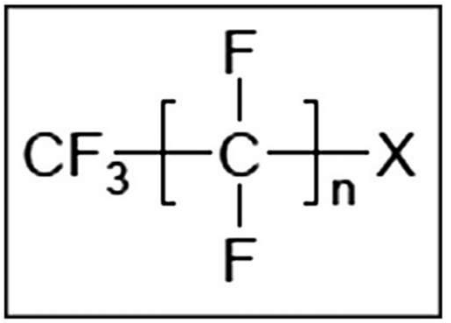
Different to other POPs - water soluble, but still bioaccumulate

Many hundreds of congeners

Found in drinking water – especially near contamination sources

Also found in fish, seafood, meat and dairy

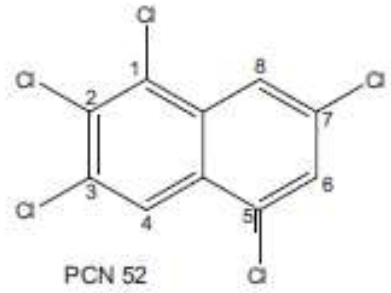
perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA) and perfluorohexane sulfonic acid (PFHxS) of most concern on basis of toxicity and exposure



Other POPs and industrial contaminants

Chlorinated paraffins - used as additives in lubricants and cutting fluids in the metal industry and are also used as flame retardants – still widely produced and used

Polychlorinated naphthalenes – no longer manufactured - mixtures containing some of congeners - uses include insulating coatings for electrical wires, wood preservatives, rubber and plastic additives, capacitor dielectrics and in lubricants



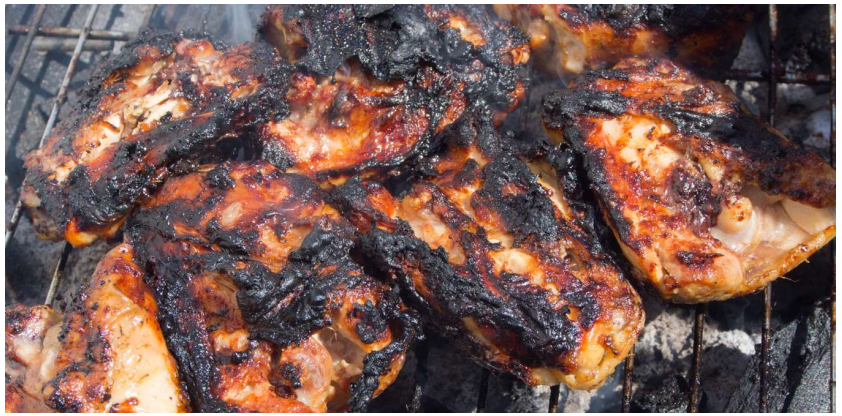
PCN 52

Processing contaminants

Heating- associated contaminants (Acrylamide, Furans, Alpha-, beta- unsaturated aldehydes, Polycyclic aromatic hydrocarbons, Heterocyclic amines, Acrolein)

Nitrosamines

(and Biogenic amines)



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Original thinking... applied

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