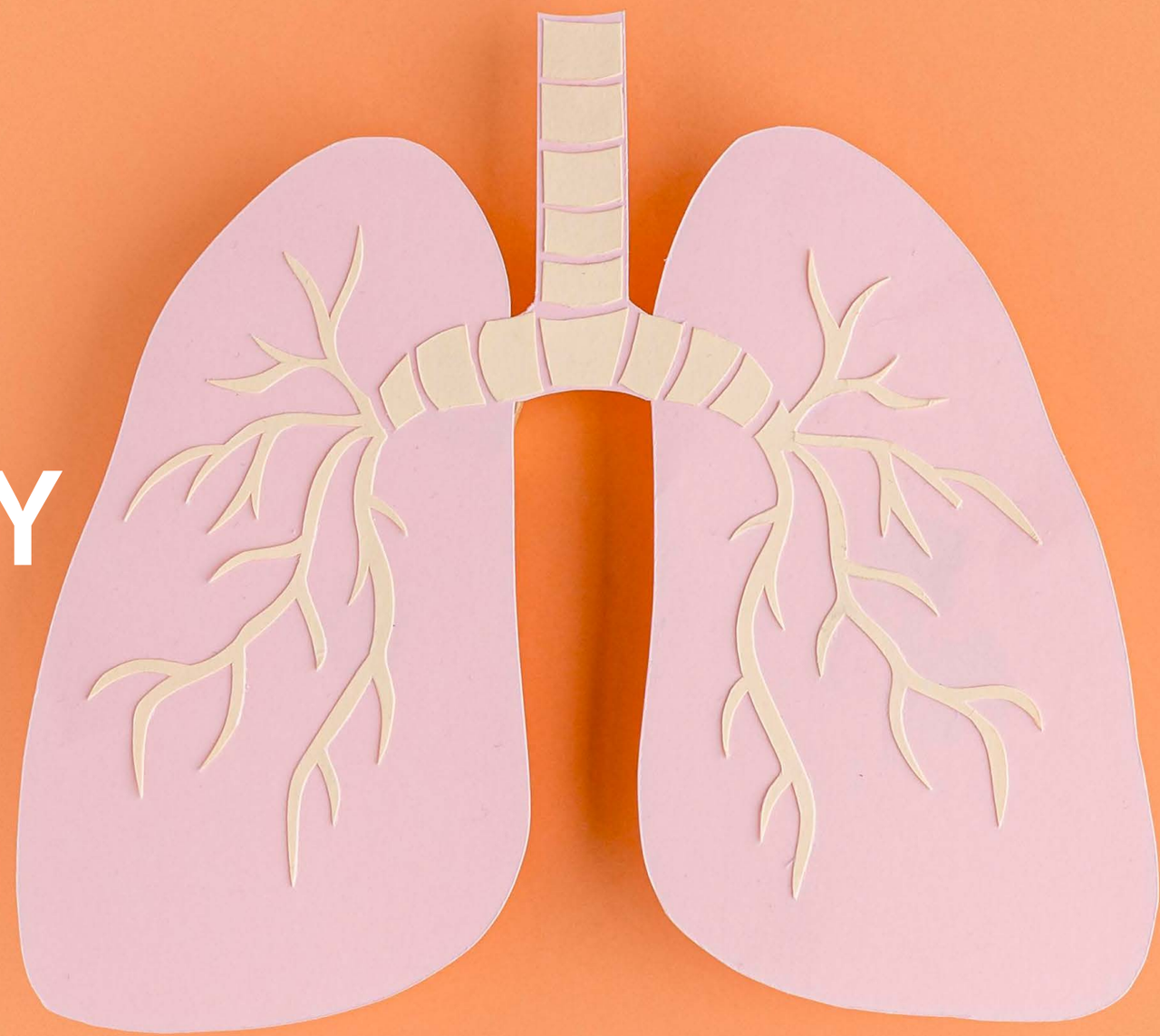
TCDD
TOXICOLOGIE

NUMMER 1
MAART 2022

SPECIAL THEME

INHALATION TOXICOLOGY



- PE-PUR QUALITY ISSUES IN RESPIRATORY MEDICAL DEVICES, WHAT IS IT ABOUT?
- A CHANGE OF AIR
- WHEN A COZY ENVIRONMENT WITH CANDLES AND INCENSES CAN INCREASE THE EXPOSURE TO A TOXIC CHEMICAL

NEDERLANDSE VERENIGING VOOR TOXICOLOGIE

Colofon

Toxicologische Communicatie, Data en Documentatie

Bestuur
Voorzitter
Juliette Legler, *Institute for Risk Assessment Sciences (IRAS), Universiteit Utrecht*
Vice-Voorzitter
Paul Jennings, *Vrije Universiteit Amsterdam*

Secretaris
Hester Hendriks, *Rijksinstituut voor Volksgezondheid en Milieu*
Nicole Nijhuis, *Rijkswaterstaat*
Penningmeester
Peter Theunissen, *CBG-MEB*
Lid
S. (Suzanne) Heemskerk, *UMC St Radboud*
Anne Kienhuis, *Rijksinstituut voor Volksgezondheid en Milieu*

Secretariaat
Secretariaat Hester Hendriks,
Rijksinstituut voor Volksgezondheid en Milieu
Postvak 1, Postbus 1, 3720 BA Bilthoven
E-mail: secretaris@toxicologie.nl

Redactie
Héloïse Proquin, *National Institute for Public Health and the Environment (RIVM)*
Damiën van Berlo, *National Institute for Public Health and the Environment (RIVM)*
Carolien Schophuizen, *Synthon BV*
Hedwig Braakhuis, *National Institute for Public Health and the Environment (RIVM)*
Maaike Steenhof, *Zwiers Regulatory Consultancy*
Barae Jomaa, *Colonial Chemical*

Webredactie
Samantha Guichelaar, *Rijksinstituut voor Volksgezondheid en Milieu*
Floris Groothuis, *Rijksinstituut voor Volksgezondheid en Milieu*
webmaster@toxicologie.nl

Bestuursvergaderingen 2022
14 maart, 25 april,
12 september, 21 november

Lidmaatschap en Adreswijzigingen
Marjan Sewradj-Mulder
Ledenadministratie NVT, p/a KNCV
Postadres: Postbus 249, 2260 AE
Leidschendam
tel. 070 - 337 87 97
Via NVT website na inloggen
http://www.toxicologie.nl
E-mail: ledenadministratie@kncv.nl

Het lidmaatschap wordt automatisch verlengd tenzij de NVT-ledenadministratie vóór 1 december van het lopende jaar schriftelijk of per e-mail een opzegging heeft ontvangen. Hiervan ontvangt u een bevestiging.

Contributie NVT
Incl. abonnement TCDD 53,= euro
(extra kosten EEMS: 10,= euro)

Sluitingsdata kopij 2022
22 april, 30 september,
25 november

Kopijbus
redactie@toxicologie.nl

Website NVT
http://www.toxicologie.nl

Vormgeving
Marleen Mulder
Green Bean Design, Nunspeet
www.greenbeandesign.nl

TCDD
TOXICOLOGIE

Inhoud

3 Editorial/redactioneel

4 News from the board

5 Announcement for The Annual NVT Meeting

6 Nieuws van de Secties

8 A response to “A review of the Herzler et al. critical paper on the EU Chemicals Strategy for Sustainability” (TCDD no. 3 – 2021)

Special theme articles: Inhalation Toxicity

9 PE-PUR quality issues in respiratory medical devices, what is it about?

10 A Change of Air

11 When a cozy environment with candles and incenses can increase the exposure to a toxic chemical; formaldehyde

Overig

18 Proefschrift promopraatje by Ruiwen He

18 Toxafette by Kelly Niermans

20 Tox in het nieuws: Proposal to ban ‘forever chemicals’ in firefighting foams throughout the EU

25 Events and announcements

TERUG NAAR INHOUD

Editorial

Dear reader,

Welcome to a new TCDD, the first one of the year. We are only a couple of months in, but 2022 has already been more eventful than we would have liked. The developments between Russia and Ukraine are on all of our minds, and we fervently hope that the conflict will come to a peaceful solution soon.

In this TCDD themed ”inhalation toxicity”, we focus on the quality of the air we breathe. Various topics are included such as: What is the state of the art in *in vitro* inhalation testing, and how do household products such as scented candles influence the air quality in our homes? Furthermore, in the section “proefschriftpromopraatje” Ruiwen He from RIVM/IRAS elaborates on his work examining the air-liquid interface exposure of *in vitro* lung models to aircraft-related air pollutants. Also in this issue, three toxicologists from the industry comment on “A review of the Herzler et al. critical paper on the EU Chemicals Strategy for Sustainability”, as published in TCDD no. 3, 2021. Finally, there is news from the sections, and the Toxafette with Kelly Niermans from the Laboratory of Entomology and Wageningen Food Safety Research.

On behalf of the editorial team, we wish you an interesting read!

Sincerely,

Carolien Schophuizen

To breathe in life and breathe out

Like tomorrow is today

Breathe in life and breathe out

It's not so long to wait

Breathe in life and breathe out

Wipe the dust from your sweet smile

And breathe in life.

By: Lucie Silvas 2004

Photo by Jess Bailey on Unsplash

TERUG NAAR INHOUD

News from the board

Welcome to the spring 2022 edition of the TCDD. Spring is a time of hope, renewal and rebirth, yet we are now confronted with events in the world that are very distressing. Just as we seem to be emerging from a global pandemic, a war has started in the Ukraine. In response, EUROTOX has decided to suspend the Russian Society of Toxicologists' membership of EUROTOX with immediate effect, see also https://www.eurotox.com/.

As Board of NVT, our hearts go out to all those affected by the conflict in the Ukraine. I believe that the goals of our Society, which include promoting communication between toxicologists, and maintaining contacts with international organisations in the field of toxicology, were established on the basis of the principles of peace, respect, liberty, open dialogue and open cooperation. We hope for a timely solution to this conflict which speaks to these guiding principles.

Please let me remind you of our next annual meeting 'Green Deal: Toxicology Matter(s)', at conference centre 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**. All participants are encouraged to submit an abstract to present their research via a pitch or poster, please see the NVT site for more information.

Please also let me remind you of 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). It is still possible to register and submit abstracts. As mentioned on the site, ICT2022 'unites the best of toxicological scientists worldwide in the historical city of Maastricht.'

We look forward to seeing you in person in Ede on May 24-25th and in Maastricht in September.

All the best, Juliette Legler

NVT annual meeting

The Dutch society for toxicology (NVT) is organizing its annual NVT meeting on **Tuesday 24th and Wednesday 25th of May**. The theme of the annual meeting will be: **Green Deal – Toxicology matter(s)**.

The Green Deal is the EU's ambition for a "toxic-free" environment, which they hope to realize through the new Chemicals Strategy for Sustainability. How will this strategy impact the field of toxicology? And *vice versa*? In this year's annual meeting we will discuss the impact of the Chemicals Strategy for Sustainability on all fields of toxicology. Views from experts on this strategy will be provided through keynote lectures by dr. Matthias Herzler and prof. dr. Majorie van Duursen. We will also host a speaker session on Next-Generation Risk Assessment and Non-Standard endpoints, as well as several interesting workshops.

Join us for the member day on Tuesday the 24th of May and for the young scientist day on Wednesday the 25th of May in de Reehorst, Ede. We invite all participants to submit an abstract as to represent their research via pitch or poster. Registration and abstract submission will open on the 21st of February. The abstract submission will close on the 4th of April. More information regarding the NVT annual meeting will follow soon. All information, including the programme, regarding the meeting can be found on our website: www.meeting2022.toxicologie.nl.

Green Deal
Toxicology matter(s)

SECTION PHARMACEUTICAL TOXICOLOGY
AND SECTION RISK ASSESSMENT

Meeting: Tuesday, April 5, 2022

We hereby announce the meeting organized by the Dutch Society of Toxicology Section Pharmaceutical Toxicology and Section Risk Assessment.

TUESDAY APRIL 5, 2022

Leiden University Gorlaeus Lecture Hall C1
Address: Einsteinweg 57, Leiden
With an option for digital attendance

ONE SUBSTANCE – MULTIPLE ASSESSMENTS TITANIUM DIOXIDE CONSIDERED FROM A FOOD AND PHARMA PERSPECTIVE

[1] Taking into account the general corona rules for meetings that apply at that time, a physical meeting might not or only partially possible. In that case, the organizers decide to make it a fully virtual or hybrid meeting. You will be informed about it timely.

In this spring meeting of the NVT, the section Pharmaceutical Toxicology and the section Risk Assessment will give an overview of the challenges from various legal frameworks with regard to the principle of 'one substance - one assessment'. In support of the EU chemicals strategy for sustainability, the EU Commission is moving towards 'one substance – one assessment' principle. But how does this work across different regulatory frameworks? What are the differences in risk assessments and how might end-use of products be impacted? Should one regulate based on hazard or based on risk? Based on an example substance, titanium dioxide, regulatory and risk assessment considerations regarding 'one substance – one assessment' will be highlighted.

During the symposium there will be sufficient time to discuss and ask questions to the speakers and other attendees. We hope it will be an inspiring, thought-provoking, and informative meeting.

An invitation to register for this meeting will be sent in March 2022.

The annual Business meeting of the Section Pharmaceutical Toxicology will be held prior to the scientific program, starting at 13:00 hours. For the Business meeting a separate invitation will be sent.

Program

13:00 – 13.45	Business Meeting (only for members of the NVT section Pharmaceutical Toxicology)
13:45 – 14.00	Registration, coffee and tea
14.00 – 14.10	Welcome & Instructions *Day chairman: Susan Dekkers, TNO*
14:10 – 13.40	Introduction: one substance – one assessment *To be determined, RIVM representative*
14.40 – 15:10	Titanium Dioxide: regulatory and risk assessment aspects from a food perspective *Jacqueline Castenmiller, NVWA*
15:10 – 15:30	Break
15:30 – 16:00	Titanium Dioxide: regulatory and risk assessment aspects, and its implications from a pharma perspective *Kim Notenboom and Ira Koval, CBG*
16:00 – 16:30	Titanium Dioxide: Communication to patients *To be determined, KNMP*
16:30 – 16:50	Discussion & wrap-up
16:50 – 17:30	Social get together and drinks

A response to “A review of the Herzler et al. critical paper on the EU Chemicals Strategy for Sustainability” (TCDD no. 3 – 2021)

By Josje Arts, Chantal Smulders and Annette Wilschut (toxicologists working within industry)

“I wish toxicologists had only one hand, because they always say on the other hand…”, as once overheard from a legal counselor. Toxicology is not black and white, and thus professional views and expert judgment may differ. In TCDD no. 3 (October 2021), a review was published on a paper from the German Federal Institute for Risk Assessment (BfR; Herzler et al., 2021) on the EU Chemicals Strategy for Sustainability (CSS). We agree with the authors of the BfR paper that the CSS justification of several of the actions needed is based on public concern, and unfortunately not on solid scientific argumentation. Public concern is arguably a fair basis for political decision making; however, regulations need to be adapted as much as possible based on new, scientific insights. This is also underscored by representatives of the international scientific community in an editorial letter (Barile et al., 2021). Some of the statements made by the author of the TCDD paper need reflection from a toxicology perspective:

1. It is of pivotal importance to realize that we – as professionals in toxicology, regardless of the organization we are employed with – firmly share the purpose of protection of human health and the environment. Chemicals are designed to serve a performance or application need. Thus, they provide societal benefits and are not intended or designed to have any (adverse) impact on human health or the environment. It should be made clear that it is not in anyone’s benefit to bring or keep chemicals on the market that could pose a risk to human health or the environment. REACH is designed as such that as soon as a ‘chemical health threat is recognised’, immediate risk management measures are implemented.

2. The CSS foresees additional measures to address public concern on reproductive risks. According to the BfR, life expectancy and growth rate of the European population is high which does not indicate a fundamental problem; and thus, based on observed historical trends for life expectancy and population in the EU, chemical reproductive risks are sufficiently controlled. In the TCDD paper, in contrast, the suggestion is made that risks due to chemical exposure of the general population to reprotoxic chemicals are masked in epidemiology studies, e.g. by improved nutrition and healthcare. In our opinion, however, there are many confounding factors in epidemiological studies and attributing one cause (chemicals) or another (masking by more healthcare and improved nutrition) is equally speculative. Thus, if there are no solid data, any regulatory action will be based on (public) concern, and not on a causal relationship between exposure to chemicals and reproduction risks. It also underscores the concern of the authors of the BfR paper, that there is no scientific basis whether the additional measures proposed in the CSS will actually improve protection of human health and the environment. To be able to deliver on the objectives of the CSS a scientific basis for the regulatory measures is required, otherwise it will be difficult, if not impossible, to demonstrate any effect of these measures on human health and environment.

3. In the TCDD paper, it is indicated that industry has ‘multiple opportunities to intervene which causes delays’, and in case of going to ECHA’s Board of Appeal ‘usually results in a multiple-year delay’. It is acknowledged that the regulatory process could benefit from more agility, however, it is important for industry to be able to give feedback on ECHA decisions and to appeal. This is beneficial for the ▶

[1] D. van Berlo: “A review of the Herzler et al. critical paper on the EU Chemicals Strategy for Sustainability” (TCDD no. 3 – October 2021)

transparency of the process and the quality of the outcome. The recent publication from ECHA on all decisions of the Board of Appeal (ECHA, 2022) provides the informative insight that several appeal cases were made to avoid unnecessary animal testing and to comply with REACH article 25(1) to use animal testing only as a last resort.

It should also be noted that moments for appeal are limited; one cannot appeal on harmonized classification and labelling and on Substance of Very High Concern (SVHC) decisions. In addition, a lot of work is already done (incl. data generation) before any appeal, i.e. REACH registrations have been done, and full risk assessments have been carried out which has already resulted in risk management measures where needed.

4. We wonder what was meant with the statement that 'the intrinsic properties can also vary depending on the life cycle stage' as this seems to conflict with the basic principle of toxicology: the hazard is an intrinsic property, it is inherent to the chemical regardless of life cycle stage.

5. It is worth highlighting the great progress that has been made in recent years in predictive modelling of occupational and consumer exposure, which is not supporting the suggestion that 'data on exposure are virtually non-existent', although we acknowledge this area needs improvement in terms of covering all uses. Examples of models are the Advanced REACH Tool (ART; co-developed by TNO), ConsExpo (led by RIVM), and dermal uptake estimation derived from equations developed by Wil ten Berge. Also, ECHA has developed the Chesar tool that integrates hazard data (DNELs and PNECs) with the ECETOC TRA exposure model and other tools. The performance of these models has been studied using statistical approaches based on comparison of model outputs with measured data sets; some models have even been calibrated using exposure data. So, although it looks like many risk assessments of individual substances are lacking exposure data, the assessments are based on modeled data. Moreover, in several REACH dossiers the exposure assessment is based on measured data.

6. Following REACH, one can only market chemicals in the EU if safe use is demonstrated. Although the REACH information requirements for 'low tonnage' substances are limited compared to higher tonnage substances, this does not mean there is no information. As mentioned earlier, it is in no one's benefit to market substances which could pose a risk to human health or the environment. Thus, already at the design phase, as a standard practice in innovation processes, hazard assessments are done using *in silico* methods. Even more could be done by using the REACH database to develop 'big data' driven predictive toxicology tools (improved *in silico* methods) available to all companies. It is also important to realize the responsibility of the employer towards its employees in these discussions: even for low tonnage substances adequate information is needed to protect workers. Nevertheless, there is an opportunity to capitalize on the use of innovative non-animal hazard assessment methods to develop further insights in the possible hazards of low-tonnage substances.

7. Exposure to unintentional mixtures is a topic of debate and discussed in several publications. Many papers have been published on chemical mixtures indicating that low-dose combined exposures of REACH chemicals do not demonstrate synergistic effects (e.g. Kienhuis et al. 2015). In this regard we would also like to already draw your attention to the soon to be published results of a study commissioned by Cefic: with only a few exceptions, the toxicity of a mixture is well represented by the most toxic component(s). So far, in studies that were focused on the presence of chemicals at certain hotspots, the chemicals generally found were not REACH chemicals, but – besides the so-called legacy chemicals - substances regulated under different regulatory schemes such as pesticides and pharmaceuticals.

8. Regarding endocrine disrupting (ED) chemicals, such chemicals are already classified (and regulated) for the adverse effect linked to the ED mode of action (e.g. reproductive toxicity and ED, or carcinogenicity and ED). In addition, in case of substances with an ED mode of action for which adverse effects have been established during testing, risk assessment is performed based on NOAELs/ NOAECs resulting in safe use(s). In those exceptional cases where no safe use(s) can be obtained, a ban should be in place.

Conclusion

We conclude that REACH works (and the REACH reviews have concluded the same) as it has all the components to assess hazard, exposure and risk of chemicals and to take regulatory action as needed. The processes could, however, be made more efficient and there are some areas for improvement which could be worked on (like communication in the supply chain and understanding exposure scenarios). We concur that data generation is the cornerstone of any good assessment, both for hazard and risk. In this regard we would also like to refer to a recent paper by Doe et al. (2021) how to improve hazard assessment of CMR compounds to better select appropriate risk management options. The biggest dilemma to be addressed in data generation is animal testing as this should be the last resort. The CSS offers an opportunity to modernize the REACH approach to data generation and risk assessment, viz. the CSS strategy may offer opportunities to include the new and emerging non-animal hazard assessment methodologies as technology has progressed significantly since the inception of REACH. But such new ▶

regulations and guidance on chemical safety should be science based.

Coming back to the legal counselor in our introduction: luckily toxicologists have two hands, so we can offer one of ours to constructively collaborate to protect human health and the environment. ■

References (all freely available)

Barile F.A., Berry C., Blaauboer B., Boobis A. et al. (2021). The EU chemicals strategy for sustainability: in support of the BfR position. Arch. Toxicol. 95:3133–3136
Doe J.E., Boobis A.R., Cohen S.M., Dellarco V.L. et al. (2021). The codification of hazard and its impact on the hazard versus risk controversy. Arch. Toxicol. 95:3611-3621
ECHA (2022). https://echa.europa.eu/documents/10162/2314761/digest_of_decisions_of_boa_en.pdf/cad5c04e-1888-9ac3-5718-eb6f17a395a8?t=1642149879775
Herzler M., Marx-Stoelting P., Pirow R., Riebeling C. et al. (2021). The "EU chemicals strategy for sustainability" questions regulatory toxicology as we know it: is it all rooted in sound scientific evidence? Arch. Toxicol. 95:2589-2601
Kienhuis A.S., Slob W., Gremmer E.R., Vermeulen J.P., Ezendam J. (2015). A dose-response modeling approach shows that effects from mixture exposure to the skin sensitizers isoeugenol and cinnamal are in line with dose addition and not with synergism. Toxicol. Sci. 147:68-74

Special theme: Inhalation Toxicity

Door *Flemming Cassee*

Waar veel van ons zich specialiseren in één of meer orgaansystemen of werken op moleculair or cellulair niveau is inhalatietoxicologie een vakgebied waarbij meer dan gemiddeld aandacht wordt besteed aan de blootstelling. En dat heeft vooral te maken met het verschil tussen externe blootstelling – de concentratie in de lucht die je in ademt- en de daadwerkelijk biologische effectieve dosis. Wat je inademt heeft nog een lange weg te gaan, of juist niet. Er zijn daarbij een aantal fysische processen van belang. Voor gasvormige stoffen is diffusie het belangrijkste, terwijl voor vaste stoffen en druppeltjes ook nog de lading, de snelheid (impactie) en het gewicht (sedimentatie) bepalen in welke mate de stof waar terecht komt in de luchtwegen en longen. Hoewel er vaak wordt gesteld dat hoe kleiner hoe dieper het deeltjes kan doordringen is dat een versimpeling van de werkelijkheid omdat ook die hele kleine deeltjes waar je de laatste jaren steeds meer over hoort (ultrafijn stof, nanomaterialen, microplastics) op het neusepitheel terecht kunnen komen. Dit alles betekent dat je als inhalatietoxicoloog naast goed bekend zijn met de biologie/fysiologie ook kennis moet hebben van fysica. Voor elke blootstelling moet je weten hoe je de stof in de lucht krijgt en wat er dan in de lucht zit. Je moet de karakteristieken weten om met computermodellen de dosis te kunnen berekenen omdat alleen dan je resultaat van je *in vitro* of *in vivo* model goed te extrapoleren is naar de mens. Helaas zien we nog te vaak publicaties waarbij dit soort gegevens (deeltjes afmeting op basis aerodynamica of hydrodynamica, oppervlakte en aantallen, effectieve dichtheid en lading) niet worden gepresenteerd of vooral bij deeltjes er complexe handelingen worden uitgevoerd om een deeltje in een suspensie (aerosol, vloeistof) te krijgen (sonificeren, toevoegen eiwitten) waardoor het oorspronkelijke karakter geheel of gedeeltelijk is verdwenen. Dit zien we vooral wanneer er wordt gewerkt met 'submerged' celkweekmodellen. Veelal kan je met de gepresenteerde gegevens geen biologisch effectieve dosis berekenen en weet je eigenlijk niet goed wat nu de toxiciteit van de stof is. Met de mogelijkheden die er nu ook bij inhalatietoxicologie zijn voor het uitvoeren van *in vitro* 'air-liquid-interface' testen waarbij cellen direct aan de testlucht worden blootgesteld kan dit grotendeels worden voorkomen omdat je in ieder geval op een realistische manier je teststof in de lucht kan krijgen. Maar dan blijft nu nog de uitdaging om ook in dat soort systemen de dosis (snelheid) te bepalen. Ook hier wordt bij het RIVM aan gewerkt. Een toxicoloog weet het: de dosis is waar alles op draait, niet de concentratie.

Lees de bijbehorende artikelen ➔

PE-PUR quality issues in respiratory medical devices, what is it about?

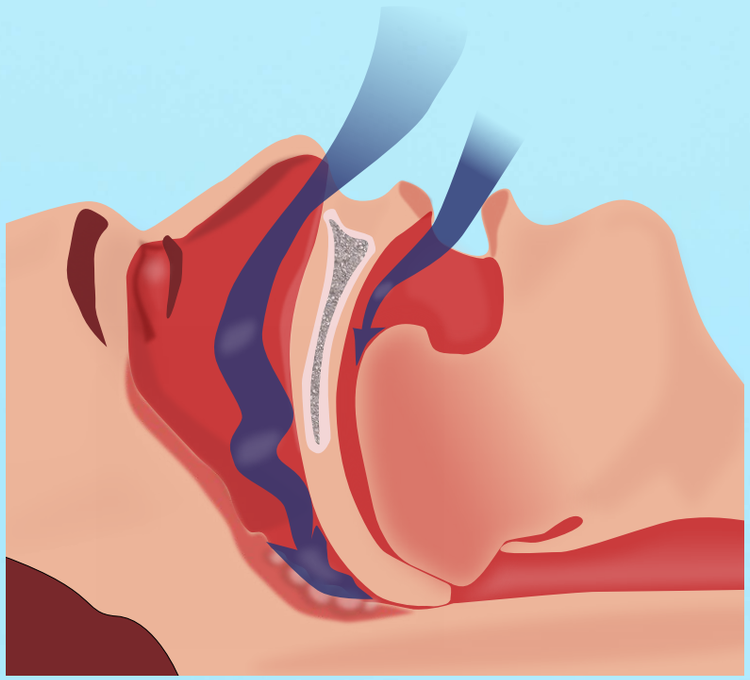
By *Carolien Schophuizen*

In June last year, Philips announced a worldwide recall of millions of copies of apnea ventilators due to health risks. The ventilators are crucial for people who suffer from sleep apnea. The machine ensures that breathing continues by pumping in air. The potential harm is in the foam inside the machines, which may disintegrate and thereby release potentially harmful gases. [6]

Injected polyurethane (PUR) foam and polyester polyurethane (PE-PUR) are commonly used insulation materials which can be applied in homes, and are also used to reduce noise or vibration of various devices. Polyurethane foam based on polyester was first introduced to the market in 1937. [1, 4]

The release of toxic gasses from insulating foam has been an issue that has been recognized before. Research by TNO in 2013 in which air samples were taken, indicated that a causal relationship between PUR-foam house isolation and resident health complaints is unlikely, though it could not be completely ruled out.[8] PUR foam is created by a chemical reaction of two components that harden. One component consists of isocyanates and the other component is a mixture of mainly polyols, catalysts, blowing agents and flame retardants. It is very important that the chemical reaction in the formation of PUR foam proceeds well and that the foam hardens well. Isocyanates can then no longer be released. However, the volatile organic compounds (VOCs) or blowing agents remain in PUR foam. These are released slowly and in low concentrations, even with well cured foam. There are no concrete indications that blowing agents are harmful to health, but the possible consequences of long-term exposure have only been investigated to a limited extent. In 2020 the Dutch Health Council has advised that research into these substances in PUR (VOC blowing agents, such as isocyanates) should also be carried out. [3]

Isocyanates are starting materials for PE-PUR foams. Exposure to isocyanates occurs mainly in industry, including construction (e.g. post-insulation), automotive, shipbuilding, painting, plastics manufacturing and electronics manufacturing. Exposure of the general public may occur when insulating PE-PUR foams used in house insulation or household product degrades, but exposures are generally low. [3, 5]



Isocyanates are a family of chemical compounds characterized by high reactivity and low molecular weight. Isocyanate exposure most commonly results in respiratory problems. These respiratory effects range from shortness of breath and dry cough to asthma, bronchitis and pneumonia, depending on the duration of exposure. Respiratory sensitsation may also occur, though no clear threshold or a dose-response relationship is available. A few studies indicate a potential for neurotoxic effects in humans exposed to diisocyanates. The data are however inadequate to establish a causal association between isocyanates and neurotoxicity. No indications of neurotoxicity have been observed in animal studies.[2]

Research has also linked isocyanate exposure to cancer. Based on the available data, some studies indicate that isocyanates may cause genotoxicity. The study results are however inconclusive/equivocal. Though evaluation of ▶

studies has not resulted in the explicit listing of PE-PUR foam as a carcinogen, (di)isocyanates are CLP-classified as Carcinogenicity Category 2; Suspected of causing cancer. Further research into the carcinogenic potential of PE-PUR foam, is therefore warranted. [2]

In the Philips ventilators polyester-based polyurethane (PE-PUR) sound-absorbing foam is present. Next to off-gassing, this PE-PUR foam may degrade into particles, which may enter the device's air pathway and be ingested or inhaled by the user. According to Philips Respironics, the affected devices were evaluated by an external medical panel, and they indicated that exposure to the amount of VOCs identified (for the first generation devices) is not expected to result in long-term health consequences for patients. According to Philips Respironics, various toxicological VOC risk assessments have been performed by certified testing laboratories and a qualified external expert based on the initial and new VOC tests performed to date. Philips Respironics has made this data available to the FDA and other competent authorities, and is in the process of sharing this data with healthcare professionals and patients. [7]

The full investigation and analysis related to the foam particles is expected to be completed in the second quarter of 2022, as test protocols to fully comply with the requirements of the relevant ISO standards for all affected devices require a long lead time of several months. ■

1. Bayer, O., Siefken, W., Rinke, H., Orthner, L., et al., A process for the production of polyurethanes and polyureas. German Patent DRP, 1937. 728981: p. 13.
2. ECHA, Scientific report for evaluation of limit values for diisocyanates at the workplace. 2019. p. 1-182.
3. Gezondheidsraad, Gespoten PUR-schuimisolatie en gezondheid. . 2020, Gezondheidsraad: Den Haag
4. Harris, J.C., Rumack, B.H., and Aldrich, F.D., Toxicology of Urea Formaldehyde and Polyurethane Foam Insulation. JAMA, 1981. 245(3): p. 243-246.
5. ISOPA, Socio-economic contribution of the polyurethane industry to growth and jobs in Europe. European Diisocyanate and Polyol Producers Association, 2014: p. 1-18.
6. Philips. Medical Device Recall Notification, Philips Respironics Sleep and Respiratory Care devices, Device registration and recall contact information. 2021; Available from: https://www.usa.philips.com/healthcare/e/sleep/communications/src-update.
7. Philips, Philips provides update on the test and research program in connection with the CPAP, BiPAP and Mechanical Ventilator recall notification. 2021.
8. TNO rapport TNO2013 R11049. Evaluatie van gezondheidsrisico's voor bewoners op basis van metingen in woningen tijdens en direct na aanbrengen van SPF-vloerisolatie. Opdrachtgever: Nuon Isolatie BV (thans United Energy Works Isolatie BV). 2013.

A Change of Air - Moving from *in vivo* inhalation toxicity studies to *in vitro* alternatives

By *Barae Jomaa and Hedwig Braakhuis*

Rodent models are the gold standard for chemical toxicity testing despite the fact that they differ from humans in anatomy, physiology and metabolism. It gets even more complicated when ethical concerns and high cost are factored in. An acute inhalation toxicity study in rats costs an estimated US$32,300 while a 90-day inhalation toxicity study in rats costs an estimated US$601,600 (EPA 2019). A step-wise testing strategy typically begins with computational approaches then moves on to simple cell-based *in vitro* methods before going to more complex cell-based methods and, if required, a more refined animal test.

In vitro lung models are usually based on a layer of epithelial cells to which immune cells, endothelial cells and/or fibroblasts can be added to enhance physiological relevance of the model. Depending on the region of the lung that is being studied, either bronchial or alveolar epithelial cells are being used. These cells can originate from an immortalized cell-line or primary cells can be used, either directly from patients or from a commercial source. The general thought is that by enhancing the physiological relevance (and complexity) of the model, the predictivity of the model is being increased (Lacroix et al. 2018, Marescotti et al. 2019).

This paper will be covering some of the most promising *in vitro* inhalation toxicity test methods available today.

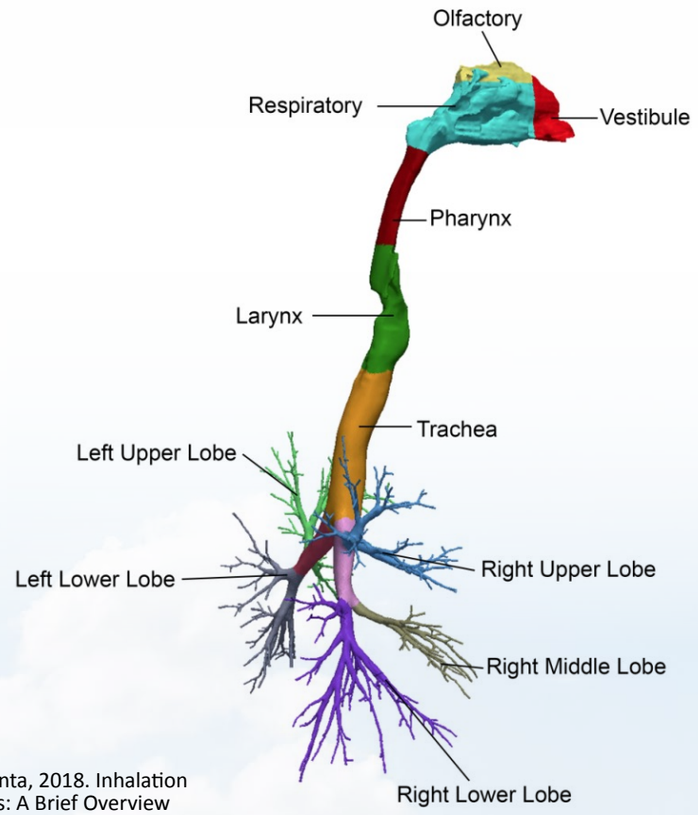


Figure 1: Human respiratory tract. Image source: Syngenta, 2018. Inhalation Risk Assessment Using Computational and *In Vitro* Tools: A Brief Overview

Nasal/Tracheal/Bronchial

Epithlix's MucilAir™ is an *in vitro* cell model of the human airway epithelium cultured at the air liquid interface. It is reconstituted using human primary cells at low passage and from different anatomical sites (Nasal, Tracheal or Bronchial).

Tracheal/Bronchial

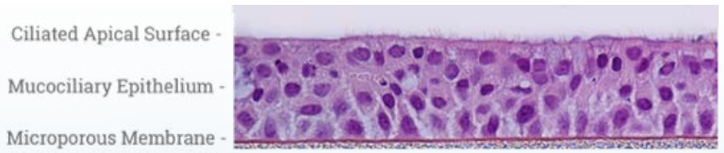


Figure 2: EpiAirway tissue model. Image credit: MatTek

MatTek's EpiAirway™ is a 3D mucociliary tissue model consisting of normal, human-derived tracheal/bronchial epithelial cells. According to MatTek, as the model is cultured at the air-liquid interface (ALI) it mimics the *in vivo* phenotypes of barrier, mucociliary responses, infection, toxicity responses and disease. EpiAirway is amenable to ▶

acute or long-term chronic studies with its 3D structure consisting of organized Keratin 5+ basal cells, mucus producing goblet cells, functional tight junctions and beating cilia.

Alveolar

EpiAlveolar is a 3D co-culture model of the air-blood barrier. According to the manufacturer, they are produced from primary human alveolar epithelial cells, pulmonary endothelial cells and fibroblasts, EpiAlveolar is an *in vitro* model system developed to mimic human-relevant biological responses. The epithelium exhibits functional tight junctions and a robust barrier that remains stable for studies lasting more than 30 days.

Figure 3: EpiAlveolar tissue model. Image credit: MatTek

Exposure

In traditional toxicity testing, cells are cultured submerged in culture medium and substances are exposed via this culture medium. However, in our lungs, we are exposed to compounds via the air. By adding substances to a culture medium, characteristics change and the results of this kind of experiments might not be predictive for the real situation. Therefore, advanced lung models are now being exposed at the air-liquid interface (ALI). This means that the cells are cultured on a porous membrane with culture medium at the basolateral side and no fluid at the apical side, thereby mimicking the situation in the lungs. Air-liquid interface models allow for more realistic toxicity testing of airborne materials. Several different exposure methods are used to apply the test compounds, ranging from cloud systems that use a nebulizer to continuous flow systems. One of the challenges of air-liquid exposure is the need for specialized equipment and the relatively low deposition of substances on the cells. In submerged cultures, one can expose up to mg/ml, while using aerosol exposure the deposition is usually in the range of ng/cm^2 or maximum of a couple of microgram/cm^2 (for particles). These deposited doses are more realistic compared to real exposure; however, they might be too low to detect the effect of substances. In some studies, the models are therefore exposed 'quasi-ALI' by adding the test substance in a very small volume.

Lung surfactant function

Lung surfactant or pulmonary surfactant is a surface-active complex of proteins and phospholipids produced in type II alveolar cells. This important complex decreases surface tension and increases the ability of the lungs to expand. It also prevents the collapse of alveoli at the end of expiration. Clearly, inhaled compounds that interfere with lung surfactant function could lead to severe lung conditions. Jorid B Sørli et al. have introduced a novel *in vitro* method to study lung surfactant functionality after aerosol exposure (Sørli et al. 2016). Such a method could prove invaluable as part of an integrated testing strategy which includes cellular models from relevant anatomical sites of the respiratory tract.

Future developments

Similar to other alternative models, the main challenge for implementation of *in vitro* lung models is their predictivity. Further unravelling the mechanism of toxicity, for example by using adverse outcome pathways, might help understand the link between measurement of cellular effects and the occurrence of toxicity at the organ level. To measure these mechanisms at a cellular level, physiologically-relevant lung models are likely the way forward. The above-mentioned primary models can be optimized by including macrophages and/or fibroblasts. Another recent development includes movement of the lung models to mimic breathing (Dos Santos Rocha et al. 2022, Cei et al. 2021). Applying mechanical strain affects cell behaviour and the cellular response to an exposure. Finally, it is generally assumed that for predicting long-term effects, *in vitro* models should also be exposed for a longer period of time. The use of primary models allows for this, as these cells can be cultured and exposed for weeks. All these developments might further enhance the predictivity of the *in vitro* models. ▶

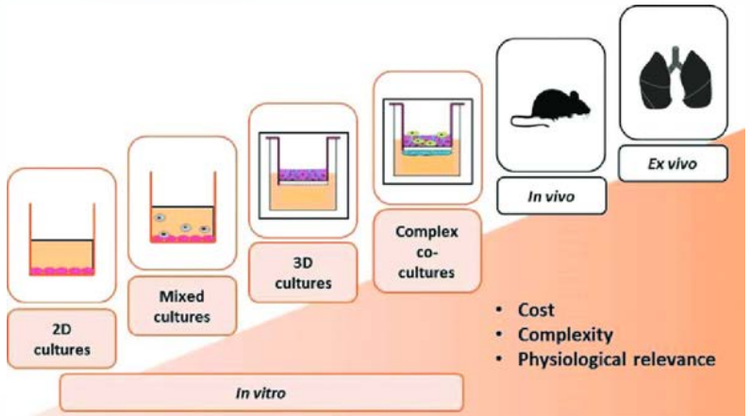


Figure 4: Respiratory models, from simple to complex.
Image credit: Lacroix et al. 2018

Relevant publications
Lacroix G, Koch W, Ritter D, Gutleb AC, Larsen ST, Loret T, Zanetti F, Constant S, Chortarea S, Rothen-Rutishauser B, Hiemstra PS, Frejafon E, Hubert P, Gribaldo L, Kearns P, Aublant JM, Diabaté S, Weiss C, de Groot A, Kooter I. Air-Liquid Interface *In Vitro* Models for Respiratory Toxicology Research: Consensus Workshop and Recommendations. Appl *In Vitro* Toxicol. 2018 Jun 1;4(2):91-106. doi: 10.1089/aivt.2017.0034. PMID: 32953944; PMCID: PMC7500038.

Dos Santos Rocha A, Petak F, Carvalho T, Habre W, Balogh AL. Physiologically variable ventilation prevents lung function deterioration in a model of pulmonary fibrosis. J Appl Physiol (1985). 2022 Feb 24. doi: 10.1152/japplphysiol.00670.2021. Epub ahead of print. PMID: 35201935.

Soriano L, Khalid T, O'Brien FJ, O'Leary C, Cryan SA. A Tissue-Engineered Tracheobronchial *In Vitro* Co-Culture Model for Determining Epithelial Toxicological and Inflammatory Responses. Biomedicines. 2021 Jun 2;9(6):631. doi: 10.3390/biomedicines9060631. PMID: 34199462; PMCID: PMC8226664.

Artzy-Schnirman A, Hobi N, Schneider-Daum N, Guenat OT, Lehr CM, Sznitman J. Advanced *in vitro* lung-on-chip platforms for inhalation assays: From prospect to pipeline. Eur J Pharm Biopharm. 2019 Nov;144:11-17. doi: 10.1016/j.ejpb.2019.09.006. Epub 2019 Sep 6. PMID: 31499161; PMCID: PMC7611793.

Marescotti D, Serchi T, Luettich K, Xiang Y, Moschini E, Talikka M, Martin F, Baumer K, Dulize R, Peric D, Bornand D, Guedj E, Sewer A, Cambier S, Contal S, Chary A, Gutleb AC, Frentzel S, Ivanov NV, Peitsch MC, Hoeng J. How complex should an *in vitro* model be? Evaluation of complex 3D alveolar model with transcriptomic data and computational biological network models. ALTEX. 2019;36(3):388-402. doi: 10.14573/altex.1811221. Epub 2019 Feb 12. PMID: 30753736.

Cei D, Doryab A, Lenz AG, Schröppel A, Mayer P, Burgstaller G, Nossa R, Ahluwalia A, Schmid O. Development of a dynamic *in vitro* stretch model of the alveolar interface with aerosol delivery. Biotechnol Bioeng. 2021 Feb;118(2):690-702. doi: 10.1002/bit.27600. Epub 2020 Nov 4. PMID: 33058147.

EPA. 2019. "Cost Estimates of Studies Required for Pesticide Registration." https://www.epa.gov/sites/default/files/2019-07/documents/studies-cost-estimates-jul-2019.pdf.

Sørli, Jorid B., Emilie Da Silva, Per Bäckman, Marcus Levin, Birthe L. Thomsen, Ismo K. Koponen, and Søren T. Larsen. 2016. "A Proposed *In Vitro* Method to Assess Effects of Inhaled Particles on Lung Surfactant Function." *American Journal of Respiratory Cell and Molecular Biology*

54 (3): 306–11. https://doi.org/10.1165/rcmb.2015-0294MA.

TERUG NAAR INHOUD

Ciliated apical surface of EpiAirway™
Image credit: MatTek

When a cozy environment with candles and incenses can increase the exposure to a toxic chemical; formaldehyde

By *Héloïse Proquin*

When we talk about inhalation toxicology, what first comes to mind is particulate matter from exhaust pipes and emission from industry but one very important source of exposure to compounds is the house where we live in. Because it is our own home, which feels like a safe place, many people do not think that they can be exposed to a larger number of compounds at home than outside.

Among the many compounds found in houses, from burning gas, wood or using sprays,… we would like to focus on a known one, formaldehyde a.k.a. CH_2O coming from the candles and incents.

Candles are, for the majority of them, made with paraffin as a major compound. Paraffin is a petroleum by-product. Paraffin wax was introduced in the 1850's when chemists were able to separate a naturally-occurring waxy substance from petroleum and refine it[1]. It was a major advancement in the production of candles because the paraffin, being odorless and bluish-white color, burned cleanly, consistently and was more economical to produce than any other candle fuel.

Incenses are made from a wide variety of substances, including resins, aromatic substances, essential oils, and synthetic chemicals[2]. While these incenses are burning they would emit a variety of (toxic) chemicals. In some countries like China, burning incenses is very important in the culture, therefore the concentrations measured in the houses can be higher than in other countries.

Formaldehyde is a known by-product produced from burning candles/incense[3,4]. Concentrations after burning a candle can range form 2-50 µg/cm³ for a scented candle, 5-50 µg/cm³ for an incent stick, and 15-60 µg/cm³ for a incense cone. Measurements made in houses in China show a mixing ratio of formaldehyde of 103 ppbv in the home during incense burning. These values exceed the World Health Organization (WHO) air quality guideline of 100 $\mu g.m^{-3}$ (88 ppbv) for formaldehyde[4]. When a candle and incense are compared, an incense releases higher concentrations of formaldehyde than a candle[3,4,5].

According to the harmonised classification and labelling (ATP06) approved by the European Union, formaldehyde is "toxic if swallowed, is toxic in contact with skin, causes severe skin burns and eye damage, is toxic if inhaled, may cause cancer, is suspected of causing genetic defects and may cause an allergic skin reaction"[6].

Candles and incense are not the only source of formaldehyde in a home environment: pressed-wood products containing formaldehyde resins, cigarette smoke and the use of unvented fuel-burning appliances, such as gas stoves, wood-burning stoves, and kerosene heaters[7].

In order to reduce in-house exposures, some simple actions can have a very big impact. Corona pandemic taught more people to ventilate their house regularly, it would be good to continue informing the public that ventilation is essential in a house to be able to reduce exposure to (potentially) dangerous compounds[5]. This is the best way and for now the only efficient way to improve air quality in the house because some sources, like fuel burning appliances, are difficult to remove.

References:

[1] Website: https://candles.org/history/#:~:text=With%20the%20introduction%20of%20mechanized,from%20petroleum%20and%20refine%20it. Visited 22 february 2022.

[2] Zhang J., Chen W., Li J., Yu S., Zhao W., VOCs and Particulate Pollution due to Incense Burning in Temples, China, Procedia Engineering, Volume 121, 2015, Pages 992-1000, ISSN 1877-7058, https://doi.org/10.1016/j.proeng.2015.09.067.

[3] Petry T, Cazelle E, Lloyd P, Mascarenhas R, Stijntjes G. A standard method for measuring benzene and formaldehyde emissions from candles in emission test chambers for human health risk assessment purposes. Environ Sci Process Impacts. 2013 Jul;15(7):1369-82. doi: 10.1039/c3em00011g. PMID: 23695106.

[4] Ho, S. S. H., & Yu, J. Z. (2002). Concentrations of formaldehyde and other carbonyls in environments affected by incense burning. Journal of Environmental Monitoring, 4(5), 728–733. doi:10.1039/b200998f

[5] François Maupetit, Fabien Squinazi . Caractérisation des émissions de benzène et de formaldéhyde lors de la combustion d'encens et de bougies d'intérieur : élaboration de scénarios d'exposition et conseils d'utilisation. Environnement, Risques & Santé. 2009;8(2):109-118. doi:10.1684/ers.2009.0235

[6] ECHA, formaldehyde, 2022 https://echa.europa.eu/nl/substance-information/-/substanceinfo/100.000.002

[7] NIH, formaldehyde fact sheet: https://www.cancer.gov/about-cancer/causes-prevention/risk/substances/formaldehyde/formaldehyde-fact-sheet

Air-liquid interface exposure of *in vitro* lung models: Improvement and application to study inhalation toxicity of aircraft-related air pollutants

By *Ruiwen He*

On September 14, 2021, I finished my PhD thesis defense entitled “Air-liquid interface exposure of *in vitro* lung models: Improvement and application to study inhalation toxicity of aircraft-related air pollutants”. I performed my PhD under the supervision of Prof. Flemming Cassee and Dr. Remco Westerink at National Institute for Public Health and the Environment (RIVM) and Institute for Risk Assessment Sciences (IRAS) at Utrecht University.

Thesis Summary:

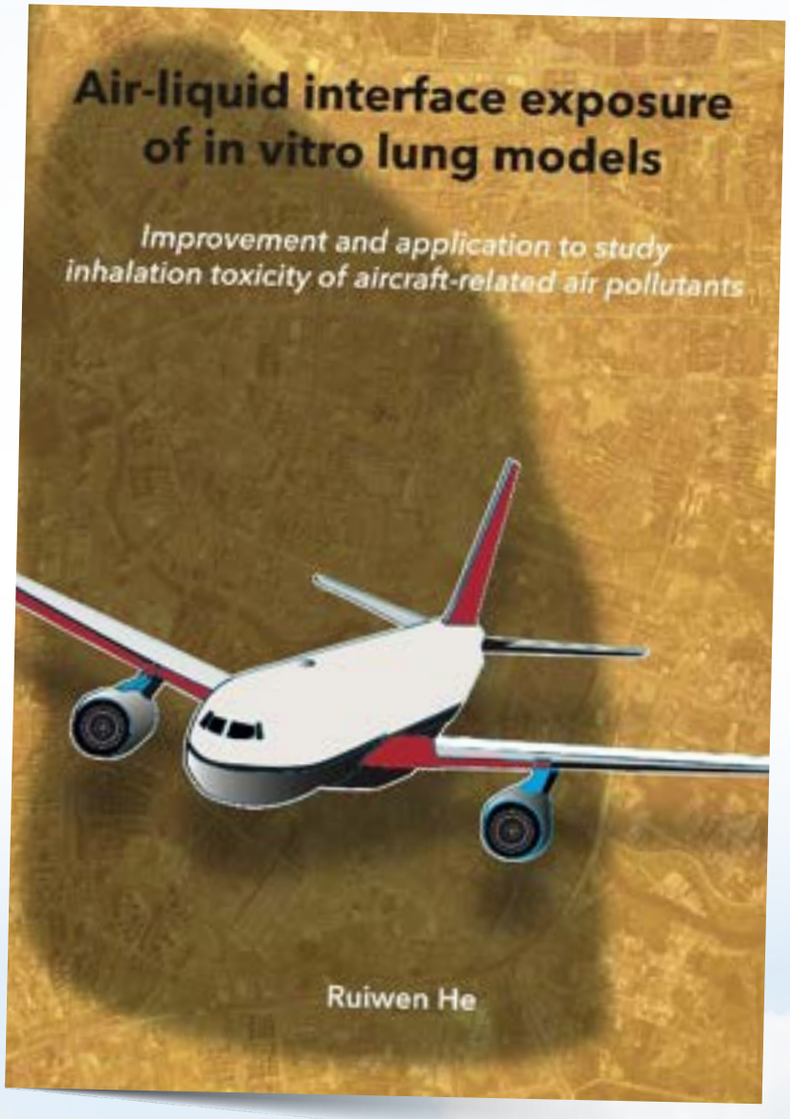
Since the aviation industry has expanded rapidly over the past decades, aircraft-related air pollution, including airport ultrafine particles (UFPs) pollution and aircraft cabin bleed-air contamination, is considered as an increasing global problem for human health. Exposure to UFPs in/near airports for airport personnel and surrounding residents as well as to bleed-air contaminants in aircraft cabins for aircrews and passengers may be related to a wide spectrum of public health problems. However, scientific information on toxicity of those air pollutants is still incomplete and thus needs to be further investigated. *In vitro* toxicity testing models using direct exposure to air pollutants have gradually become available, avoiding extensive investigations in experimental animals. To realistically mimic inhalation exposure, lung cell models need to be continuously exposed to test atmospheres under air-liquid interface (ALI) conditions. Some of the lung epithelial cell models involve co-culturing with macrophages to construct physiological traits that closely resemble *in vivo* lung epithelium in response to inhaled particles. However, many immortalized cell lines do not remain viable over long-term ALI culture. Careful selection of *in vitro* lung models that meet the aims for ALI exposure is therefore required. The main goal of my PhD study is to optimize *in vitro* lung models under prolonged ALI culture conditions for investigating the adverse health effects of air pollutants that are emitted by and in aircrafts.

In my PhD work, I studied the physicochemical characteristics, potential sources, and *in vitro* toxicity of PM0.25 collected from airport emissions (downwind Los Angeles International Airport), in comparison to well-analyzed urban traffic emissions. Aircraft emissions were found as the major contributor to the total PM0.25 mass collected from airport emissions. Compared to airport PM, urban traffic PM samples had a more complex elemental composition, suggesting multiple emission sources. To test toxicity of PM0.25 from airport and urban traffic emissions *in vitro*, human bronchial epithelial 16HBE cells were exposed to PM0.25 suspension at 10 μg/mL under submerged conditions. *In vitro* toxicological results indicate that PM0.25 from airport and urban traffic emissions can increase the generation of reactive oxygen species (ROS) and induce pro-inflammatory responses in the bronchial epithelial cells, eventually resulting in cell death. Compared to urban traffic PM, *in vitro* exposure to ▶

airport PM increases higher production of pro-inflammatory mediators in the cells probably due to their smaller size range. These findings highlight the potential health risks of aircraft emissions as a major source of PM0.25 in airport surroundings.

In the meantime, I optimized the *in vitro* mono-/co-culture cell model of human airway barrier under ALI conditions for aerosol exposure. Human bronchial epithelial Calu-3, 16HBE, H292 and BEAS-2B cell lines were evaluated regarding epithelial morphology, barrier function and cell viability over long-term ALI culture. Only Calu-3 cells can exhibit a monolayer structure and maintain a strong barrier function with high cell viability at least up to 2 weeks. Therefore, Calu-3 cells were used as structural barrier to create different co-cultures with monocyte-derived macrophages (MDM) and THP-1 derived macrophages (TDM). Following optimization of the protocol for co-culture, adhesion of macrophages onto the epithelial carpet was allowed for 4 hours with a seeding density of 5×10^4 macrophages/cm^2. When challenged with lipopolysaccharide (LPS) as a positive control, the two co-culture models showed higher sensitivity in inflammatory responses compared to the monoculture of Calu-3 cells, in which the co-culture of Calu-3 + MDM gave a stronger response than the Calu-3 + TDM. Therefore, the optimized monoculture of Calu-3 cells and co-culture of Calu-3 + MDM were used in my following studies for testing toxicity of airport UFPs as well as fumes generated from aircraft engine oils and hydraulic fluids toxicity.

I separately collected UFPs predominantly derived from airport emissions (Airport UFPs) or traffic emissions (Non-Airport UFPs) at a location near Amsterdam-Schiphol airport (AMS), depending on wind directions, with my colleagues' help. The mean size of Airport and Non-Airport samples in suspension falls within the ultrafine range (particle size < 100 nm). Using a cloud exposure system (CES), the optimized monoculture of Calu-3 cells was exposed under ALI conditions to Airport and Non-Airport UFPs, ranging from 0.09 to 2.07 µg/cm^2. ALI exposures revealed that pro-inflammatory responses can be induced in the lung cells at high viabilities (> 80%) after exposure to Airport and Non-Airport UFPs at doses > 0.09 µg/cm^2. Airport and Non-Airport UFPs exerted a comparable *in vitro* toxicity in the Calu-3 cells under ALI exposure conditions. Afterwards, I investigated toxic effects of exposure to cabin bleed-air contaminants under ALI conditions. To realistically mimic inhalation exposure to cabin bleed-air contaminants and subsequently evaluate their toxicity *in vitro*, a mini Bleed-Air Contaminants Simulator (Mini-BACS) system was connected to an aerosol exposure system (AES). This unique combination integrates generation of fumes from aircraft engine oils and hydraulic fluids under controlled conditions, deposition of fumes onto lung cell models with a continuous airflow, and online physicochemical measurements of test atmospheres. The obtained results indicate that exposure to high levels of engine oil and hydraulic fluid fumes under ALI conditions can reduce TEER and cell viability, induce LDH release and increase the production of pro-inflammatory cytokines in the Calu-3 monoculture and Calu-3 + MDM co-culture models. Hydraulic fluids fumes are more toxic than engine oil fumes, likely due to higher abundance of organophosphates (OPs) and smaller particle size distribution (PSD) of hydraulic fluid fumes. Taken together, these *in vitro* toxicological data from my PhD study reveal that exposure to aircraft-related air pollutants, airport UFPs and the generated cabin fumes, can induce considerable lung toxicity, highlighting their potential inhalation risks under real-life exposure conditions. ■



AIO toxafette - Kelly Niermans

Can you introduce yourself?
Hi, I'm Kelly Niermans and I'm originally from Ilpendam which is a tiny town right above Amsterdam. I studied Nutrition and Dietetics, and did some cool internships during that time which made me realize I really wanted to continue with a master in Food Safety. To finalize my studies, I did in internship in the BfR in Germany, which is the German Foody Safety Institute. After I graduated, I stayed there for another half-a-year to finalize my project and then I moved to Parma to do a one-year-traineeship in EFSA. After those adventures I moved back to Wageningen to start a PhD at the Laboratory of Entomology and Wageningen Food Safety Research. This PhD is part of the InsectFeed consortium where we investigate the possibility to use insects as sustainable feed for a circular economy. In this consortium we study many different topics, like the ethics and welfare of insect production, insect immunology and behavior, among others, but I focus on whether we could upgrade low-quality contaminated, with mycotoxins in particular, side-streams into high-quality insect protein and lipids.

How would you explain the subject of your research to a layperson?
Mycotoxins are toxic compounds that are produced by specific types of moulds (fungi) and they can affect human and animal health severely, therefore we don't want them present in our food or feed. Contamination with moulds that produce these mycotoxins is affected by, for example, non-ideal storing conditions of harvested crops, climate change and is especially a problem in countries with a warmer humid climate. This makes mycotoxin contamination of crops also an economical issue as a lot of crops that are highly contaminated need to be destroyed. From previous research it seems that certain larvae of insects, can still grow very well on feed substrates that are contaminated with mycotoxins and that they do not seem to take up these mycotoxins in their bodies. We therefore want to try to figure out whether we could use insect larvae to transform these low-quality contaminated substrates into safe insect protein and lipids and could reduce the concentrations in the feed residues to become safe.

What was your motivation to start a PhD program?
During the time I have spent in Food Safety institutes I realized that the jobs that I like all require a PhD, so that would be the practical reason of why I wanted to start one. Further, I was really happy when I saw that this PhD topic was offered, because funnily enough, this was the exact topic I also worked on during my time in the BfR and which I became really passionate about.

Why did you choose a subject in toxicology?
I like the field of toxicology because I believe that it is very important to understand the effects caused by chemicals, substances and the mechanisms behind this. There are still so many questions left that I believe that every answered question has a big impact.

How do you see the future of your research topic (follow-up research / social impact)? What do you hope for?
Of course, we still need more research to prove whether using insects this way is really safe. But I really believe that, if we manage to prove this is safe, we could provide, for example, farmers an opportunity to transform their mycotoxin contaminated crops into something valuable rather than having to destroy their harvest. Besides that, it's really fun and easy to grow insects.

What is the best advice that you have received as a PhD student or would like to give to another PhD student?
Never compare your progress with anyone else. Every PhD project is different and it would therefore not be fair to yourself to make this comparison. ▶

What goals do you have regarding your career after finishing your PhD? Would this be inside or outside academia, and why? Would you consider going abroad?
I would like to keep working in the Food Safety field, maybe in one of the Food Safety Institutes and I'm definitely open for more adventures abroad.

Please answer the question from the last toxafette PhD-candidate: "What would you investigate if you had unlimited resources?"
If I had unlimited resources, I would set up a huge experiment in which I would not only study what I need to do for my PhD, but also whether we could use other side-streams like food waste from households or restaurants, manure and other organic streams to grow insects and study all possible microbiological, chemical and physical hazards to figure out whether insects could really be, at least partly, the solution to some of the issues we're facing.

Could you propose a question for the next PhD-candidate for the Toxafette?
Question: if everything is possible, what would you like to do during your PhD? ■

Proposal to ban 'forever chemicals' in firefighting foams throughout the EU

The European Chemicals Agency brings forward a proposal for an EU-wide restriction on all per- and polyfluoroalkyl substances (PFASs) in firefighting foams. The restriction would prevent further groundwater and soil contamination and health risks for people and the environment.

ECHA/NR/22/05

TERUG NAAR INHOUD

Helsinki, 23 February 2022 – ECHA has investigated the environmental and health risks posed by the use of PFASs in firefighting foams at the request of the European Commission. The Agency concluded that an EU-wide restriction is justified as the risks posed by PFASs are currently not adequately controlled and releases should be minimised.

Firefighting foams containing PFASs have caused many cases of environmental contamination in the EU, both in soil and drinking water. All PFASs, or their breakdown products, are very persistent and some are known to harm human health or the environment. The combination of persistence and the potential to cause harm means that it is important to minimise further releases of these substances to reduce the likelihood of, potentially irreversible, harm in the future.

ECHA has assessed the strengths and weaknesses of five different options to control the risks of PFASs in firefighting foams. The proposed option would **ban the placing on the market, use and export of all PFASs in firefighting foams** after use or sector-specific transition periods. These transition periods would give time for industry to replace PFAS-containing foams without compromising fire safety. During the transition periods, those still using PFAS-based foams will have to ensure that releases to the environment are minimised. Expired foams and any waste foams would also need to be appropriately disposed.

If adopted, the restriction could reduce emissions of PFASs into the environment by more than 13 000 tonnes over 30 years. The estimated costs to society would be around EUR 7 billion over the same period. These costs include, among others, the price of modifying equipment for using PFAS-free foams, the cleaning of equipment to remove PFAS foam residues and the price difference between PFASs and alternative foams.

The proposal is based on information that was available at the time it was prepared and can be updated if new information comes to light. A six-month **consultation is planned to start on 23 March 2022** that is open for anyone to give evidence-based comments on the proposal. ECHA will also organise an **online info session on 5 April** to explain the restriction process and help those interested to take part in the consultation.

Additionally, five European countries (The Netherlands, Germany, Denmark, Sweden and Norway) are working on a restriction proposal that will cover all PFASs in other uses. They are planning to submit their proposal to ECHA in January 2023. The risk assessment introduced in the proposal to restrict PFASs in firefighting foams is relevant for all PFASs. This means that it will also pave the way to assessing risks in the wider PFAS restriction.

Next steps

ECHA's scientific Committees for Risk Assessment and Socio-Economic Analysis will now start assessing the proposed restriction options. In their assessment, they will consider the scientific evidence received during the consultations. The combined opinion of the two committees is expected in 2023. Together with the 27 EU Member States, the European Commission will take the decision on the restriction and its conditions – based on the proposal and the committees' opinion.

Background

The EU's chemicals strategy for sustainability places PFAS policy front and centre. The European Commission commits to phasing out all PFASs, allowing their use only where they are proven to be irreplaceable and essential to society. The restriction proposal on PFASs in firefighting foams is mentioned in the strategy as one action to further limit the use of PFASs. ■

Uniting in toxicology

ICT2022
THE XVITH INTERNATIONAL
CONGRESS OF TOXICOLOGY
MAASTRICHT, THE NETHERLANDS
SEPTEMBER 18-21,2022

It is with great pleasure that the Dutch Society of Toxicology (NVT) is inviting you to the XVIth International Congress of Toxicology in Maastricht, the Netherlands, from September 18 to 21, 2022. This congress is jointly organized with the International Union of Toxicology (IUTOX) and the European Society of Toxicology (EUROTOX), and unites the best of toxicological scientists worldwide in the historical city of Maastricht.

When we chose **'Uniting in Toxicology'** as theme of the congress, we could hardly have imagined how appropriate it would be and how much we would be longing to re-unite after a long period of separation due to the COVID-19 pandemic. In order to make this re-union a memorable and unforgettable event, we have set-up an inspiring scientific program and prepared a warm welcome in a lovely city that offers plenty opportunities to meet and greet in the nicest places you can imagine.

We have managed to create an exciting scientific program in which the state of the art is presented as well as reflections on great achievements in recent years. We pay special attention to the early career toxicologist by giving them a special platform for oral communications.

The main venue of the conference is the Maastricht Exposition and Conference Centre (MECC), which has recently been completely renovated and has ample space to accommodate large groups for our keynote lectures, debates and exhibitions as well as many breakout rooms for smaller symposia and workshops. The program will have well-balanced inputs from academia, industry and regulators and will challenge you to interact and participate in lively debates and discussions. In a smaller side-programme we aim to step out of our regular conference setting to unite in local pubs and bars with citizens and international students and discuss how toxicological research can contribute to safe products, environmental protection and a more sustainable society.

We cordially invite you to come to the ICT2022 in Maastricht and to reunite with all your colleagues in Toxicology!

Prof. Theo de Kok
Chair of the Local Organizing Committee

Prof. Flemming Cassee
Chair of the Scientific Program Committee

IMPORTANT DATES:

March 31, 2022
Deadline abstract submission

May 15, 2022
Deadline early registration

September 18-21, 2022
ICT 2022, Maastricht, NL

Maastricht University

Afscheidscollege Prof. dr. Jos Kleinjans

woensdag 4 mei 2022

De Rector Magnificus van de Universiteit Maastricht maakt bekend dat Prof. dr. Jos Kleinjans hoogleraar 'Milieugezondheidkunde' in de Faculteit Health, Medicine and Life Sciences verband met zijn emeritaat de universiteit zal verlaten.

Zijn afscheidscollege vindt plaats op woensdag 4 mei 2022 om 16.00 uur in de Aula van de Universiteit Maastricht, Minderbroedersberg 4-6 te Maastricht.

De titel luidt: ''Milieu en gezondheid, een marginale kwestie?" Belangstellenden worden uitgenodigd deze plechtigheid bij te wonen. Universiteit Maastricht volgt de richtlijnen van het RIVM. Na afloop is er een receptie.

Prof.dr. Pamela Habibović
Rector Magnificus

In de naaste omgeving van de Aula is parkeren vrijwel uitgesloten. Gelegenheid tot betaald parkeren is er in de garage onder het Vrijthof.

Aan Hoogleraren:
Indien u voornemens bent dit afscheidscollege bij te wonen en deel te nemen aan het cortège wordt u verzocht dit uiterlijk vóór 26 maart 2022 door te geven aan phd-office@maastrichtuniversity.nl. Verzoeke tevens aan te geven of uw partner u zal vergezellen.

De oratie zal ook te volgen zijn via een livestream. Indien u de oratie via de livestream wil volgen, vragen wij u dit bij uw aanmelding kenbaar te maken. U ontvangt dan uiterlijk een week van tevoren een link.

TERUG NAAR INHOUD