TCDD

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SPECIAL THEME

FOREVER CHEMICALS

- THE EFFECTS OF PFAS EXPOSURE TO LIPID HOMEOSTASIS IN HUMANS
- THE EFFECTS OF PFAS ON GENE EXPRESSION IN HUMAN HEPARG CELLS AND QIVIVE FOR PFAS HEPATOTOXICITY
- CAN WE GET RID OF PFAS?
- PFAS: WEL OF NIET BAKPAPIER?
- ORGANOHALOGENS AND OUR PERSISTENT SKI WAX PROBLEM

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Toxicologische Communicatie, Data en Documentatie

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TCDD
TOXICOLOGIE

Inhoud

TERUG NAAR INHOUD

Editorial

Dear reader,

A year ago, we reflected in the TCDD about 2020 being dominated by COVID. At that time, we were not expecting that 2021 would also be a COVID-year. We are again in a lockdown, and it can sometimes be difficult to keep positive as the end of this pandemic seems far away. Despite this, a lot of work is going on within the toxicology community and there is, in the media, attention given to topics related to the toxicity of substances. One group of substances that has recently taken over many headlines is PFAS popularly known as “forever chemicals”, which is the theme of this issue of the TCDD.

Igor Znidarsic of the Chemie Magazine summarizes the background and main issues of PFAS, Stella Fragki from RIVM updates us on the latest research on the toxicity of PFAS, and we look into options for removal of PFAS form the environment. Also in this issue, you can learn what an Environmental Health and Safety manager does from Barry Blankvoort in the ‘what’s next?’ section. Paul Scheepers from Radboud University discusses the impact of face masks on human and environmental health. Finally, there is news from the sections and the Toxafette with Annemijne van den Berg.

We hope you enjoy reading this TCDD. And we wish you a Merry Christmas and a happy 2022 that is hopefully not all about COVID. Stay healthy!

On behalf of the editorial team,

Hedwig Braakhuis

Photo by Jess Bailey on Unsplash

News from the board

Welcome to the November 2021 issue of TCDD. I hope you are all well in these challenging times of a third (or is it fourth?) lockdown. The main theme of this issue is 'forever chemicals.' When I hear the word 'forever,' I can't help but draw a parallel to the current Covid-19 situation. Will this virus be with us forever? We know that the it will very difficult to truly eliminate this virus. I hope that we can learn from the forever chemicals case in how to take bold steps to restrict and manage risks.

Despite the current Covid-related measures, we still looking forward to a 'live' NVT annual meeting and member assembly next year at the Reehorst in Ede. Due to conflicts with other important meetings, we have changed the date. Please save the new date: **May 24-25, 2022.** The regular NVT meeting for members will be on May 24, and the PhD days on May 25. One of the highlights of the annual meeting is the Joep van den Bercken prize. For all supervisors of PhD candidates who defended their thesis in 2021, please consider nominating your PhD candidate for this prize! More information will be provided in the coming months, or feel free to contact me.

I'm pleased to announce that NVT members are well represented in the board of EUROTOX, as decided at the last EUROTOX meeting. Congratulations to Paul Scheepers (member, SubCommittee Registration/ERT), Martin van den Berg (second term as chair of the Education SubCommittee), Theo de Kok (treasurer, Executive Committee (EC)) and Manon Beekhuijzen (member, EC). Thank you for representing our Dutch viewpoints at the European level! Regarding EUROTOX, a call has been launched for the nomination of potential candidates for EUROTOX Awards (EUROTOX Merit Award and EUROTOX Lecture Award) and subcommittees. Please let us know the NVT board know if you have suggestions for nominees. Also, a reminder to you all that it is now possible to register and submit abstracts for the International Congress of Toxicology (ICT2022) in Maastricht, September 18-22, 2022, which is hosted by NVT and jointly organised with the International Union of Toxicology (IUTOX) and the European Society of Toxicology (EUROTOX). As mentioned on the site, ICT2022 'unites the best of toxicological scientists worldwide in the historical city of Maastricht.'

Finally, we are looking for new web editors to update and maintain the NVT website (www.toxicologie.nl). The website is made in Wordpress, which is a pretty accessible system. Basic computer skills are enough to help with this. Knowledge of programming or anything like that is absolutely not necessary. If you are interested, let us know! Many thanks to Floris Groothuis for his contribution to updating and maintaining the NVT website over the past years.

On behalf of the entire NVT board: happy holidays, and stay well!

Juliette Legler

president NVT

The Annual NVT Meeting
'Green Deal - Toxicology matter(s)'

The European Green Deal sets the EU on a course to become a sustainable climate neutral and circular economy by 2050. An important part of the Green Deal is the Chemicals Strategy for Sustainability. It is a first step towards the EU's zero pollution ambition for a "toxic-free" environment. How will this strategy impact the field of toxicology? And vice versa? During the annual scientific meeting of the NVT several important aspects of the Chemicals Strategy will be discussed; Safe-by-design, next generation risk assessment, non-standard endpoints, and the policy-science interface. As toxicology matters to all, every toxicology sector will be covered by tackling these important aspects.

All participants are encouraged to submit an abstract to present their research via a pitch or poster (instructions will follow).

We are happy to invite you to the meeting at Congrescentrum de Reehorst, Ede. The new date for the 'NVT-member' day, including the annual NVT business meeting, is **May 24th**. The 'young scientists'-day is scheduled on **May 25th**. Keep an eye on the Annual Meeting website (https://toxicologie.nl/jv2022/) as more information will come.

President NVT
Juliette Legler

Organizing committee
Annemijne van den Berg, Joyce van der Heijden, Merel van der Most, Lennart van Melis, Nienke Ruijter, Tessa van Tongeren, Fabian Wagenaars, Hans Bouwmeester, Paul Jennings, Martijn Rooseboom, Peter Theunissen

RISK ASSESSMENT

- Online - Autumn symposium: Mixture Toxicity

On October 5th 2021, an online autumn symposium with the title “Mixture Toxicity” was organized. The meeting was attended by approximately 100 participants. On the program were 5 speakers. Harry Buist from the Risk Assessment Section chaired the meeting.

Theo Vermeire – General introduction
Theo provided an introduction to mixture toxicity, hazard and risk assessment, explaining definitions and currently ongoing initiatives worldwide. Theo provided further information on the different available risk assessment approaches, such as the assessment approaches of SCHEER and US-EPA and the WHO framework for risk assessment of mixtures. Attention was paid to the problem formulation with regard to both exposure and hazard assessment. In a recent publication of Herzler (2021) further information is provided on which mixtures should be considered, e.g. substance which act together, individual substances of high concern, as not all mixtures will be considered for mixture risk assessment and risk management approaches.

Bruno Dujardin (EFSA) - Combined exposure to multiple chemicals - EFSA’s recent achievements and future perspectives
Bruno spoke about ongoing initiatives and activities on mixture toxicity within EFSA, especially for non-intentional exposure to mixtures. Initially, the focus was at pesticides, with the Cumulative Assessment Groups (CAGs) for thyroid and central nervous system (CNS) effects. In parallel, a guidance on risk assessment of combined exposure to multiple compounds was also issued.

Cumulative risk assessments were performed (2019-2020) retrospectively with focus on acute and chronic exposure of the central nervous system and chronic exposure of the thyroid. It included a hazard part (identification, characterization, cumulative risk assessment groups), an exposure part, based on market sampling (120.000 samples) which were combined with consumption data (20.000 subjects), and resulted in a risk assessment part with an uncertainty analysis. Main findings were: 1) the outcome is driven by a limited number of compounds 2) highest exposure was often due to 1 pesticide, 3) model estimations are very conservative, leading to an overall conclusion that the cumulative exposure to pesticides that have chronic/acute thyroid/CNS effects does not exceed the thresholds of regulatory consideration.

Future actions on the cumulative risk assessment of pesticides are scheduled by EFSA, in cooperation with DG Santé, e.g. prioritization of new CAGs. Furthermore, by 2030 EFSA and partners should be equipped for implementation for risk assessment of multiple chemicals, with a focus on dietary and non-dietary exposure for human health, with a stepwise implementation for dietary and aggregate exposure to pesticides and chemical in general, and with further development of methods (harmonized grouping criteria, OMICs data, aggregate exposure) and tools (open source).
An EFSA guidance document, on hazard driven criteria and prioritization methods, is expected to be finalized by December 2021.

Stephanie Melching – Kollmuss (BASF) - Experiences with cumulative risk assessments in the agrochemical industry and views
Stephanie shared the experience of Croplife on the cumulative risk assessment addressing different compounds (within the group of pesticides), products and applications. As an introduction to the EU approach, Stephanie mentioned that initial work involved the establishment of CAGs to cover all relevant target organs, together with performing probabilistic exposure and risk assessments. As also presented by Bruno, from the retrospective cumulative risk assessments, the thresholds for regulatory consideration were not reached, after hazard and exposure-based refinements. However, future work is required, as is indicated in the EFSA/DG Santé action plan. This would also include prioritization with regard to hazard ➔

assessment (relevance CAGs, number of compounds in CAGs, dose at which the effect occurs, excluding compounds with low individual hazard quotients) and exposure assessment (realistic retrospective exposure, focus on major crops and uses). Croplife looked at specific groups, e.g. liver (with a focus on primary lesion, rather than the secondary lesions) or the reproduction/ developmental CAGs. In addition, prioritization based on exposure is required. In order to avoid extensive refinements in mixture risk assessment, it is proposed to refine upfront by e.g. apply more stringent criteria to substance for inclusion into CAGs, consider only compounds for which the common toxic effect is very close to effect driving the reference value, use realistic exposure scenarios (e.g. maximum market share), monitoring background exposure, etc. Future challenges are aggregate exposures, availability of open data bases and risk management.

Lonneke van Leeuwen (RIVM, bureau REACH) – The EU Chemicals Strategy for sustainability towards a toxic-free environment: A Mixture Assessment Factor under REACH
Lonneke presented on the EU Chemical Strategy for Sustainability (CSS) and recent ongoing work on the Mixture Assessment Factor (MAF) with a focus on the environment.

2009 is taken as a starting point with the Kortenkamp 'State of the art report on mixture toxicity'. It concludes an assessment can be done, but should it also be regulated? In 2016 the RIVM published a thought starter on this topic. This report introduced a data driven mixture assessment factor (MAF) for the environment, and indicated that further work was needed to quantify a MAF. In 2020 the EU CSS was published describing a route to a toxic free environment with the goal to better protect human health and the environment and boost innovation. One of the strategic priorities to achieve this is to build a stronger EU legal framework to deal with mixtures. The focus is on unintentional mixtures.

In 2021 the RIVM has a publication in preparation that uses monitoring data for EU surface waters to identify trends in number of chemicals responsible for toxic pressure due to cumulative (environmental) exposure.

The first outcomes show time-place combination where in most situations 1 or 2 chemicals are present. There are only 376 time-place locations with more than 25 substances present. Further, it was observed that a large portion of the toxic pressure on freshwater bodies (> 90%), is caused by 20% of the chemicals. The chemicals that cause the issues are different between the monitoring locations. The current monitoring data shows that not all surface waters in the EU are properly protected. A general reduction of the RCR for single substances to 0.33 leads to a large improvement of the protection of EU surface waters.

RIVM will further investigate whether the same observations can be made based on a wider set of freshwater modelling data.

Annette Wilschut (DSM) – Mixed feelings
Annette gave us a warming up for the discussion on the proposal for a Mixture Assessment Factor (MAF). Industry is recognizing the issue of combined exposure, however, is questioning whether the MAF is the right solution. How to balance the aim and the impact of the measure? Will the MAF solve the issue (e.g., legacy chemicals)? Is it proportional & targeted (e.g., via other targeted frameworks/permits)? What is the scientific basis (i.e., more insight in environmental compared to human risk)? How will it be implemented (e.g., prioritization, one-fits-all solution)? According to Annette, the complexity of the situation does not warrant a generic MAF. A set of targeted science-based solutions is the best way forward.

Discussion
There was a lively discussion from all areas of the playing field with experts highlighting the pros and cons of a generic MAF:

- *Risk management has been trying to handle this for 30 years. When does the precautionary principle take over from science-based solutions?*
- *Only a few chemicals determine the effects, the balance does not seem right in this respect.*
- *Is there really an issue? Let's target the active substances.*
- *Would the focus on better exposure and mechanistic data (and making this data publicly available) give us the opportunity for a more targeted approach to come to the critical scenarios and protect human health and the environment?*

Diverging opinions were expressed. In the end it is up to policy makers to decide on the best approach in the coming years. Will this be a more general precautionary approach or a science-based data driven approach in the end … The future will tell!

The presentations can be found on the NVT website (Autumn symposium: Mixture Toxicity - Nederlandse Vereniging voor Toxicologie).

TERUG NAAR INHOUD

ARBEIDSTOXICOLOGIE

Vooraankondiging **Middagsymposium Groepsaanpak van stoffen**

Op donderdag **10 maart 2022** organiseert de sectie arbeidstoxicologie samen met de Contactgroep Gezondheid en Chemie (CGC) een voorjaarsbijeenkomst. Het onderwerp is: Groepsaanpak van stoffen voor de hazard- en risicobeoordeling op de werkplek. Afhankelijk van de situatie op dat moment wordt de bijeenkomst fysiek (in Eindhoven) of digitaal georganiseerd.

Om de blootstelling aan schadelijke stoffen op de werkplek te reguleren kan worden gekozen voor een groepsaanpak. Voorbeelden hiervan zijn te vinden bij de restricties van CMR-stoffen (carcinogene, mutagene en reproductietoxische stoffen) in REACH en CLP, en bij wettelijk vastgestelde grenswaarden voor bijvoorbeeld PAK's en cadmiumverbindingen. Het definiëren van groepen stoffen blijkt echter een uitdaging en zo'n groepsaanpak wordt in de praktijk nog maar weinig toegepast. Dit symposium is bedoeld om arbo-professionals (toxicologen, arbeidshygiënisten, bedrijfsartsen) inzicht te geven in de laatste ontwikkelingen door stil te staan bij wat onder een groepsaanpak wordt verstaan, wat de barrières zijn om het in de praktijk toe te passen, wat de wetenschappelijke en wettelijke mogelijkheden zijn voor het groeperen van stoffen en door voorbeelden uit de praktijk te geven. Tijdens het symposium is er voldoende ruimte om met de sprekers en andere aanwezigen in discussie te gaan en vragen te stellen.

Zodra het definitieve programma is vastgesteld wordt het op de website van de NVT gepubliceerd.

Noteer de datum alvast in uw agenda!

Special theme: Forever Chemicals

Per- and polyfluoroalkyl substances (PFAS) are hydrophobic and have a very high (chemical and thermal) stability, and are therefore widely used in a variety of consumer products, including water-proof fabrics, firefighting foams, non-stick cooking pans, food packaging material and shampoos. The group of PFAS consists of many different chemicals including PFOS and PFOA. The widespread use of PFAS has resulted in their ubiquitous presence in the environment. Because of their stability, they are barely degraded and they can accumulate in humans, animals and plants. They are therefore also known as 'forever chemicals'. The accumulation of PFAS in humans and the environment has raised concerns about the toxic effects. In this section, we highlight some of the recent insights in PFAS toxicity.

See the following articles ➔

The effects of PFAS exposure to lipid homeostasis in humans

By *Stella Fragki from RIVM*

Per- and polyfluoroalkyl substances (PFASs), like perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) are manufactured chemicals possessing unique physicochemical properties, such as oil and water repellence, high temperature and chemical resistance, and emulsifying/surfactant characteristics; therefore, they have a wide range of industrial and consumer applications. PFASs contain at least one fluoro-carbon chain of different length with varying chemical groups attached, which makes especially the long-chain congeners extremely persistent in the environment. Measurable blood concentrations of PFOA and PFOS, have been found in populations worldwide. The production and use of the most studied PFASs, PFOS and PFOA, have been restricted due to concerns of adverse effects to human health and the environment, whereas several EU countries are at the moment working on a REACH restriction proposal for all PFASs.

PFASs have been repeatedly associated with increased blood lipids in humans, but a causal relation has been debated. Rodent studies show opposite effects occurring, however, at PFAS serum levels at least 100-fold higher than those in humans. Next to this, the liver, which is tightly controlling lipid homeostasis, has been identified as an important toxicity target organ in animal studies. We[1] have reviewed and presented the main issues regarding the modulation of lipid homeostasis by the two most common PFASs, PFOS and PFOA, by emphasizing the main underlying mechanisms relevant for humans. Overall, the apparent contrast between human and animal data may be an artefact of dose, with different molecular pathways coming into play upon exposure to PFASs at very low versus high levels. It can be said that the interpretation of existing rodent data on PFOS/PFOA-induced lipid disturbances for to the human situation is rather complex. Mechanistically, studies with human liver cells demonstrate that PFOS/PFOA activate the PPARα pathway, whereas studies on the involvement of other nuclear receptors, like PXR, are less conclusive. Suppression of the nuclear receptor HNF4α signalling pathway, and perturbations of bile acid metabolism and transport are identified as important cellular events that require further examination. Future studies with human-relevant test systems would help to obtain more insight into the involved mechanisms relevant for humans. When such studies are finetuned to the human situation and interpreted in the context of the intact human, they can generate valuable information that will contribute to a better understanding of PFAS-mediated lipid perturbations and the issues involved in their interpretation for human health risk assessment.

[1] This work is conducted within the HBM4EU project www.HBM4EU.eu. For all contributors please have a look at the published manuscript: Fragki et al. 2021 https://doi.org/10.1080/10408444.2021.1888073

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The effects of PFASs on gene expression in human HepaRG cells and QIVIVE for PFAS hepatotoxicity

By *Stella Fragki from RIVM*

PFASs have been shown to exert a wide range of adverse effects, including hepatoxicity, developmental toxicity, and immunotoxicity (EFSA CONTAM Panel, 2020). Toxicity to the liver has been recorded very often in experimental animal studies, manifested as hyperplasia and hypertrophy, accompanied by hepatic lipid accumulation and blood hypolipidemia. In humans, exposure to PFOS and PFOA has been correlated with increased lipid levels in the blood, but also elevated serum levels of the hepatic enzyme ALT (alanine transferase), which is considered a biomarker for liver damage.

We[1] are currently working on obtaining a better insight into the cellular effects of PFASs on the human liver, by studying their effects on cellular triglyceride accumulation (AdipoRed assay) and gene expression in human HepaRG liver cells, with DNA microarrays and RT-qPCR. In addition, we are evaluating the potential of such *in vitro* data to predict the hepatotoxicity relative potencies of 18 congeners of the PFAS group. The approach facilitated for a selection of marker genes that can be used to assess *in vitro* relative potencies of PFAS in relation to liver (effects), which showed to be reasonable predictors for *in vivo* liver toxicity, when compared to animal data. In parallel, we assessed the *in vitro* biokinetics of PFOS and PFOA in the HepaRG cells by measuring time-and concentration-dependent cell-associated PFAS levels. Although equal concentrations were applied for both substances, cellular exposure was different, underpinning the importance of generating information on cellular concentrations and *in vitro* kinetics. These results provide relevant *in vitro* dosimetry data that will be used for a quantitative *in vitro* to *in vivo* extrapolation (QIVIVE) based on Physiologically Based Kinetic (PBK) modelling.

[1] This work is conducted by WFSR (Wageningen Food Safety Research) and RIVM (National Institute for Public Health and the Environment) and it is performed within the HBM4EU project www.HBM4EU.eu

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Can we get rid of PFAS?

By *Hedwig Braakhuis*

The main issue of PFAS is its persistency in combination with its widespread use. This has led to an accumulation of PFAS in humans and the environment up to concentrations that can induce toxicity. An option to reduce the health and environmental risks of PFAS is by enhancing its degradation to prevent it accumulation and subsequent effects. In addition, research is ongoing on how to remove PFAS from contaminated environments.

There are several ways to degrade substances, including using solvents or using micro-organisms. The success of using microbial species for PFAS depends on the structure of the PFAS, the type of micro-organism and the environmental conditions (Zhang et al. 2022). For example, a mixed microbial culture from aerobic sediment showed a much higher capability to degrade some PFAS species (about 80% degradation) compared to culture from aerobic sludge (6% degradation). Unfortunately, there is no confirmed biodegradation pathway yet. This is also related to the different structures of PFAS as the biotransformation mechanisms vary per type of PFAS. In addition, biotransformation is mainly limited to removal of the non-fluorinated moieties and does not break the carbon-fluor bonds. This leads to the risk that, after removal of the functional groups, the short-chain PFAS could even be more resistant and thus persist longer in the environment (Li et al. 2020).

Currently, PFAS biodegradation approaches do not provide complete degradation and combinations with other degradation processes such as physicochemical processes might help to achieve complete PFAS degradation (Zhang et al. 2022).

Physical methods for degradation include adsorption (e.g. activated carbon, polymers), (nano)filtration, reverse osmosis, sonication (Pilli et al. 2021). Chemical degradation methods include oxidation. For removal of PFAS from contaminated water, adsorption is considered the most suitable (Mukhopadhyay et al. 2021). Especially organically-modified clay minerals (modified with surfactants, polymers and amines) seem promising for the removal of PFAS from contaminated water. However, more research is needed and the removal of short-chain PFAS remains challenging. For soil and sediments, sonication treatment is predicted to be an effective removal technique for PFAS from a solid phase and can be investigated further (Uriakhil et al. 2021).

Taken together, the stability of PFAS gives the chemicals their functionality but also leads to their environmental persistence and toxicity. Removal of PFAS by biodegradation or other physicochemical processes is challenging and there is no method yet that can be used to remove all types of PFAS. Research could focus on options for removal of specific PFAS from environmental compartments. In the meantime, efforts are being made to ban the use of PFAS. The Netherlands is working with Denmark, Germany, Norway and Sweden on a proposal for a European ban on PFAS (PFAS restriction proposal | RIVM). Given the widespread presence of PFAS in humans and the environment, this ban is the way forward to prevent additional PFAS accumulation.

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TERUG NAAR INHOUD

Organohalogens and Our Persistent Ski Wax Problem

Persistent industrial chemicals are forcing us to rethink safety assessments and tighten regulations

By *Barae Jomaa*

Persistent Organic Pollutants (POPs) are sometimes referred to as “Forever Chemicals” since they remain in the environment for extended periods of time and, due to their potential to bioaccumulate, are more likely to reach levels that impact human health and the environment. The elimination or restriction of POPs is part of an international treaty signed in 2001, known as the Stockholm Convention.

The full list of substances that are earmarked for restriction or elimination (table 1) includes PFOS and PFOA have hydrolytic half-lives of 41 years and 92 years respectively[1,2]. PFOS and PFOA are part of a larger group of substances known as per- and polyfluoroalkyl substances (PFASs). There are thousands of such organofluorine chemicals and the listing of PFOS and PFOA on the Stockholm Convention is said to have led to “regretful substitution” with other related chemicals that are also a cause of concern. The new generation of PFAS chemicals includes the HPFO-DA (GenX) group of substances which have been added in 2019 to the European Chemicals Agency’s (ECHA) list of substances of very high concern (SVHCs).

In order to avoid other “regretful substitutions” with structurally related substances having similar properties, the Netherlands, Germany, Sweden, Denmark and Norway announced the intention to submit a restriction proposal for PFAS to ECHA by 19 July 2022.

Why is persistence a cause of concern?

The more we read about forever chemicals the quicker we are to jump to the conclusion that persistent chemicals are detrimental to human life and the environment. What about “non-toxic” chemicals that persist in the environment? In a paper by Cousins et al., the authors argue that the continuous release of highly persistent chemicals increases the probability of an effect occurring and since some of these effects are bound to be adverse, it will take “decades, centuries or even longer to reverse contamination”. This combination of high persistence and continuous release would inevitably lead to thresholds for potentially unexpected effects to be exceeded. The authors propose that high persistence alone should therefore suffice for the regulation of a chemical and call this a “P-sufficient approach”. The paper defines high persistence as a degradation half-life exceeding an indicative value, and give 6 months as an example. In addition, while bioaccumulation is an additional cause for concern, the authors point out that for highly persistent chemicals which will tend to be widespread in the environment, low bioaccumulation does not protect against continued and likely increasing exposure. Highly persistent chemicals with low toxicity should therefore be regulated. An example given in the article is synthetic polymers which are poorly degradable but are seen as a low concern due to their low bioavailability. These chemicals could also, with time, reach exposure levels that cross expected or unexpected effect thresholds and lead to adverse physical, chemical or biological effects.[3]

Why are halogen compounds persistent?

POPs are often halogenated organic compounds. These substances are of particular concern since they are typically lipid soluble (tend to bioaccumulate) and contain highly stable carbon-halogen bonds (tend to persist). Bond dissociation energies of carbon–halogen bonds increase as we go up the periodic table (C—I < C—Br < C—Cl < C—F). This is also why discussions revolving around organohalogens are often focused on fluorine, chlorine and bromine. As a real-world example, Teflon is a polymer of fluorine bonded to carbon with the chemical formula (C2F4)n. Due to the fluorocarbon bonds, it is highly resistant to thermal and chemical degradation – properties that have led to its widespread commercial success. One of the basic tenets ➔

of chemistry is that halogens are very eager to gain an electron in order to achieve a full outer shell. The reactivity of elements decreases with an increasing size of atoms because the nuclear pull/attraction decreases with increasing distance. The halogen bond has been captivating scientists since the 1920s and will continue to captivate our attention for years to come[4].

Replacements

Replacement fluorochemistry has been touted by industry ever since PFOA and PFOS were phased out. Second-generation PFAS have shorter chain lengths and shorter biological half-lives. These second-generation PFAS are still difficult to degrade and have higher environmental mobility. Moreover, some studies have suggested that this new generation of organohalogens is even more toxic than its predecessor. In a paper written in collaboration between the Swedish Chemicals Agency and Stockholm university, toxicity was ranked using modeled serum concentration (GenX > PFOA > PFHxA > PFBA) and liver concentrations (GenX > PFOA ≈ PFHxA ≈ PFBA) concentrations and the results are not promising[5,6]. The best way forward might be to do away completely with non-essential uses of organohalogens. Teflon coating, as used in cookware, can be successfully replaced with silicon dioxide (ceramic coating). PFOA Containing Ski Waxes are harder to replace (figure 1) but there many efforts under way to find suitable replacements[7]. While clearly essential for skiers, Cousins et al. have deemed it non-essential and have given a clear definition of essential, substitutable use and non-essential use[8].

In conclusion, there is an increasing amount of evidence that some of the alternative chemistries that have been developed as replacements to prohibited POPs are suffering from the same drawbacks. For example, the substances that are being developed to be resistant and water repellent ➔

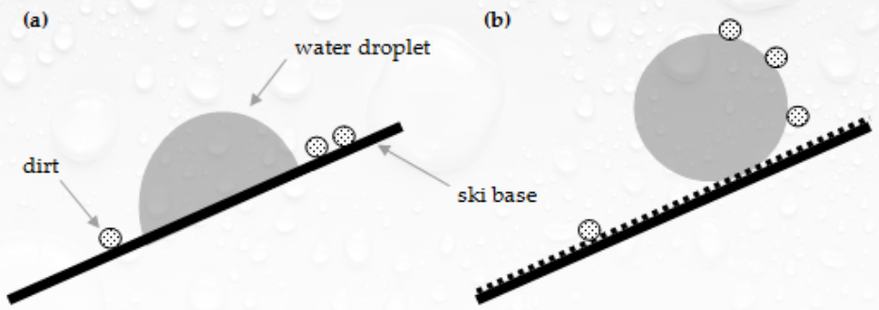

Figure 1. The difference between hydrocarbon (**a**) and fluorocarbon paraffin (**b**) waxes. Source: Pavla Svermova and Miroslav Cernik[7]

a)

Aldrin 🟢	Chlordane 🟢	Chlordecone 🟢
Decabromodiphenyl ether (commercial mixture, c-decaBDE) 🔺	Dicofol 🟢	Dieldrin 🟢
Endrin 🟢	Heptachlor 🟢	
Hexabromobiphenyl 🔺	Hexabromocyclododecane (HBCDD) 🔺	Hexabromodiphenyl ether and heptabromodiphenyl ether 🔺
Hexachlorobenzene (HCB) 🟢🔺	Hexachlorobutadiene 🔺	Alpha hexachlorocyclohexane 🟢
Beta hexachlorocyclohexane 🟢	Lindane 🟢	Mirex 🟢
Pentachlorobenzene 🟢🔺	Pentachlorophenol and its salts and esters 🟢	Polychlorinated biphenyls (PCB) 🔺
Polychlorinated naphthalenes 🔺	Perfluorooctanoic acid (PFOA), its salts and PFOA-related compounds 🔺	Short-chain chlorinated paraffins (SCCPs) 🔺
Technical endosulfan and its related isomers 🟢	Tetrabromodiphenyl ether and pentabromodiphenyl ether 🔺	Toxaphene 🟢

b)

DDT 🟢	Perfluorooctane sulfonic acid, its salts and perfluorooctane sulfonyl fluoride 🟢🔺

c)

Hexachlorobenzene (HCB) 🟪	Hexachlorobutadiene (HCBD) 🟪	Pentachlorobenzene 🟪	Polychlorinated biphenyls (PCB) 🟪
Polychlorinated dibenzo-*p*-dioxins (PCDD) 🟪		Polychlorinated dibenzofu-rans (PCDF) 🟪	Polychlorinated naphthalenes 🟪

Pesticide 🟢	Industrial chemical 🔺	Unintentional Production 🟪

Table 1: POPs listed in the Stockholm Convention for a) elimination b) restriction and c) reduction of the release of unintentionally produced substances

are often, due to their inherent chemical properties, also persistent and bioaccumulative. Even persistence alone, it has been argued, can be a cause for concern. This means that we might have to do away with the perfect ski wax or ultimate water-repellent surfer shorts in order to avoid risking long-term implications on human health and the environment. Moreover, the categorization of uses into non-essential, substitutable and essential, could prove to be a useful approach as we transition away from chemicals with an undesirable risk profile.

Category	Definition	PFAS examples
(1) “Non-essential”	Uses that are not essential for health and safety, and the functioning of society. The use of substances is driven primarily by market opportunity	Dental floss, water-repellent surfer shorts, ski waxes
(2) “Substitutable”	Uses that have come to be regarded as essential because they perform important functions, but where alternatives to the substances have now been developed that have equivalent functionality and adequate performance, which makes those uses of the substances no longer essential	Most uses of AFFFs, certain water-resistant textiles
(3) “Essential”	Uses considered essential because they are necessary for health or safety or other highly important purposes and for which alternatives are not yet established[a]	Certain medical devices, occupational protective clothing

Table 2 Three essentiality categories to aid the phase out of non-essential uses of chemicals of concern, exemplified with PFAS uses. Source: Cousins et al., 2019[8]

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PFAS: wel of niet bakpapier?

By *Igor Znidarsic*

Sinds de uitvinding in 1938 hebben per- en polyfluoralkylstoffen (PFAS) ons veel gemak en welzijn gebracht. Dankzij PFAS laat onze regenkleding geen water door, bakken onze pannen niet aan en zijn allerlei medische toepassingen mogelijk. Inmiddels zijn er ook nadelen bekend en is er veel discussie over hoe om te gaan met deze stoffen.

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“Door de oersterke verbinding tussen het fluor- en het koolstofatoom kun je er mooie producten mee maken”, zegt Jacob de Boer, hoogleraar milieuchemie en toxicologie aan de VU Amsterdam. “Maar het zijn ook producten waar je vanwege hun persistentie bijna nooit meer vanaf komt.”

Zie hier het dilemma van PFAS (spreek uit: péfas), een groep van zo’n zesduizend per- en polyfluoralkylverbindingen. De huidige discussie over deze stoffen is volgens De Boer vergelijkbaar met die over eerder toegepaste gehalogeneerde koolwaterstoffen zoals DDT(zie kader). Volgens De Boer kunnen PFAS nier- en teelbalkanker veroorzaken en het immuunsysteem schaden. Hij pleit dan ook voor uitfasering, met uitzondering van een aantal stoffen waarbij sprake is van essential use, bijvoorbeeld voor medische toepassingen, zolang de industrie geen alternatief heeft gevonden.

Martijn Katan, biochemicus en hoogleraar voedingsleer aan dezelfde universiteit, concludeerde vorig jaar in NRC echter dat PFAS weinig of geen effect hebben op de gezondheid van de mens. Als we iets tegen kanker willen doen kunnen we volgens hem veel beter zonnebanken uitfaseren. Bijna tegelijkertijd verbaasde Majorie van Duursen, hoogleraar toxicologie aan de VU, zich bij de NOS erover dat, hoewel PFAS-varianten PFOA en PFOS inmiddels in de ban waren gedaan, er ‘nog duizenden stoffen met veelal dezelfde eigenschappen overblijven’, waarvoor ‘nog gewoon vergunningen worden afgegeven’.

PFAS maken een pizzadoos vetafstotend.

Tegenspreken

Ondertussen valt op de website *Waarzitwatin.nl* van het ministerie van VWS te lezen dat producten met PFAS erin bij normaal gebruik veilig zijn. ‘Dat komt doordat de stoffen meestal vastzitten in het materiaal.’ Zoals bij een pan met een PTFE-antiaanbaklaag. ‘Maar soms zitten ze ook los in een product. Bijvoorbeeld bij brandblusmiddel, ski-wax, waterafstotend impregneermiddel voor textiel of smeermiddel voor fietskettingen.’ De hoeveelheden die hierbij vrijkomen zijn volgens VWS echter zo klein dat we ons geen zorgen hoeven te maken.

De discussie over PFAS gaat kortom al enige tijd alle kanten op, waarbij de deskundigen elkaar niet zelden tegenspreken. Een van de redenen hiervoor is dat ze het niet altijd over hetzelfde hebben. Waar de een het alleen heeft over PFOS, PFOA en GenX, stoffen die volgens het RIVM toxisch zijn, scheert de ander alle PFAS over één kam, terwijl met name de fluorpolymeren zoals PTFE volgens Chemours absoluut veilig zijn en er over de stofeigenschappen van het gros van de andere PFAS nog weinig tot niets bekend is. “Dat maakt de discussie nogal ondoorzichtig”, zegt Manon Bloemer, directeur van de VNCI. “De gemiddelde consument weet nu nog steeds niet of hij wel of niet bakpapier kan blijven gebruiken.” Bloemer wil de discussie op een evenwichtige manier voeren. “Omdat we veel nog niet weten moeten we wel voorzichtig zijn, maar we moeten ons ook niet door angst laten regeren.”

Pacemakers

PFAS zijn niet voor niets zo’n enorm succes geworden. In 1938 maakte een chemicus van het Amerikaanse DuPont ➔

per abuis het polymeer polytetrafluoretheen (PTFE), dat bijzondere eigenschappen bleek te hebben. Het was water-, vuil- en olieafstotend, kon goed tegen hitte en werd niet makkelijk aangetast door andere chemische stoffen. DuPont verkocht PTFE onder de merknaam Teflon. Later maakten vele producenten variaties op PTFE, zoals FEP, PFA en EFTE. Deze fluorpolymeren worden vanaf de jaren vijftig massaal toegepast. Naast de bekende toepassing als antiaanbaklaag in pannen zijn ze essentieel voor het goed functioneren van dagelijkse producten zoals auto's (onder andere slangen), elektronica (computers, smartphones) en zonnepanelen en zijn ze onmisbaar in veel industrieën en in de gezondheidszorg (pacemakers, katheters, hechtdraad, kunstmatige bloedvaten). PFAS zijn daarnaast veel gebruikt in het vuil- en waterafstotend maken van regen- en buitensportkleding, papier met een afstotende coating, zoals bakpapier en pizzadozen, cosmetica, flosdraad, meubels en tapijt. Binnen de grote verzameling van circa zesduizend PFAS valt ook de groep non-polymeren zoals PFOA en PFOS. Na een brand op een Amerikaans vliegdekschip in 1967, waarbij 130 mensen omkwamen, werd blusschuim met PFOS ontwikkeld, effectief tegen branden met licht ontvlambare stoffen.

"We moeten de voor- en nadelen van PFAS goed tegen elkaar afwegen", zegt Bloemer. "Ze worden gebruikt bij de productie van heel veel nuttige producten, die ons veel gemak en welzijn hebben gebracht. Als blijkt dat er gezondheidsrisico's aan kleven, moeten ze uiteraard worden verboden of streng genormeerd, zoals nu gebeurd is met PFOS, PFOA en GenX." Over de overige PFAS kunnen we volgens Bloemer nog weinig concreets zeggen, simpelweg omdat er nog zo weinig over bekend is. De stoffen worden bovendien niet in Nederlandgeproduceerd en komen door import ons land binnen. Het is niet altijd duidelijk welke producten pfas bevatten en welke niet.

PFAS zijn veel gebruikt in het vuil- en waterafstotend maken van regen- en buitensportkleding

Essentieel

Volgens Annemarie van Wezel, professor milieu-ecologie aan de Universiteit van Amsterdam, is nog maar een beperkt deel van alle PFAS binnen REACH geregistreerd. Het gaat om 107 van de duizenden stoffen. De andere PFAS – met uitzondering van de circa duizend mengsels of polymeren – zouden volgens haar niet in grotere volumes in de EU gemaakt, verhandeld, toegepast of gebruikt mogen worden. Daarnaast zou de toelating beperkt kunnen worden tot 'essentiële stof- en toepassingscombinaties'. Voor wat essentieel gebruik is verwijst zij naar het Montreal Protocol, een internationaal verdrag uit 1987 om de ozonlaag te beschermen. Daarin wordt gesteld*: 'The two elements of an essential use are that a use is "necessary for health, safety or is critical for the functioning of society" and that "there are no available technically and economically feasible alternatives".'*

Als voorbeeld van essential use van PFAS worden vaak medische toepassingen zoals bloedzakken genoemd, waar vooralsnog geen alternatief zonder PFAS voor zou bestaan. Over andere toepassingen zal de komende tijd ongetwijfeld een discussie losbarsten. "We moeten goed gaan nadenken over essential use", zegt Bloemer. "Zijn bijvoorbeeld smartphones onmisbaar voor het functioneren van de samenleving? Ik heb drie pubers thuis, ik denk dat die het antwoord wel weten."

Politiek heeft het laatste woord

Eind vorig jaar maakte minister Van Veldhoven van Milieu en Wonen tijdens de milieuraad in Brussel bekend een procedure te beginnen om toepassing van PFAS in de EU aan banden te leggen. Dit jaar zal Nederland een 'restrictievoorstel' indienen bij het Europees ➔

Agentschap voor Chemische Stoffen (ECHA). Dat komt vervolgens met een definitie van te verbieden stoffen en uitzonderingsgronden voor stoffen waarvoor geen alternatief is. De Europese Commissie besluit vervolgens over een voorstel voor een verbod, waarover de lidstaten en het Europees Parlement het laatste woord hebben.

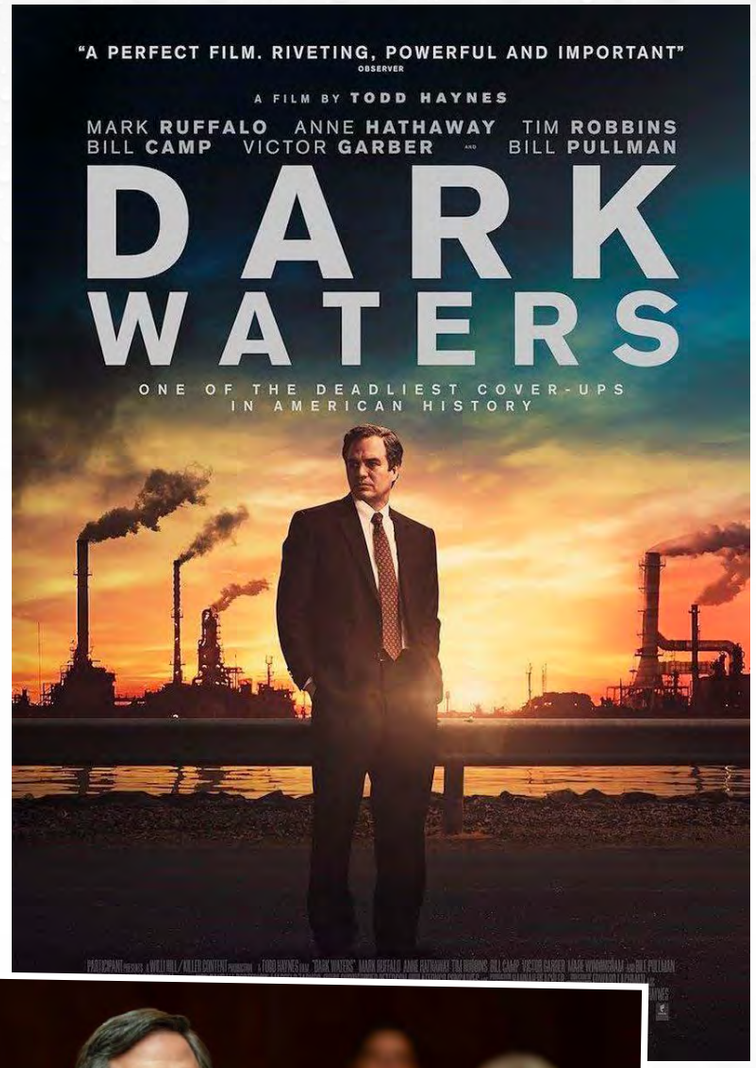
Dark Waters

Bij de productie van Teflon bij DuPont in het Amerikaanse Parkersburg en bij DuPont in Dordrecht (de locaties vallen sinds 2015 onder Chemours) is de stof PFOA(C8) als hulpstof gebruikt. Volgens de recente documentaire *The Devil We Know* en de speelfilm *Dark Waters*, deze maand in Nederland in première, zijn in Parkersburg vanwege lozingen van PFOA mensen ziek geworden en heeft DuPont voor 670 miljoen dollar geschikt. Ook in Dordrecht loosde DuPont jarenlang PFOA, overigens met vergunning, evenals het Helmondse bedrijf Custom Powders. Toen de gezondheidsrisico's van PFOA bekend werden, schakelde DuPont in Dordrecht in 2012 (vergund) over op GenX. Afgelopen zomer heeft de Europese overheid de stof gelabeld als een *substance of very high concern*. Daardoor is de stof ook in Nederland een 'zeer zorgwekkende stof' en geldt er een verplichting om emissies te minimaliseren. Chemours in Dordrecht is bezig de uitstoot van GenX terug te dringen, met als doel een reductie van minimaal 99 procent voor het eind van 2020. Ook produceert het bedrijf inmiddels de biobased en fluorvrije Teflon EcoElite, waarmee textiel water- en vuilafstotend gemaakt kan worden.

DDT: van Nobelprijs tot (bijna) verbod

Dichloordifenyltrichloorethaan (DDT), in 1948 goed voor de Nobelprijs, is het meest effectieve middel tegen de malariamug geweest en heeft tientallen miljoenen mensenlevens gered. Dankzij DDT verdween malaria uit de VS, Europa, Rusland, Japan, Australië en delen van Zuid-Amerika en grotendeels uit India. Het middel was ook zeer effectief tegen muggen die de gele koorts en knokkelkoorts veroorzaken en tegen katoen- en aardappelkevers.

Dankzij DDT werden VS en Europa in een korte tijd verlost van dodelijke ziektes als de pest en vlektyfus. Vanaf de ontdekking werd het wondermiddel dan ook in enorme hoeveelheden geproduceerd. Tot in 1962 het boek *Silent Spring* uitkwam. DDT stapelde zich volgens de schrijfster via de voedselketen op in dieren en mensen en was verantwoordelijk voor onder meer genetische defecten en kanker en het uitsterven van dieren. DDT belandde in de verdomhoek. Inmiddels mag DDT weer op beperkte schaal binnenshuis worden gebruikt in enkele Afrikaanse landen.



Een vasthoudende advocaat ontdekt een duister geheim dat een groeiend aantal onverklaarbare sterfgevallen verbindt met een van 's werelds grootste bedrijven. Hij probeert de waarheid te onthullen.

AIO toxafette - Annemijne van den berg

By *Annemijne van den Berg*

Can you introduce yourself?
My name is Annemijne van den Berg and I am a first year PhD student at Utrecht University. I finished the bachelor Health Sciences at VU Amsterdam and the master Toxicology and Environmental Health at Utrecht University. Right after obtaining my master's degree in May 2021, I started my PhD adventure at the immunotoxicology department of the Institute for Risk Assessment Sciences (IRAS), Utrecht University. Under the supervision of dr. R.H.H. Pieters and prof. dr. ir. J. Legler, I am currently working on an EU wide project called POLYRISK. Essentially, this project aims to unravel the human health risks of micro- and nanoplastics.

How would you explain the subject of your research to a layperson?
Today, it is hard to imagine a world without plastic. Plastics that have been degraded into small plastic particles in the micro- and nano-size range are found in our food, drinking water and even in the air. Consequently, it has become evident that we get exposed to these tiny plastic particles daily. Therefore, the very important question arises whether these particles form a threat to our health. During my PhD-project, I focus mainly on the effects of plastic particles on our immune system after ingestion. I investigate if the particles affect our intestines and if they cross the intestinal barrier, possibly leading to systemic exposure. Furthermore, I examine the effect of the particles on critical immune cells.

What was your motivation to start a PhD program?
While doing my masters internship at IRAS, I realized that I really enjoyed the different aspects of research. For me, it feels like a giant, complex puzzle and by solving this puzzle I will, hopefully, contribute to public health. I love to advance and create knowledge and to develop new skills. Furthermore, I am always eager to take on new challenges and responsibilities. Lastly, I hope that acquiring a PhD degree will pave the way for a successful further career.

Why did you choose a subject in toxicology?
I've always been quite the "girly" girl, interested in all sorts of cosmetics and personal care products. While slathering myself in a great variety of creams, serums and lotions I started wondering what I was actually putting on my skin, and as important, what I was washing through the drain afterwards. This passion gradually evolved into a broader interest in toxicology and the environment. Hence, I started the master Toxicology and Environmental Health. During this master, I got introduced to immunology and micro- and nanoplastics and I quickly realized that I wanted to explore these subjects in more detail.

How do you see the future of your research topic (follow-up research / social impact)? What do you hope for?
I really hope my research project will contribute to the risk assessment of micro- and nanoplastics so we can make science-based decisions regarding the global problem of plastic pollution. I am very happy to be part of a big consortium in which experienced researchers all over Europe put their heart and soul into this important subject. Therefore, I expect that in the coming years a lot of groundbreaking science will be presented about to what extent and how micro- and nanoplastics affect our health. I really hope that these results will give extra intention for the generation of solutions to the plastic problem.

How do you combine your PhD project with your personal life? Are there choices you have to make?
I've always been a busy bee, which results in quite some hobbies that got out of hand. I have been very passionate about (antique) jewelry and during my masters, I became a registered appraiser and certified gemologist. I started my own online jewelry shop (Het Goudmijntje) which takes up a considerable part of my free time. I must admit ➔

that, unfortunately, starting a PhD comes at a cost since I have less time and energy to maintain my side business. But still, having the right work-life balance is crucial in order to stay productive at work, so I definitely make sure that I have time left for some relaxation, to go outside and to enjoy quality time with my friends. Furthermore, I try to exercise very regularly since I feel that it gives me fresh motivation and increases my creativity.

What is the best advice that you have received as a PhD student or would like to give to another PhD student?
At the end of my masters, I was doing an internship at KWR Nieuwegein. When I told my colleagues that I was going to do a PhD, one of them, Dr. Stefan Kools, gave me some advice that really stuck with me. He told me that it can feel like a PhD is mostly done in solitude and that it can become a lonely process. Therefore, it is very important to talk to your colleagues and your supervisor. Your colleagues will almost always be eager to help and talking/brainstorming can help you in continuing and advancing your research process.

What is the biggest challenge for you in doing PhD research?
To this question, I would like to give a very honest and humble answer. Sometimes it scares and overwhelms me that I am surrounded daily by all these intelligent, experienced and hard-working people. It can make me feel rather insecure about my own abilities; “Am I smart enough? Do I work hard enough? Am I doing it right?”. But then I try to turn the tables by changing this challenge into something positive and I realise that I am blessed to have these people around me, from whom I can learn so much.

Do you consider research communication as an important aspect of your PhD research and why so? If yes, to what kind of audience?
In the last couple of years, you can almost consider discussing the risks of (micro-)plastic pollution a hype. This has resulted in a discrepancy in how science and media frame microplastic risk. The media might tend to deform scientific information/ data just to boost their story. However, the microplastic issue has still many uncertainties and unanswered questions. So therefore, I would strongly agree that research communication in my PhD field is very important.

What goals do you have regarding your career after finishing your PhD-project? Would this be inside or outside academia, and why? Would you consider going abroad?
I regularly find myself brainstorming about my future, hemming and hawing about which direction I want to go. But in my most honest opinion, it is very difficult to get a grip on the future. Up until now, I got constantly surprised with new career opportunities which meant that I had to adapt the plans I made for the future. I can envision myself working outside academia after my PhD so I can put all the skills I picked up during research into use in a new context and gain some experience in working in the industry. But one can never know what comes on his or her path, and right now I am still open to all the different possibilities.

Please answer the question from the last toxafette PhD-candidate: “What is something you wish someone told you about before you started your PhD research?”
Doing a PhD consists of many processes that take a lot of time such as reading, learning new methods, conducting experiment, analysing results, supervising students, giving or following education, etc. Sometimes it is very important to take a pause and schedule in some ‘thinking time’ to really make sense of the things you are reading and finding. Focus on what you are doing and don’t lose track of where you want to go.

Question for the next toxafette candidate: What would you investigate if you had unlimited resources?

Working in the chemical industry

I have been told that the section "what's next" is intended to provide new toxicologist insights into the different career paths and opportunities that they may encounter. It is a different type of writing than normally performed but I'll try my best. For sure a starting position as a toxicologist provides many job (crafting) opportunities allowing for constant evolution in one's career while leaning on and expanding knowledge and experience from the past.

By *By Barry Blankvoort - EHS-manager at Synthon BV*

Start of my career

My career started about 25 years ago when I embarked upon a PhD study at Wageningen University and TNO as part of a joint project. One of the aims was to develop a biomonitoring tool to be applied in the control on the use of illegal growth hormones in cattle. This was appealing since it was on the edge of science and the direct application thereof. It was a rewarding period, including hard work, successes and also a fair share of frustration but ultimately doing a PhD represents a great learning experience.

Career crossroads

After finishing a thesis, one is at a crossroad; continue a career in academics, contract research organizations or switch to the industry? While still being in doubt and applying for all types of positions I received a phone call from a recruiter. He saw a potential connection between my study in environmental sciences, my PhD toxicology experience and a position in his portfolio. Being focused on toxicology during my PhD, I kind of forgot to include my study specialization in labor and health in my job search; a good recruiter can be valuable. So, in 2004 I started working at Synthon, a generic pharmaceutical company headquartered in Nijmegen. At the time I did not yet fully realize how very wide the scope of work at a relatively small pharmaceutical company can be. Essentially all disciplines can be touched upon from animal to human to environmental toxicology. In general, focus will be on applied toxicology utilizing research performed by universities and elsewhere and supplementing it with contract research and expert knowledge. More specialized functions are those at the toxicology (TOX) department that supports product development and safety thereof; perhaps something to elaborate on by one of my TOX colleagues in a later issue.

Responsibilities as a EHS-toxicologist

In the area of environment health and safety, where I job crafted myself to, a toxicologist can perform a broader (albeit less specialized role) touching upon issues such as:

- Employee safety including compound classification in line with EU legislation (REACH/CLP) and compiling safety data sheets
- Deriving occupational exposure limits.
- Supporting occupational hygiene by contributing to occupational exposure banding and supporting (interpretation of) exposure assessment.
- Environmental risk assessments of pharmaceuticals.
- Regulatory toxicology; surrounding areas such as shared facility use, hazardous waste disposal, transport classification etcetera.
- Risk assessment after accidental exposure on the work floor or after spillage at customers
- Contributing to shared facility requirements
- And more areas where toxicology turns out to be relevant… ➔

Being in an EHS department ensures a wide variety of activities and, if one is committed to it, also offers ways to contribute to more sustainable ways of doing business. For instance, in an emerging economy, we will soon be realizing a wastewater treatment plant that performs above legal requirements amongst others due to an in-house eco-toxicological risk assessment.

A toxicologists' responsibility regarding risk assessment
Lastly, it is important to realize that toxicology is very much a "niche-area". Since there are not many of us out there, we often have to make or influence/motivate/advise on decisions (often based on limited data) keeping a risk-based approach in mind. We have to be able to explain our work to a wide range of people ranging from peers, to regulators, to work floor colleagues or even society at large. In doing so we should not submit to the (in my humble opinion) overall increasing tendency of only accepting (or believing in) "zero chance". It is our task to persist in explaining the nuances in toxicology, stressing (additional) caution where it is warranted but also defusing unnecessary fears where it is responsible. And not only at work, but also in the canteen after sports, at a birthday or wherever you find yourself in a surprise discussion, but perhaps this is a topic more suitable for another section of the TCDD...

Practical example:
Within pharmaceutical production the minimization or prevention of "carry-over" is an important aspect in production safety. Carry-over can occur when traces of medicine A end up in medicine B when they are produced in the same shared facility. To prevent (negative) side effects scientifically justified cleaning limits (based on toxicological data) are increasingly applied at the switch of production to another medicine. Although many countries and companies already apply such a risk based approach, a dedicated facility requirement for "cytotoxic" compounds is still required in a considerable number of cases. At the same time, no clear definition of what cytotoxicity actually means (and it is in fact a broad term) is provided. Sometimes this results in a blanket requirement for dedicated facilities for all anticancer medicines, thereby ignoring the myriad of mechanisms of action through which many modern medicines work. A toxicologist can contribute to this discussion by delivering a useful definition of cytotoxicity supplemented with a motivation indicating for which antineoplastic medicines it is sensible to use a dedicated facility. This is relevant since such decisions can for instance influence production capabilities, availability of medication and the cost of medicines (since dedicated production is much more expensive).

Inschrijving TiO

Voorletters	Achternaam	Opleider	Datum inschrijving
X.	Li	Prof.dr.ir. I.M.C.M. Rietjens	13/12/2021
J.E.M.	van der Heijden	Prof.dr. F.G.M. Russel	13/12/2021
T.M.J.A.	Moerenhout	Prof.dr.ir. I.M.C.M. Rietjens	13/12/2021

Inschrijving Register

Voorletters	Achternaam	Datum inschrijving	Datum afloop registratie
P.C.C.	Sijnesael	13/12/2021	13/12/2026

Mondneusmaskers: impact op gezondheid en milieu

By *Paul T.J. Scheepers, Radboudumc, Nijmegen*

Mondneusmaskers hebben een bedenkelijke reputatie. In het straatbeeld staan mondneusmaskers hoog genoteerd in het zwerfafval (Roberts et al., 2021). Wat ook niet helpt in de beeldvorming is dat ze goedkoop geproduceerd kunnen worden, maar bij schaarste tegen woekerprijzen ingekocht zijn. Aanvankelijk werd nogal getwijfeld aan het effect van het dragen van een mondneusmasker als middel om het de overdracht van het virus terug te dringen. Inmiddels zijn er studies die laten zien dat dit effect op het verloop van de pandemie dusdanig is dat deze interventie wereldwijd ook in de toekomst veel zal worden gebruikt (Kwon et al., 2021). Laten we daarom de effecten van mondneusmaskers op gezondheid en milieu eens op een rij zetten.

Hoe kom je aan goede en betaalbare mondneusmaskers?

De goedkoopste chirurgische maskers zijn een beproefd ontwerp dat zich volgens een aantal grote systematic reviews bewezen heeft in een klinische setting. Deze maskers zijn in de laag-risico situatie even goed als de professionele en gecertificeerde FFP2 of N95 mondneusmaskers. De kwaliteit van het chirurgisch masker komt voort uit het gebruikte materiaal: non-woven spunbound meltblown polypropyleen. Deze maskers halen een zeer hoge efficiency doordat ze opgebouwd zijn uit verschillende laagjes. Tijdens de eerste golf bleek dat Nederland afhankelijk was van import omdat er geen eigen productiecapaciteit was. Als je dit materiaal groot kunt inkopen kun je met moderne machines honderdduizenden maskers per week produceren. Voor zover deze machines nog niet in Nederland voorhanden waren zijn ze aangekocht om aan de grote vraag te kunnen voldoen. Zo is er een productie van eigen bodem van de grond gekomen, wel met geïmporteerde grondstoffen.

Weggooien of hergebruiken?

De mondneusmaskers die worden gebruikt in de zorg vormen een enorme afvalstroom, maar gaan mee in een nog veel grotere stroom ziekenhuisafval. Met een bijdrage van 7 % levert de zorgsector als geheel een forse bijdrage aan de uitstoot van broeikasgassen in Nederland (Zijp et al. 2020). Daar komt nog bij dat er op deze hogere kwaliteit gecertificeerde producten een maximale houdbaarheid zit die samenhangt met de lading die is aangebracht op het filteroppervlak. Deze zg. electreet maakt het mogelijk dat hoge filtratie efficiency is te combineren met een niet al te hoge ademweerstand. Maar die lading wordt met de tijd minder waardoor de overheidsvoorraad nog ongebruikte mondneusmaskers voor de zorg inmiddels een afvalberg is ‘waar je vanaf kunt skieën’ aldus de Volkskrant van vorige week. Voor de maskers die door het publiek worden gebruikt liggen er ook bergen in de grijze stroom moeilijk herbruikbaar afval. Waarschijnlijk wordt hier CO_2 van gemaakt in de afvalverbranding. Er is ook nog geen goede manier gevonden om uit gebruikte mondneusmaskers grondstoffen terug te winnen. Dat is al wel mogelijk voor de enorme afvalstroom van wegwerpbabyluiers in huishoudelijk afval en incontinentiemateriaal in afval van de zorg. Recycling van non-woven filtermateriaal was al wel beschreven (Bhat et al. 2008). De vraag is waarom deze technologie nog niet op grote schaal wordt toegepast. Mogelijk dat het ontwerp van mondneusmasker zich nog niet leent voor grootschalige recycling. De logistiek vormt natuurlijk ook een probleem wat we al kennen uit het verwerken van verzameld kunststof afval. Verzamelpunten in winkelstraten en op parkeerplaatsen zou een mooi begin zijn.

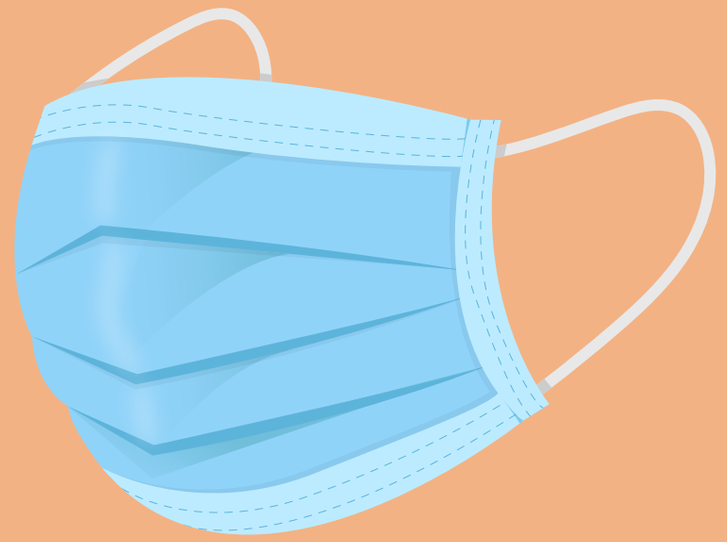
Veel consumenten geven gelukkig al de voorkeur aan herbruikbare mondneusmaskers. Wat helpt is dat studies laten zien dat deze producten qua effectiviteit bijna op gelijke hoogte kunnen komen als de wegwerpmaskers. Het prijsverschil is alleen nog erg groot. Alleen als je een masker heel vaak (50-100x) hergebruikt kun je dat prijsverschil terugverdienen. Voor het schoonmaken van herbruikbare maskers adviseert de overheid wassen op 60°C. ➔

TERUG NAAR INHOUD

Impact op gezondheid

In de dermatologische literatuur wordt melding gemaakt dat formaldehyde verdacht wordt van een huidreactie op het dragen van mondneusmaskers (Clawson and Pariser, 2021). De eerste rapporten van een contact dermatitis door mondneusmaskers zijn in Nederland ook al gemeld (persoonlijke communicaties binnen het Radboudumc). Dit fenomeen was al bekend uit de textielindustrie waar formaldehyde bijdraagt aan kreukvrije kleding. Het advies is dan: eerst wassen, wat voor mondneusmaskers niet erg praktisch is. Fabrikanten passen ook andere stoffen toe zoals nanozilver, titaniumdioxide en biociden (Singh et al. 2021). Over de veiligheid is weinig bekend, maar van het inademen van stoffen of deeltjes die vrijkomen uit het materiaal van mondneusmaskers is de veiligheid onvoldoende aangetoond (Sciensano https://www.sciensano.be/nl/pershoek/verduidelijking-bij-de-mogelijke-risicos-verbonden-aan-de-avrox-maskers). Volgens een brief van het ministerie van VWS aan de Tweede Kamer is een lading van 20 miljoen mondneusmaskers met grafeen ingekocht door het Landelijke Consortium Hulpmiddelen (LCH) uiteindelijk afgekeurd door het RIVM.

Gelukkig zijn er ook voor de gezondheid positieve ontwikkelingen te melden. Zo is een onderzoek gedaan naar een aangepast mondneusmasker voor patiënten die moeite hebben om te voldoen aan de draagplicht in openbare binnenruimtes en het OV. Hiervoor zijn bij Longfonds ervaringsdeskundigen en het Longpanel benaderd. Tijdens het onderzoek is het corona transmissie reductie (CTR) mondneusmasker getest. Dit concept masker is speciaal voor dit doel ontwikkeld door een Nederlandse fabrikant en afgeleid van het ontwerp en een al bestaand FFP2 mondneusmasker voor zorgprofessionals. De ademweerstand is met meer dan de helft verminderd terwijl het filter bijna net zo goed filtreert als een FFP2 masker, maar niet voldoende voor een FFP2 certificering.



Aan het onderzoek deden 84 astma en COPD patiënten mee. De deelnemers aan het onderzoek kregen het masker thuisgestuurd en hebben het enkele weken getest. Vooral bij traplopen was dit masker een verbetering. Bij andere activiteiten (wandelen, boodschappen doen) werd nog wel steeds een verhoogde ademweerstand ondervonden maar bijna de helft van de deelnemers zou het CTR mondneusmasker willen gaan dragen als het beschikbaar zou komen.

Impact op milieu

Zodra wegwerpmondneusmaskers in het zwerfvuil terecht komen, dragen ze bij aan het ontstaan van milieubelasting waaronder het microplasticsprobleem (Dissanayake et al., 2021). Waterafstotende coatings gemaakt van perfluorverbindingen leiden tot emissies van persistente schadelijke stoffen. Fabrikanten zijn niet erg open over de toepassing van deze coatings. Online zijn wel producten te vinden waarbij het gebruik van fluorkoolwaterstoffen wordt opgegeven in de productspecificatie. In de vakliteratuur is ook te vinden dat fluorverbindingen worden toegepast in de coating of telfon (PTFE) als filtermateriaal (Chua et al., 2020). Er zijn ook goede redenen om bij herbruikbare mondneusmaskers geen fluorkoolwaterstof toe te passen vanwege gezondheidsbezwaren (zie kadertekst). ➔

Bron: Nederlands Normalisatie Instituut (NEN, 2021)

*"**4.3.5.2 Schadelijkheid voor slijmvliezen en longen***
Materialen die stoffen in de ingeademde lucht kunnen afgeven, mogen geen gevaar voor de gezondheid vormen of irritatie voor de drager veroorzaken. Mondkapjes die op de markt worden gebracht, moeten voldoen aan Verordening (EG) nr. 1907/2006 (REACH) en aan Verordening (EU) 2019/1021 van het Europees Parlement en de Raad van 20 juni 2019 betreffende persistente organische verontreinigende stoffen. Dit betekent dat het niet is toegestaan textiel te gebruiken dat is behandeld met biociden, pyretroïden of een waterafstotende finish van fluorkoolwaterstoffen.

Ook strijkvrij textiel wordt afgeraden. Dit textiel bevat vaak stoffen (bijv. formaldehyde) die bij verkeerd gebruik schadelijk kunnen zijn voor de gezondheid. Het gebruik van basismaterialen die voldoen aan ISO 10993-1, categorie A, wordt aangeraden, aangezien het product voor de mond wordt gedragen.

4.3.6 Gebruik van biociden Het is niet toegestaan om materialen te gebruiken die zijn behandeld met een biocidecoating op synthetische basis, omdat biociden: — niet zijn bedoeld voor inhalatie; — gevaarlijk kunnen zijn voor de algemene gezondheid. De meeste biociden zijn onderworpen aan Verordening (EU) nr. 528/2012 betreffende het op de markt aanbieden en het gebruik van biociden. Zie ook www.biociden.nl/behandelde-voorwerpen."

Oplossingen

Een gunstige ontwikkeling is voor preventie van gezondheidseffecten van het dragen van mondneusmaskers is dat er een NEN certificering is ontwikkeld waarin ook gezondheid aandacht krijgt (zie kader). Op de website https://www.nen.nl/certificatie-mondkapjes-voor-publiek-gebruik is een lijst opgenomen met producten waarvoor een certificaat is afgegeven en die ook geen fluorkoolwaterstoffen bevatten, wat een milieuvoordeel is. Op Europees niveau buigt CEN technical committee CEN (CEN/TC 248/WG 39 – *Community face coverings - guide to minimum requirements, methods of testing and use*' zich inmiddels ook over dit onderwerp. Hierin worden waarschijnlijk ook voorwaarden opgenomen om schade aan gezondheid en miilieu te voorkomen. Verder blijkt dat de productie van het filtermateriaal (meltblown polypropyleen) in Nederland klimaatneutraal is gerealiseerd. Alleen is een goede oplossing voor het inzamelen en hergebruik van grondstoffen van wegwerp mondneusmaskers is nog ver weg.

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Uitnodiging Netwerkdag
Medicijnresten in het Milieu
8 maart 2022

Datum en tijd:
8 maart 2022
09.00 – 16.30 uur

Plaats:
RIVM
Antonie van Leeuwenhoeklaan 9
3721 MA Bilthoven

Het RIVM Rijksinstituut voor Volksgezondheid en Milieu organiseert op 8 maart 2022 de Netwerkdag Medicijnresten in het milieu. Afgelopen jaren is er veel werk verzet rondom dit thema. Tijdens deze netwerkdag krijgt u een update van de meest recente ontwikkelingen en kunt u meepraten tijdens verschillende workshops. Deze dag is bedoeld voor iedereen die betrokken is bij het onderwerp of erin geïnteresseerd is, vanuit de zorgsector én de watersector. De Netwerkdag bestaat uit een ochtendprogramma (fysiek en digitaal) en een middagprogramma (alleen fysiek). Gedurende de dag is er voor de deelnemers aan de fysieke bijeenkomst voldoende tijd en ruimte om elkaar te ontmoeten.

Het programma
Ochtendprogramma: In de ochtend geven een aantal sprekers presentaties over initiatieven om de impact van medicijnresten in het milieu aan te pakken. Denk hierbij aan onderwerpen als de Ketenaanpak Medicijnresten, de Green Deal en het Innovatieprogramma Microverontreinigingen uit Afvalwater.

Middagprogramma: In de middag worden er interactieve workshops gegeven over actuele onderwerpen.
Thema's die aan bod komen zijn onder meer Antibioticaresistentie, Educatie in de Gezondheidzorg, Medicijnresten in een Circulaire Economie en Innovaties in Rioolwaterzuiveringen.

Organisatie en aanmelden
Dit jaar is ervoor gekozen om de Netwerkdag in hybride vorm te laten plaats vinden. Dit betekent dat u de presentaties in de ochtend zowel fysiek als digitaal kunt bijwonen. Het middagprogramma (workshops rondom diverse thema's) kan alleen fysiek bijgewoond worden. Voor de fysieke bijeenkomst is het aantal deelnemers beperkt. Mocht u alleen de ochtend willen komen, dan willen we u vragen om de bijeenkomst online bij te wonen.

Aan deelname zijn geen kosten verbonden. Aanmelden voor zowel de fysieke als de online bijeenkomst kan via de volgende link: Netwerkdag Medicijnresten 2022.

TERUG NAAR INHOUD

TCDD is de nieuwsbrief van de Nederlandse Vereniging voor Toxicologie (NVT).