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SPECIAL THEME

Toxic lifestyles

- FACTORS CONTRIBUTING TO FALLING SPERM COUNTS WORLDWIDE
- DECAY OF LIFE EXPECTANCY IN THE USA: ANY TOXIC LIFE STYLE RESPONSIBLE?
- VAPING; HEALTH EFFECTS OF E-CIGARETTE AND ACTIONS TO MAKE IT LESS ATTRACTIVE
- HIGH FRUCTOSE CORN SYRUP AND OBESITY

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TERUG NAAR INHOUD

Editorial

This year was eventful for the toxicology community in the Netherlands. From the 18th to the 21st of September, Maastricht was the location of the 16th International Congress of Toxicology (ICTXVI). The general feedback was that this event was a resounding success and a chance to finally meet up face-to-face with peers from around the world. The NVT Annual Meeting on May 24-25 titled 'Green Deal – Toxicology matter(s)' was another importer event for our members and gave them the chance to participate in lively discussions. These large gatherings came in addition to various symposia set up by the different sections of the NVT.

The editorial team of the TCDD was also busy this year, covering the special themes, inhalation toxicology, petroleum toxicology and water. For this issue, and in line with the holidays which are typically associated with festive food and drinks, we decided to focus our attention on our lifestyles. The theme for this issue is therefore 'Toxic Lifestyles'. Carolien discusses 'Factors contributing to falling sperm counts worldwide', Heloise takes a closer look at the 'Decay of life expectancy in the USA', Ali covers the 'Health effects of e-cigarettes' and I take a look at the link between 'High Fructose Corn Syrup and obesity'.

On behalf of the editorial team, I wish you happy holidays and an interesting read!

Sincerely,

Barae Jomaa

Photo by Jess Bailey on Unsplash

RISK ASSESSMENT

NVT Risk Assessment: Understanding chemical micro-pollutants in water

“It was fun to work together in a group to solve the issue”

On the fourth of October the section Risk Assessment organized a symposium on chemical micro-pollutants in water. The symposium was the first face-to-face only meeting of the section Risk Assessment since the COVID-19 pandemic. Around 30 participants attended the meeting, which was held at KWR Water Research Institute in Nieuwegein. Annette Wilschut, the chair of the meeting, thanked KWR for hosting this meeting and providing the very timely topic. The meeting consisted of three presentations and a serious game.

Freshwater is a finite resource, and this is realized more in the recent decennia, especially by younger generations. Over the years the perception of the most pressing issues in water management changed to the current awareness of water quality and availability. KWR is the independent research organization in the drinking water sector and is concerned with water research in the broad sense. The core work is part of the Joint Research Programme with the water companies. There are threats towards the quality of the drinking water sources, which is most pressing in surface water. Another activity by KWR is wastewater monitoring and sewer surveillance, to detect drug use and virus particles amongst others. Emissions of anthropogenic chemicals (either local or diffuse) can represent a threat to drinking water sources. For emerging contaminants there is a signaling value of 0.1 µg/l, to prioritize the most important substances for further research. In addition to the legal limits, there are health-based guidance values, based generally on 20% of the tolerable daily intake. The TTC approach is used to further prioritize substances, as well as QSARs and read-across, with preferably multiple models applied in parallel. Effect-based monitoring is also used as a method to assess water quality, by applying toxicity tests such as Daphnia, Ames test and CALUX. Innovative chemical screening is used to find substances and prioritize them on expected toxicity. Overall, currently innovative approaches are required for hazard and risk assessment. More information can be found in the KWR online library (library.kwrwater.nl).

“It was a successful afternoon”

The next presentation was by Julia Hartmann from RIVM and she told more about the RIVM and its activities ➔

related to drinking water quality. RIVM is an independent agency of the ministry of Health, Welfare and Sport (VWS). The scope of the organization is very broad, including many topics related to environmental and human health. The drinking water related activities lie in development of guideline values, emergency response, and research into new challenges, amongst others. Some further information can be found at https://www.rivm.nl/drinkwater. From source to tap, there are a lot of parties involved with different responsibilities. The proposals for limits by RIVM are based on exposure and health effect information, which go to the ministry of Infrastructure and Water Management (I&W) for the actual setting and implementation. The responsibility for the water quality is spread over several stakeholders and regulations, both national and at EU level. In addition to health-related values for substances, there are signaling values for substances without limits of 1 µg/l in drinking water or 0.1 µg/l (long term presence in surface water used for the production of drinking water). Julia's PhD project (PS-Drink) focused on the early identification and assessment of emerging chemical and microbial drinking water contaminants. An integrated approach was developed for this purpose, which included a decision support tool based on the concept of value-focused thinking. The goal was to develop a tool to prioritize components for further action (e.g. monitoring). The model provides the expected risk and the uncertainty. For more information on the prioritization model see this article. The thesis can be found here.

The third presentation given by Robert Overhof of Sitech addressed the activities performed to prepare for a new permit for the wastewater treatment plant of the chemical site Chemelot, which is very close to the production site and next to the river Meuse (Maas). The plant collects all the water from the Chemelot site. The preparations for the permit involved a lot of stakeholders, including the local water companies, Rijkswaterstaat, province and companies at the chemical site. Due to tighter regulation for permits, all substances have to be assessed, also those coming into the treatment plant (partially in analytics and mass balance as the composition of some products is kept secret). Assessments consider information on degradation, ecotox, chemical properties and grouping into categories which determines the effort necessary for the reduction in discharge. The policy for substances of very high concern (SVHC) is (in principle) zero discharge, which is achieved by maximizing removal and evaluation via discharge tests. Also included in the assessment of the discharge are the background levels, dilution factors and environmental standards. Data availability is an issue: MSDS, ECHA, ECOTOX, QSARs, and literature are used to fill the gaps. If there are no standards available, Sitech has to derive indicative standards and make them available. This also requires quite some explaining to companies, who have to cooperate on providing substance information. The whole assessment also included Whole Effluent Assessment (WEA) and Continuous Biomonitoring with mussels. To note is that for any change in use or production at the companies at the chemical site, the whole process of chemical substance evaluation should be reconsidered. Deriving the standards also requires laboratory capacity as well as experts and approval. Much more is required under the new permit system, but this also results in more substance specific standards. A hot item at this moment is micro-plastics.

After the break the serious game was introduced by Tessa Pronk and Adele Ferrario. In the game the participants were divided in groups and given the role of a commission that has to suggest a solution to an acute river pollution incident. Each group was provided with a budget and could buy analytical results or hire other experts, decisions had to be made wisely. We learned about all the complicated steps involved in water quality management, finding the cause (hazard assessment, analysis with bioassays) and the solution. Interesting tools can be found at https://www.sleutelfactortoxiciteit.nl/

The presentations can be found here: Summary and Presentations | Serious game: 'Understanding chemical micropollutants in water' | Section Risk Assessment | October 4th 2022 - Nederlandse Vereniging voor Toxicologie

"Tessa Pronk explaining the serious game"

TERUG NAAR INHOUD

RISK ASSESSMENT

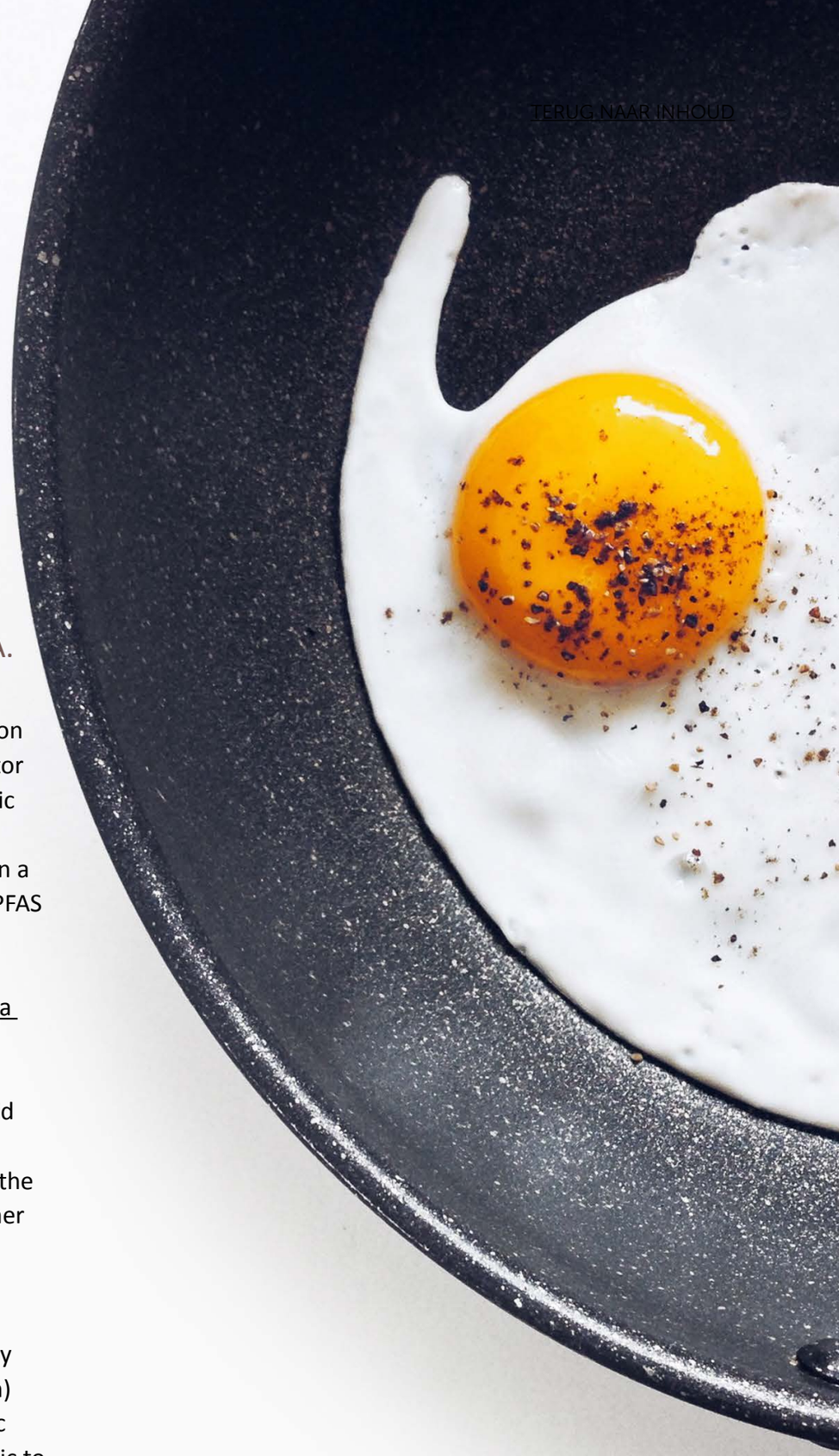
Environmental occurrence, hazard and risk of PFAS

Symposium organized by Kees van Gestel (VU) and Michiel Kraak (UvA) on behalf of the section Environmental Chemistry & Toxicology (KNCV/NVT-MCT) on Friday September 16th 2022 at the UvA.

The symposium was divided into three parts, on *Exposure*, *Hazard* and *Risk*.

The *Exposure* part of the symposium started with an overview, by Leonard Oste (Deltares), of currently found PFAS concentrations in soils, groundwater, sediments, surface water and suspended matter. The number of PFAS detected depends on their properties (long- versus short-chained), but also on the method of analysis. Several sources were identified, and levels are expected to stabilize in the future, but the composition of the PFAS mixture may change with 'old' ones being phased out and replacements popping up. Mohammad Sadia (UvA) briefly discussed methods for producing PFAS and for removing PFAS from water. In drinking water, he measured many branched PFAS compared to other media, while the ultra-short PFAS like TFA dominate in both groundwater and drinking water. Ioanna Gkika (UvA) presented preliminary results of a mesocosm study with sediment from a pond next to the 3M factory in Antwerp, in which she assessed PFAS bioaccumulation in plants, and from a field sampling of biota from the same pond. In both cases, many PFAS compounds were present, and they also showed rather high bioaccumulation factors in biota. In the general discussion on exposure, the high biota-sediment accumulation factor (BSAF) levels were further discussed in relation to trophic levels. It was concluded that such studies should try to measure as many PFAS compounds as possible, to obtain a better overview of the presence and concentrations of PFAS in the environment.

The *Hazard* part of the symposium was started by Jessica Legradi (VU), who reported on the toxicity and modes of action of PFAS in zebrafish determined by the use of different omics methods. Oxidative stress, effects on lipid metabolism and on the immune system seemed to be most relevant, while also behavior and development of the zebrafish may be affected. Lackson Kashobwe (VU) further explored the mechanisms behind the lipid metabolism effects of PFAS using cellular assays. Activation of PPAR receptors seems to be important in these mechanisms. Skylar Xie (VU) presented results of toxicity tests done by herself but also by colleagues (Cara Byns, Thimo Groffen) of the University of Antwerp. FBSA was much more toxic than PFBS, although both compounds were not very toxic to daphnids, but toxicity increased over generations. ➔



In the Asian clam, oxidative stress was seen at lower concentrations of PFAS. But in great tits (*Parus major*) from the area near the 3M factory in Antwerp, no clear effects of PFAS were seen on reproductive success, even though the eggs contained extremely high PFAS concentrations. In the presentation of Anna Huang (WUR), it was shown that aquatic insects like midge larvae are much more sensitive to PFAS than other aquatic invertebrates, but the reason for this big difference in sensitivity remained unclear. In the general discussion on hazard, it was concluded that immune responses and endocrine disruption also may be of importance for effects of PFAS. More studies are needed to unravel the possible relation between PFAS fate and effects and chemical properties/molecular descriptors. The application of the One Health approach to further investigate the effects of PFAS was also advocated.

In the *Risk* part of the symposium Erik Verbruggen (RIVM) discussed the current EU approaches for the risk assessment of PFAS. A universal restriction of PFAS is proposed by several countries, which applies to all PFAS. For the risk of PFAS mixtures, a toxic potency factor approach is used, and this has resulted in the new Tolerable Weekly Intake (TWI) for 4 PFAS compounds set by EFSA. New RIVM guidance related to this, leading to an Environmental Risk Limit of PFAS In surface water of 7 pg/L has been published. This risk limit is frequently exceeded, nearly everywhere in the Netherlands. Joris Quik (RIVM) described how PFAS fate and exposure can be modelled. Major challenges relate to the detergent like behavior (foaming), transformation and partitioning of PFAS. Risk limits for soil and sediment for PFAS were discussed by Arjen Wintersen (RIVM). Point of departure for the risk limits is the TWI set by EFSA, and risk limits for soil may be differentiated based on the use of the soil (e.g., residential versus industrial). Since the TWI is only based on 4 PFAS compounds, more data is needed to develop risk limits for other PFAS.

In the vivid final *plenary discussion* led by Annemarie van Wezel (UvA), a co-worker of the Health Service Authority GGD Dordrecht expressed his concerns about the recent statements of some experts in news items on PFAS in Belgium and the rather strict risk limits for human health. It confuses him and he does not really know what to tell his patients. This made clear that in addition to risk assessment, also risk communication and risk management are crucial. The extremely low risk limits for human health also triggered the question whether further ecotoxicological research still is needed, as it seems unlikely to find organisms more sensitive than the currently maximum allowable concentrations. On the other hand, further research on the environmental fate of PFAS, including its bioaccumulation potential seems crucial for a proper assessment of exposure and therefore of its potential risk, also to human health. Finally, the audience was challenged to give their opinion about the future needs for PFAS research.

MILIEUCHEMTOX

Symposium Environmental Crime

Wageningen University, 30 September 2022

Are we all environmental criminals? What is environmental crime, how is it investigated, and how does the legal system deal with it? How many different roles does the government play? How can environmental scientists contribute to environmental crime investigations?

These questions were all discussed during a symposium on Environmental Crime, organised by Kennisnetwerk Milieu (KNM) and the section Milieuchemtox of NVT/KNCV. Around 50 participants from the environmental sector and criminal investigation services linked their expertise during a very interesting and lively meeting.

After Caroline Moermond (KNM) and Willie Peijnenburg (Milieuchemtox) welcomed the participants, Rudie Neve (Police Academy) introduced the topic of environmental crime, which can be defined as 'Behaviour punishable through criminal or administrative environmental law and/or morally culpable behaviour, enacted to pursue economic advantage and/or immaterial gain, resulting in environmental damage'. This type of crime is different than common crime, as environmental crime is mostly corporate crime (mixed with permitted economic activities) or is a crime of omission (e.g. when procedures on safety are not followed). Examples of environmental crime are manure fraud, illegal use of plant protection products, illegal waste dumping, emissions of substances of very high concern, fraud with bunker fuels, illegal fireworks, wildlife crime, and illegal timber trade. The chance of being caught and sanctions are usually very low, and regulations are complicated.

Bram van Diggele (Waterschap Rivierenland) explained the difficulties a water board is confronted with while investigating environmental crime and actually getting companies in front of a judge. It is often already difficult to determine who is responsible: is it the contractor, the sub-contractor, the sub-sub-contractor, or the licensee? To be convicted of a crime does not require criminal intent – (not) doing something because of financial gain is also criminal. He ended with the quote that 'to be negligent is to be held accountable', saying that who closes their eyes can also be guilty.

Ingeborg Koopmans (Prosecutor at Openbaar Minsterie) focussed on the many roles of the government in environmental crime (besides the investigative/court processes). The government has a role as legislator, licensing authority, enforcer, and as the suspect to be brought before court. Often, subsidies are the basis of environmental crime, when money is to be gained. Again, she stressed that knowing environmental crime happens but looking away and not acting, is also a criminal act in itself. The government often does this, but the national government cannot be brought to court. 'Toleration is to be indifferent to the inadmissible for so long until it is too late'.

Roos van den Munckhof (Judge at district court Oost-Brabant) explained the view of a judge. She stressed that judges in environmental law know a lot about how to apply law but are not environmental experts. They lean on information from environmental experts. It is also important for a judge to know how the public feels about a certain topic, which can be steered by environmental scientists seeking publicity.

Finally, Edwin Lakerveld (director of the Special Intelligence and Investigation Service (ILT-IOD)) explained the process of investigating environmental crime, with a couple of interesting examples on biodiesel fraud, tapping of pipelines, a company not obeying regulations aimed at protecting environmental and human health, and an internationally working laboratory that forged their reports to meet their client's needs. Their unit is going to be strengthened from 70 to 130 employees. Both Rudie Neve and Edwin Lakeveld also pointed out that there are many vacancies; check out werkenbijhetom.nl; omgevingsdienst.nl/over-ons/vacatures; kombijdepolitie.nl.

In the final discussion involving the speakers and the audience, it was stressed again that the expertise of environmental experts is essential in environmental crime investigations and in taking the right decisions at all levels of jurisdiction. We might all be environmental criminals in one way or the other, but environmental scientists have the knowledge to contribute to effectively combat the true environmental criminals.

Factors Contributing to Falling Sperm Counts Worldwide

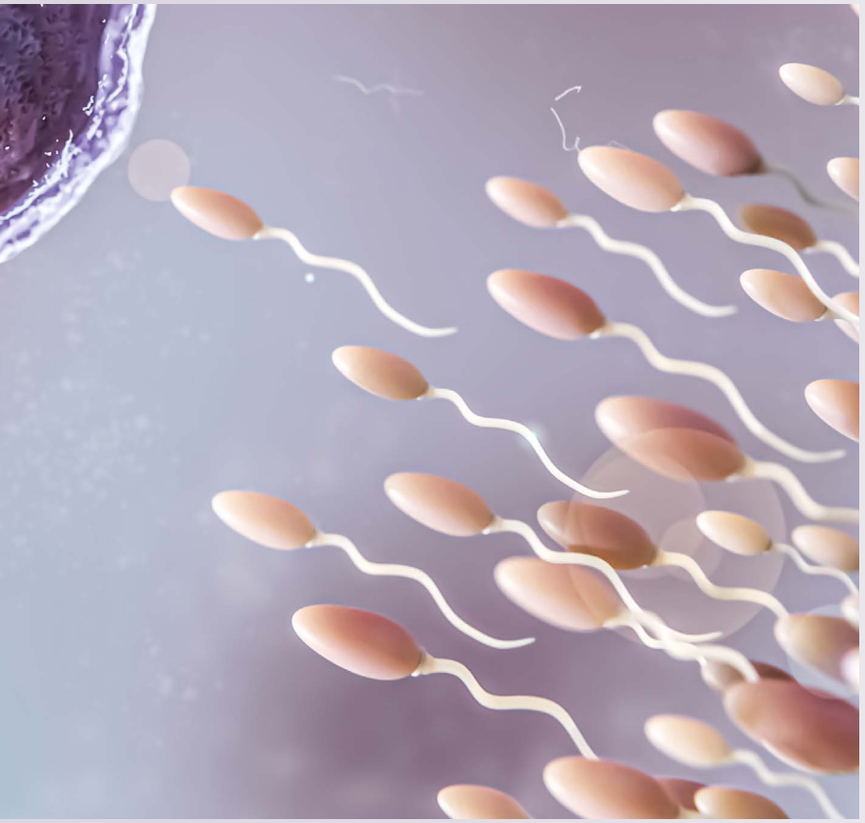
By *Carolien Schophuizen*

Last November headlines appeared in various media stating that a worldwide drop in sperm counts is taking place faster than expected. The news originated from a publication by Levine et al. (2022) in the journal Human Reproduction Update 6. The publication sparked discussions ranging from “averting a sperm-crisis that would threaten humankind”, to “this is exactly what this overpopulated earth needs”. Nevertheless, it is yet to be determined what would be the cause of this decrease. It could be lifestyle related, related to lifetime chemical exposure, or may there be other reasons involved?

In their original 2017 publication [7], Levine et al. related the importance of sperm count for public health to several key elements. Sperm count is linked to male fecundity and an essential component of semen analysis. Reduced sperm count is viewed as a predictor of all-cause mortality and morbidity, and re-associated with diseases such as cryptorchidism, hypospadias and testicular cancer, suggesting a shared prenatal etiology. Furthermore, sperm count and other semen parameters are possibly associated with multiple environmental influences. Therefore, in an updated study a systematic review and meta-regression analysis of trends in sperm concentration (SC) and total sperm count (TSC) was performed, with focus on their modification by fertility and geographic group. The study included data on sperm counts from scientific studies published since 1981. The researchers published some of this data previously [7], but have updated the dataset to include 38 newer studies (14233 samples) from 2014 – 2019, from all areas of the globe. Sperm counts are falling by around 1.16% post-1972 to 2.64% post-2000, showing that the rate of decline has doubled since 2000. In the ‘wider implications’ section they conclude: research on the causes of this continuing decline and actions to prevent further disruption of male reproductive health are urgently needed.

The causes of a decline in sperm count are thought to be plentiful, and many are thought to be lifestyle related. As the effects occur within a single generation, genetics are unlikely to be involved. Exposure to lifestyle and environmental factors (i.e. pollution, plastics, alcohol, smoking) [3,7], drug (ab)use [12], high temperatures [5], obesity [9] and poor diet [2], have all been suggested to be contributory factors [10]. For example, the use of marijuana is associated with hormonal imbalance by lowering estradiol levels and inhibiting aromatase function [12]. ➔

Dietary factors can influence sperm concentrations. Specifically, supplementation with zinc, selenium, omega-3 fatty acids, and CoQ10 are reported to significantly increased sperm concentration and motility, with omega-3 fatty acids and CoQ10 additionally increasing total sperm count [2]. CoQ10's play a central role in the electron-transport chain whereby inhibition of the organic peroxide formation this may reduce sperm-cell oxidative stress in seminal fluid. At the same time, some other lifestyle factors such as perceived stress, have not been associated with a change in semen volume, sperm concentration, or total sperm count [8] . Also, research towards a proposed relationship between the increased exposure to mobile phone radiofrequency and sperm quality decline, has not been conclusive [3, 11]. The actual effects of these individual factors, on such a large and variable group are generally complicated to measure. The different lifestyle and environmental factors may all be involved.



Aside from the likely effects that these environmental and lifestyle factors undoubtedly have on sperm quality, there is some controversy regarding the interpretation of the study data by Levine et al. In an expert reaction to the published sperm-count study, published on the website of the Science Media Center, Professor of Andrology at the University of Sheffield; Allan Pacey, even disputes the conclusion that the sperm quality has dropped over time [1]. He suggests that the reduction in sperm counts may be related to improvements in the training and quality control programs used for hemocytometry (the gold standard technique to count sperm). Since the meta-analysis performed involves studies published in a time range between 1981-2019, there have undoubtedly been changes and improvements in standards and protocols over time.

Regardless of the critical notes, the data are difficult to ignore and quite consistent, which at least indicates that the findings would require further investigation. The authors themselves indicate that methods for measuring SC have remained largely unchanged. They say that counting by hemocytometer is the classical way to assess SC and has been recommended by the World Health Organization in all versions of organizations semen analysis manuals.

So, are we facing a semen crisis? No, not yet, normal sperm counts range from 15 to >200 million sperm per milliliter of semen. Anything less than 15 million sperm per milliliter, or 39 million sperm per ejaculate, is considered low [4]. That threshold has not yet been reached according to the paper. Also, since the drop in SC may be multifactorial, individual men may easily change their lifestyles and thereby take the lifestyle effects out of the equation on a personal level. In addition, if personal factors are involved, improvement could be possible within a few months. However, environmental factors or (western) societal characteristics are much more difficult to change if they are the reasons for the long-term decline. Some may see this drop in SC as a blessing, a self-regulating mechanism of this overpopulated earth, and a few may even go as far as considering it evidence of a feminist plot to undermine and even ultimately eliminate the western male. But hey, let's not go into dystopian futures or farfetched conspiracy theories here. Let's keep our focus, as toxicologists, on the science behind the effects observed.

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Decay of Life Expectancy in the USA:
Any Toxic Life Style Responsible?

By *Héloïse Proquin*

Quality of life in the United States of America is evolving along with a reduction in life expectancy. Between 2019 and 2021, life expectancy has dropped 2.7 years meaning that, from 2021, an American citizen can expect to live to the age of 76.6 on average, same as 25 years ago[1]. Since 2019, a virus known as SARS-Cov-2 a.k.a. COVID-19 a.k.a. corona virus a.k.a. "the reason we got all confined" had a major impact on life expectancy worldwide. However, in the USA 2.7 years were lost as compared to 0.7 years in the Netherlands.

Even if SARS-cov-2 was responsible of more than a million death in USA, this does not explain that the first decrease of life expectancy was observed in the period 2014-2017 (-0.3)[2]. A toxic lifestyle made 95,000 victims in 2020 and 110,000 in 2021 according to the estimations of CDC[3]: the opioids. The opioid crisis started when opioids started to be delivered without a prescription in the USA in the 90's. Additionally, companies like Prudue Pharma, producing OxyContin, was, in 2020, convicted for violating anti-kickback laws by paying doctors to write more OxyContin prescriptions and for misleading regulators about its efforts to restrict the overprescription of the drug[4]. Such violation led to an increase of prescription from 670,000 to 6.2 million between 1997 and 2002[5].

The second possible reason for the decrease in life expectancy in the USA is the deterioration of the diet and lack of physical exercise leading to an increase of cardiovascular diseases. CDC calculated that 41.9% (2017-March 2020) of the American citizens aged 20 and over are considered obese as well as 22.2% of adolescents aged 12-19 years, which has an impact on the mortality ratio of the country[6].

Last but not least, a possible reason would be the difficulties to obtain health insurance and access to health care. One example would be the maternal mortality rate. The USA is one of the richest countries in the world but has the highest mortality rate among high-income countries. Studies by the OECD[7] shows that, in 2020, the maternal mortality ratio is 23.8 for every 100,000 live births, a ratio more than double that of most other high-income countries such as Canada (8.4) or the Netherlands (1.2). A big difference is also observed between Afro-American women: 55.3 for every 100,000 live births and white women: 19.1 for every 100,000 live birth[8,9]. Health care access has a high impact on this ratio.

Toxic lifestyles are partially responsible for the life expectancy decay. This decay also shows that being a high-income country does not mean that the population is having a healthy lifestyle and sufficient access to health care to keep on increasing the life expectancy.

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TERUG NAAR INHOUD

Vaping; Health Effects of E-cigarette and Actions to Make It Less Attractive

By *Ali Dehghani*

What is an e-cigarette? E-cigarettes are known by many different names. They are sometimes called “e-cigs,” “e-hookahs,” “mods,” “vape pens,” “vapes,” “tank systems,” and “electronic nicotine delivery systems (ENDS).” An e-cigarette (electronic cigarette) vaporizes a liquid that contains a mixture of flavorings and other substances. The liquid, or e-liquid, is heated to create vapor that the user can inhale. The liquid does not contain tobacco, like a regular cigarette, but often contains nicotine. The e-cigarette is available in all kinds of models and flavors. A total of 16,300 different liquid flavourings with the taste of tobacco, menthol, alcohol, fruit, chocolate, and sweet flavourings such as ethyl-maltol are used. A specific type of e-cigarette is the shishapen. This mimics the taste of a water pipe (shisha). A shisha pen contains no tobacco and usually no nicotine.

Attractive flavourings

The flavorings in an e-cigarette give a nice taste and disguise the bitter taste of nicotine. Young people find the e-cigarette especially attractive because of the extensive choice of (especially sweet) flavors. In 2022, 2.55 million U.S. middle and high school students used e-cigarettes in the past 30 days, including 3.3% (380,000) of middle school students and 14.1% (2.14 million) of high school students. Adults also use e-cigarettes as a tool in order to stop smoking. In the Netherlands, most users of e-cigarettes are (ex-)smokers. Adult (ex-)smokers, as well as young non-smokers are particularly fond of sweet tastes and fruity tastes. Tobacco smokers who are just starting out with e-cigarettes especially appreciate the tobacco flavors and the experience similar to smoking a regular cigarette. For non-smoking young people, an e-cigarette can be a stepping stone to regular smoking. ➔

Health effects of e-cigarette

E-cigarettes are not safe for youth, young adults, pregnant adults, as well as adults who do not currently use tobacco products. The e-cigarette aerosol that users breathe from the device and exhale can contain harmful and potentially harmful substances, including:

- Nicotine: A CDC study found that 99% of the e-cigarettes sold in assessed venues in the United States contained nicotine.
- Ultrafine particles that can be inhaled deep into the lungs
- Flavoring such as diacetyl, a chemical linked to a serious lung disease
- Volatile organic compounds
- Cancer-causing chemicals
- Heavy metals such as nickel, tin, and lead

It is difficult for consumers to know what e-cigarette products contain. For example, some e-cigarettes marketed as containing zero percent nicotine have been found to contain nicotine. Inhaling these substances can irritate or damage the airways. Heart palpitations can also occur and the user has an increased risk of cancer. The vapor that a smoker exhales from an e-cigarette can have effects on bystanders. Their throat, nose and/or eyes can become slightly irritated. An e-cigarette releases fewer harmful substances than a regular cigarette, and in lower concentrations. Nicotine is a health danger for pregnant adults and their developing babies. Additional research can help understand long-term health effects.

Figure 1: shapes, sizes and device types of e-cigarette products (2)

Actions to make it less attractive

Actions could include incorporating e-cigarettes into smoke free policies, preventing access to e-cigarettes by youth, price and tax policies, retail licensure, regulation of e-cigarette marketing likely to attract youth, and educational initiatives targeting youth and young adults. For example, in the US, in August 2016, the FDA began enforcing a ban on vending machine sales unless in adult-only facilities and a ban on free samples and sales to minors.

The Dutch government tries to make e-cigarettes less attractive, particularly to young people. Specific flavourings (sweet, fruity) make e-cigarette use more attractive, so the government has decided to allow only flavourings that have a tobacco-taste. If only these substances are used, RIVM expects that the use of e-cigarettes will become less attractive. This will support one of the goals of the National Prevention Agreement: ensuring that young people and non-smokers are less likely to use e-cigarettes (that means there are no children or pregnant women who smoke. And that a maximum of 5% of adults smoke by 2040). The point of departure is that only liquids with tobacco flavourings will be allowed to enter the market. At the request of the Ministry of Health, Welfare and Sport, RIVM previously assessed over 500 flavourings that are currently being used in e-liquids. This led to the recommendation to limit the number of allowed flavourings to 23 . The Dutch government only wants to allow 23 e-cigarette flavourings with a tobacco-taste. RIVM examined whether these 23 flavourings are harmful to people's health. Seven of the flavourings were found to be potentially harmful. RIVM advises the Ministry of Health, Welfare and Sport to ban these flavourings.

The study shows that two flavourings may cause cancer. Another flavouring may cause allergies. For such substances, it is not possible to determine which quantity is safe. Three other flavourings may pose a health risk at the highest concentrations in liquids in e-cigarettes. Another flavouring may irritate the lungs and thereby may cause harm. For some of these substances' information on the health effects after swallowing was available. Three substances could cause health risks at the highest concentrations in liquids found in e-cigarettes. Another substance is an irritant for the lungs and can therefore potentially cause harm. For the remaining 16 substances, there is insufficient information to assess their health risk for use in e-cigarettes. RIVM proposes two options for these 16 substances. One option is to prohibit these substances from a precautionary principle. The other option is to use these substances in e-liquids to keep the product available for smokers to help them quit smoking.

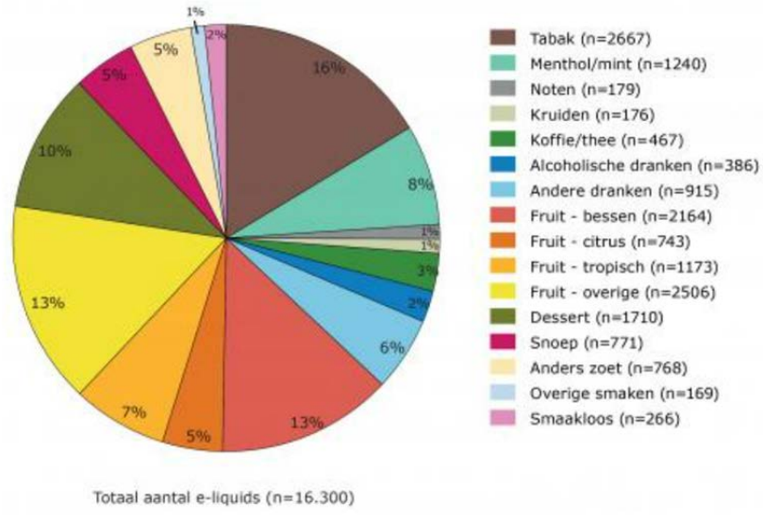

Figure2: liquid flavors in the Netherlands (1).
Overview of the main flavor categories of e-liquids registered for the Dutch market in 2017. The total number of classified e-liquids is 16,300. The classification is based on information reported by manufacturers.

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High Fructose Corn Syrup and Obesity

High Fructose Corn Syrup is a caloric sweetener so overconsumption can lead to obesity, but is it the cause of the obesity pandemic?

By *Barae Jomaa*

Corn, the food of a nation: Poster showing a woman serving muffins, pancakes, and grits, with canisters on the table labeled corn meal, grits, and hominy. Source: Lloyd Harrison for the United States Food Administration

Corn's worldwide production growth has gone hand in hand with the obesity pandemic and yet, there is widespread uncertainty as to whether corn, or a by-product such as High Fructose Corn Syrup (HFCS), is a leading cause of obesity. While sedentary behavior and inactivity may play a role in weight gain[1], there is widespread concern about caloric sweeteners, especially relatively new sweeteners such as HFCS.

Corn, better known as maize in Europe, was domesticated in the region that corresponds to modern day Mexico some 10,000 years ago. The major types of corn are dent corn, flint corn, pod corn, popcorn, flour corn, and sweet corn. Dent corn is better known as field corn and is widely use as animal feed. Sweet corn is the type of corn that is typically boiled or roasted and meant for human consumption. Besides its delicious taste, corn keeps finding new applications. Today, roughly 40% of corn produced in the United States goes towards the production of bioethanol and another 40% goes to a more traditional use, animal feed[2]. 6% of the corn goes to make corn sweeteners, including HFCS[3]. As can be seen in figure 1, corn production has been in the lead over wheat and rice since the early 2000's and the gap keeps getting bigger.

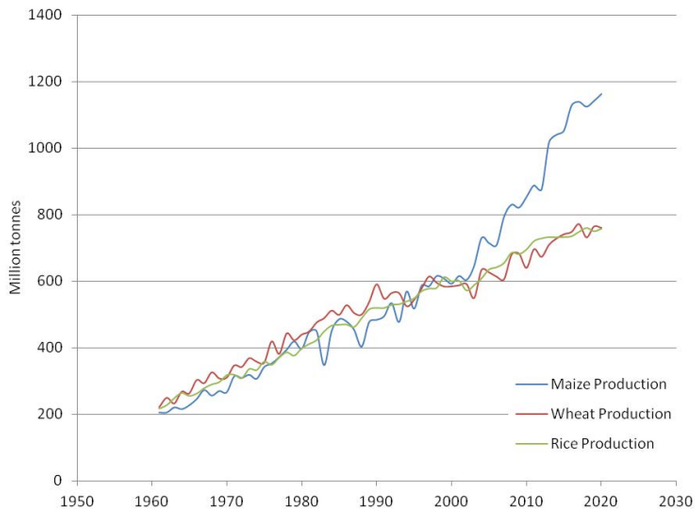

Figure 1: Worldwide Maize, Wheat and Rice production, 1961 to 2020. Source: UN Food and Agriculture Organization (FAO)

With commercial production commencing in 1964, HFCS is a modern invention. US farming subsidies and quotas on imported sugar put in place in 1981 gave HFCS a competitive advantage and led to its adoption, in 1984, by Coca-Cola and Pepsi as a full replacement for sugar[4]. At the time, it was still unclear, at least to the general public, what the difference is between HFCS and sugar. ➔

Table sugar is made up of sucrose molecules, which themselves contain one glucose moiety bonded to a fructose moiety. HFCS on the other hand is a mixture of glucose and, typically, 42-55% fructose, depending on the grade. Sucrose is metabolized in the dueodenum by sucrase or isomaltase glycoside hydrolases, yielding glucose and fructose, which are absorbed into the blood stream. Fructose and glucose from HFCS are not bonded so they can be directly absorbed into the blood stream. The end result is the same. A 2008 review of HFCS explained this well by stating: “Sucrose, HFCS, invert sugar, honey, and many fruits and juices deliver the same sugars in the same ratios to the same tissues within the same time frame to the same metabolic pathways.”[5]

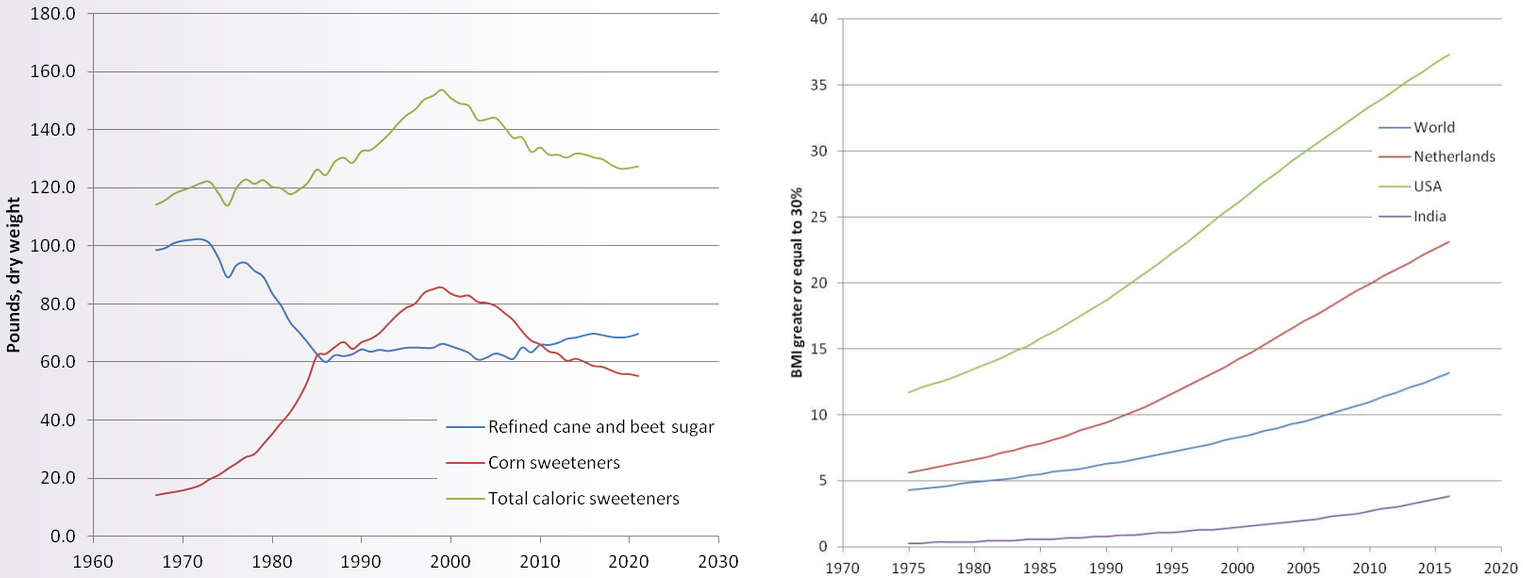

Figure 2: a) Caloric sweeteners, US per capita availability. Source: USDA, Sugar and Sweeteners Yearbook Tables. b) Share of adults that are obese, 1975 to 2016. Obesity is defined as having a body-mass index (BMI) equal to, or greater than, 30. BMI is a person’s weight (in kilograms) divided by their height (in meters) squared. Source: WHO, Global Health Observatory (2022).

Being synthetic, therefore not considered to be “natural”, already raises fear among many. However, the real confusion came following a 2004 study with data showing a correlation between obesity and the consumption of HFCS. As can be seen in figure 2, while high fructose corn syrup consumption has gone down since the early 2000’s, obesity has kept increasing. Though the authors were careful to highlight that correlation does not imply causation, the lasting misconception about the role of HFCS in the obesity pandemic is here to stay.

There is often also mention of HFCS’s role in appetite regulation with many believing that HFCS stimulates people to consume more calories even though the research that is pointed to is specific to fructose rather than HFCS[6,7] A 2008 review concluded the following: “Collectively, scientific evidence suggests that high consumption of pure fructose may be problematic to energy intake regulation. However, HFCS is more similar to sucrose than it is to fructose in terms of its content, appetitive responses, and aspects of its metabolism that have been measured to date. Thus, existing theoretical and empirical evidence suggests that fructose-induced problems are not more related to HFCS than sucrose consumption.”[8]

It can be concluded that HFCS is just as unhealthy, in excess, as other forms of sugar. Instead of focusing on the natural vs synthetic part of the story, it would be better to focus on consuming the right amount of calories needed for one’s height, age, sex and level of activity. This, while keeping in mind the importance of variety in one’s diet, keeping up an active lifestyle, and, last but not least, limiting overall sugar consumption.

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The story and lessons behind the article

By *Marcha Verheijen*

This month (November 2022) I finally published the article entitled “Multi-omics HeCaToS dataset of repeated dose toxicity for cardiotoxic & hepatotoxic compounds” (10.1038/s41597-022-01825-1) in Scientific data from Nature group. While many of us focus on publishing research articles, this article is actually a data descriptor that describes what type of data generated and how the data was obtained. With this publication, the HeCaToS data was also made publically available (https://www.ebi.ac.uk/biostudies/hecatos/studies). We really hope other researchers will use it and benefit from our hard work. In a way it ensures that the project lives on, even after it has ended. This publication really marked the end of an era for me, and I learned some valuable lessons along the way.

HeCaToS (**He**patic and **Ca**rdiac **To**xicity **S**ystems modeling) was a EU/FP7 project that ran from October 2013 till September 2018, coordinated by Prof Dr. Jos Kleinjans. I myself joined the team on 14th of April 2014 as a young PhD-student, at the department of Toxicogenomics, Maastricht University. The project generated massive amounts (8.7TB) of multi-omics data from repeated dose toxicity exposures for 10 hepatotoxic and 10 cardiotoxic compounds. Generating this data of course took time and at the end of the project, much was not analyzed yet.
To give the project partners time for their research and publications, it was agreed to release the data in 2020. But the project had ended, communication started to fade and people (including myself) spend their time on other active projects.

September 2021, I started working as a data manager on the H2020 ONTOX project (https://ontox-project.eu/). This project focusses on the creation of New Approach Methodologies (NAMs) that will be primarily fed by available data. The HeCaToS data may be a valuable source for ONTOX, but it was not made publically available yet. Since I did my PhD on the HeCaToS project with the HeCaToS coordinator as my promotor, I was allowed to write the data descriptor and release the data. But there the trouble started. I did know many of the ins-and-outs of the data, but not all of them. So I had to reach out to HeCaToS partners to obtain details on data generation, processing and quality control. Much of the actual work was done by PhD’s and Postdocs at the time, who moved on, got jobs elsewhere and where unreachable. Other people wanted to contribute, but had limited time to do so because of other work. Luckily, the HeCaToS project did a good job in recording the information, even when it meant spending some time to dig it up. This taught me the value of detailed documentation during the project.

Us researchers have all heard about the FAIR (Findable, Accessible, Interoperable, Reusable) principles. And I hope that most of us take them seriously. But for many datasets that I have worked with, I noticed that I could find it, I could access it and that I had the details necessary for reusing it. This does not directly mean that others can as well. So what if I leave? Who will be able to find and work with the data? What valuable information gets lost just because we don’t document what we know? Or if nobody took the initiative to make data of finished projects publicly available? How many buried data treasures are still out there that will probably never be found?

Of course I do know that documenting the information means to fill out many boring forms and datasheets. And ensuring that the information is complete is even harder. Since we know our data so well, we forget to include details that are obvious to us, but they are necessary for other users. And sure, when we publish our results, we include the methods. But are they really, I mean REALLY, detailed enough that others can repeat it?

My experience with the HeCaToS data motivates me to bug the ONTOX partners for their detailed (meta)data to ensure the FAIRness of the ONTOX legacy. But in the end, it is up to the researchers generating and processing the data to make sure that it actually is. So think about it, is your own data FAIR or will it be a buried lost treasure?

Funding for implementation and acceptance of animal test free research

Juliëtte Legler (Professor of Toxicology) and her team have received a NWO grant of approximately €1 million for the project “Animal testing for endocrine disruption - from science to regulatory acceptance”. She is working with experts from the Faculty of Veterinary Medicine, Geosciences, REBO and the RIVM, as well as various stakeholders from industry, regulation and NGOs.

As first published by Utrecht University https://www.uu.nl/en/news/funding-for-implementation-and-acceptance-of-animal-test-free-research with additional information on the Virtual Human Platform https://vhp4safety.nl/

Endocrine disrupting chemicals (EDCs) are harmful to humans and animals. The European Commission has created legislation for the identification of EDCs, but animal tests are still needed to determine these substances. Apart from the ethical concerns, the relevance of these animal tests to humans is questionable and tests are not available for all EDC-related effects. Current testing strategies are therefore not suitable for identifying all EDCs.

Several innovative, non-animal testing models for testing EDCs have been developed, although these are not always accepted by science, regulatory authorities and society at large. The main question remains: how do we achieve legal and societal acceptance of non-animal models?

Over the next five years, they will bridge the gap between science and regulation with the main goal: the implementation and acceptance of existing non-animal test research, to ensure it is covered by legislation. The results of this project will serve as input for ongoing projects such as the NWA-ORC Virtual Human Platform for Safety Assessment and the European EURION projects like GOLIAT H. Read more about the content of the project here: https://www.nwo.nl/nieuws

The Virtual Human Platform

VHP4Safety – the Virtual Human Platform for safety assessment project NWA 1292.19.272 is part of the NWA research program ‘Research along Routes by Consortia (ORC)’, which is funded by the Netherlands Organization for Scientific Research (NWO). With a budget of over 10 million Euros, the project starts on June 1, 2021 and will last for the duration of 5 years.

The mission of the Virtual Human Platform is to improve the prediction of the potential harmful effects of chemicals and pharmaceuticals based on a holistic, interdisciplinary definition of human health by developing the Virtual Human Platform and accelerating the transition from animal-based testing to innovative safety assessment. The Virtual Human Platform integrates data on human physiology, chemical characteristics and perturbations of biological pathways, ➔

for the first time in an inclusive and integrated manner that incorporates:

1. human-relevant scenarios to discriminate vulnerable groups, such as disease state, life course exposure, gender and age
2. chemicals from different sectors: pharma, consumer products and chemical industry
3. different regulatory and stakeholder needs

The Virtual Human Platform addresses the emerging societal challenge of the transition to animal-free safety assessment, by integrating various scientific disciplines in the consortium and working with all stakeholders towards implementation and societal acceptance of an approach to chemical safety assessment that is based on human data rather than animal data.

How: Moving away from animal experimentation

Current legal and regulatory frameworks for the assessment of the safety of chemicals and pharmaceuticals for human health rely predominantly on data from *in vivo* animal studies. However, the accuracy of animal studies to predict toxicity in humans is limited. In addition, current animal testing regimes do not reflect human-relevant scenarios, such as differences in susceptibility due to age, sexe, timing of exposure, or disease state.

The Virtual Human Platform will be developed within three interacting research lines (RL):

- RL1: building the platform
- RL2: feeding the platform with newly generated data
- RL3: implementing the platform to ensure stakeholders' acceptance, governance and sustainability

In a national and international arena urgently calling for the reduction of animal testing, the current approach to gradually refine, reduce and replace animal testing has not led to the necessary and desired pace of innovation in animal-free safety assessment. Furthermore, the opportunities offered by state-of-the-art technologies in human health and data science have hardly been yet explored in the realm of safety assessment.

VHP4SAFETY
virtual human platform for safety assessment

The General Court annuls the harmonised classification and labelling of titanium dioxide as a carcinogenic substance by inhalation in certain powder forms

At the 23rd of November, the General Court published its judgement on the classification and labeling of titanium dioxide. Titanium dioxide was classified by the European Chemicals Agency (ECHA) as category 2 carcinogen upon inhalation. Manufacturers, importers, downstream users and suppliers of titanium dioxide brought actions before the General Court for partial annulment.

The General Court judged that the reliability and acceptability of the studies was not sufficient. In addition, the Court found that the classification and labeling is not in line with the criterion that the classification can only apply to a substance that has the intrinsic property to cause cancer. The carcinogenic hazard is linked to respirable titanium dioxide particles in a specific form, physical state, size and quantity. Taken together, the General Court annuls the classification and labeling of titanium dioxide.

The rule concerning the specific state of the particles might have consequences for other nanomaterials of which the bulk form is not inducing toxicity and thus the toxicity cannot be linked to an intrinsic property of the substance. It is therefore expected that an appeal will be brought before the Court.

(Bron: ESFA)

Proefschriftpromopraatje
Juan Ochoteco Asensio

I am Juan Ochoteco Asensio, Ph.D. I defended my doctoral thesis last 9th of November, 2022, at Maastricht University, after finishing my doctorate at the Toxicogenomics department.

By *Juan Ochoteco Asensio*

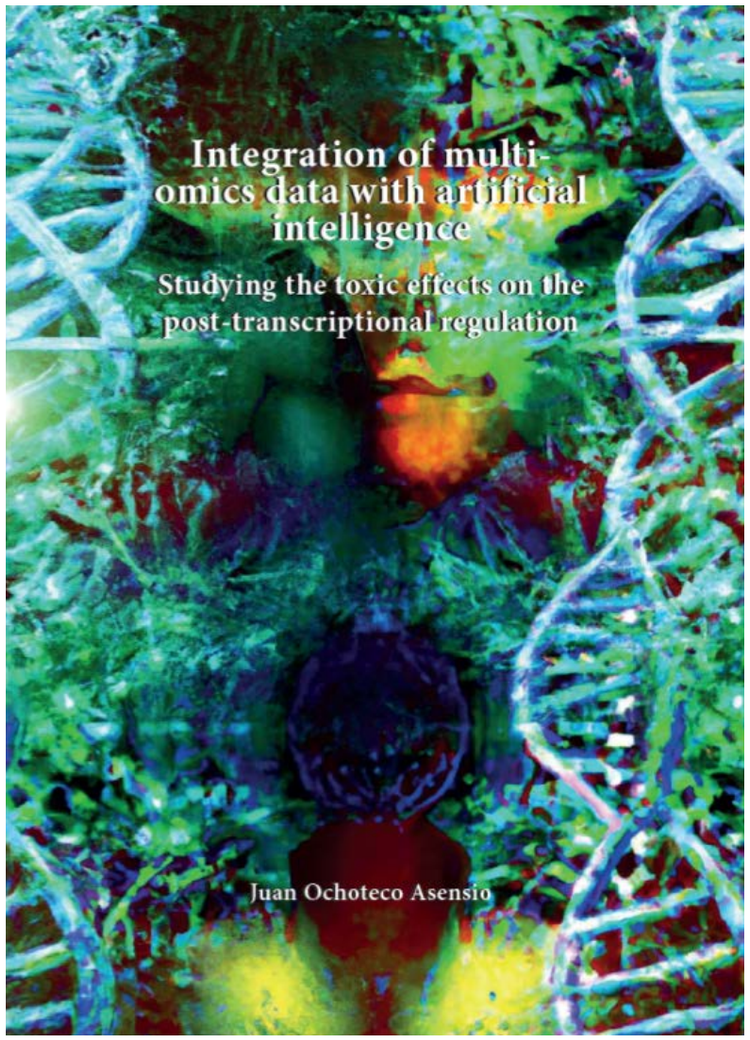
Currently, regulatory agencies rely on the use of animals for testing drugs. There are several reasons for this: first, the most accurate way of testing drugs would be testing them in humans, which is not ethically possible. Second, modeling everything that happens in our bodies in a Petri dish is nowadays unfeasible: the complexity of a human body requires 30 trillion cells to keep functioning. In addition, each of those cells also involves its level of complexity: even a simple yeast cell contains 42 million proteins[1], which does not include other essential molecules like sugars and fatty acids. Even so, recent incentives (such as the cosmetic products regulation (EC) No 1223/2009 of the European parliament[2]) have pushed the scientific community to search for alternative testing methods without the use of animals. Specifically, the area of Toxicology is impacted, as it studies the potentially toxic effects of drugs both before and after being released on the market. A popular method for studying the effects a compound can have in humans is by testing them *in vitro*, that is, by exposing human cells. Doing so helps to narrow the bridge between what is being tested (human cells outside the body) and the actual goal of the study (human cells inside the body) when compared to animal testing, where the model and the end goal belong to different species. Nowadays, the development of induced pluripotent stem cell (iPSC) technology allows reverting any human skin cell to another tissue type (such as cardiac cells that contain the same DNA as the donor of the skin cells), without the need for surgery or invasive biopsies. Although some drugs may kill cells by simply destroying the membrane that encapsulates the cell, most of them disturb the cell in more subtle ways. One of these ways is the deregulation of the number of proteins synthesized by a cell. Proteins are essential molecules, as they perform most of the cell functions. For this reason, disturbing or blocking their production can lead to the disruption or death of a cell and/or the cells that depend on it. The processes that lead to the synthesis of proteins involve mainly RNAs, molecules that work as messengers from DNA to proteins. Therefore, in Toxicogenomics, studying how specific treatments can affect these molecules can help understand their mechanisms of toxicity.

In **one chapter of my thesis**, I assessed how a recently discovered class of RNA, called circular RNAs (circRNAs), are disturbed in heart cells by known toxicants. These circRNAs have been hypothesized to regulate microRNAs (miRNAs) by letting the latter bind to the former. When messenger RNAs (mRNAs) are not bound to miRNAs, they can provide the instructions to produce proteins. When miRNAs are occupied binding circRNAs, they are not able to bind to mRNAs. For this reason, by assessing changes in the number of circRNAs, miRNAs, mRNAs, and proteins; I helped better understand how these compounds (that are still in use) are being toxic in the human heart without the use of animal testing. Going further into the thesis, I realized that knowing how many proteins are present in a cell, is crucial to understanding how a drug (or disease, or any other perturbation) affects a cell. Unfortunately, the technology used for doing it, mass spectrometry, does not measure all proteins in a cell. Instead, researchers tend to use transcriptomics, which exhaustively measures the quantity of RNAs. Nevertheless, the number of RNAs and the number of proteins do not always perfectly correlate with each other.

In **the third research chapter**, I designed an equation to estimate how many RNAs are available to produce proteins. I did that by counting the total number of mRNAs and subtracting the ones that will be affected by miRNAs, but only those miRNAs that are not binding to other RNAs (like another mRNA or circRNA). Nonetheless, the formula, which is focused mainly on RNA molecules, demonstrated an added value for only a subset of proteins. As a result, in **the following chapter**, I went a step further. I built a large dataset with RNAs and their corresponding proteins and trained a machine learning model to predict the latter. Machine learning algorithms “learn” how to predict values by looking at how other similar values behave. Using our ➔

data, our model predicted the increases and decreases of proteins well, which can help others to predict how many proteins there are in a sample of cells based on how many there are in similar ones.

As mentioned before, in the area of Toxicogenomics it is of great interest to study the changes happening in a cell. Transcriptomics is exceptionally good at counting how many RNAs there are, consequently using this technology helps us understand which molecules change in quantity due to a specific cause. The statistical tools used to detect changes, though, do not work without fault. For this reason, experts in this technology can manually detect these errors. On the flip side, this manual curation is pretty time-intensive when taking into account the number of genes to be evaluated, and requires specialist knowledge to do so. That is why, in **my last chapter**, I again trained a machine learning model. In this case, I taught the model to recognize the profile of genes that are typically of interest to the researcher. I built several of them with different characteristics and selected the best one, which I named 'AutoRel'. Even though AutoRel was not flawless, it showed improvements by removing genes that were not of interest.



In an era of increasing societal pressure against animal testing, added to the inherent shortcomings of animal assays, regulatory agencies need to re-evaluate their historical procedure of risk assessment. With the rapid development of methodologies that allow the analysis of the complete set of biological entities in a cell exposed to any substance, regulators will need both a better understanding of all the complex interactions behind molecular biology and powerful data analysis tools to integrate them. The work within this thesis contributes to this necessary transition toward a next-generation risk assessment. This is achieved by the discovery of new changes that happen when a toxic compound affects a cell, predicting protein measures that are usually unknown with artificial intelligence, and filtering results in an automated way to have a better understanding of the changes that occur in a cell. In summary, this contributes to assess more accurately how toxic a drug is, making the use of treatments safer and more reliable.

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URL to the thesis:
https://cris.maastrichtuniversity.nl/en/publications/integration-of-multi-omics-data-with-artificial-intelligence-stud

AIO toxafette - Devon Barnes

In the toxafette, PhD-students working in the toxicology field get the chance to open up about their experiences in performing research. Every issue a new candidate answers a series of questions, and then pass the baton to a fellow PhD-student. This time Devon Barnes, from Utrecht University tells us about his project.

Can you introduce yourself?
Hello, my name is Devon Barnes, and I am from a town called Reading (pronounced Red-ding) in the UK. I did my bachelor's at the University of the West of England in Bristol where I studied Biomedical Sciences, and then moved to the Netherlands to do my master's in Biofabrication at Utrecht University. I also obtained a second master's degree from the Queensland University of Technology in Brisbane, Australia after completing a dual-degree during my studies. I started as a PhD candidate at the Utrecht Institute for Pharmaceutical Sciences at Utrecht University in July 2021. I work in the Division of Pharmacology under the supervision of Prof. dr. Roos Masereeuw and Dr. Manoe Janssen.

How would you explain the subject of your research to a layperson?
Nephrotoxicity refers to the toxicity of the kidneys. It is caused by the harmful effects of toxic chemicals and medications that negatively affect kidney function. Most current methods of exploring human nephrotoxicity involve the use of animal testing, which has been shown to not translate optimally to represent the human condition. The aim of my PhD is to develop innovative new approach methodologies toward predicting systemic dose toxicity for the human kidney without the use of animals. I seek to use and validate different techniques and methods in the laboratory that improve upon pre-existing animal models in a bid to reduce the number of animals used for such studies and provide a more sustainable alternative to monitor human risk-assessment.

How is your research related to the field of toxicology, and why did you choose this subject?
The research for my project is tied to the goals of the Ontology-driven and Artificial Intelligence-based repeated dose toxicity testing of chemicals for next generation risk assessment (ONTOX) consortium, an H2020 EU-wide collaborative project coordinated by the University of Brussels of which our groups forms a part of. In short, we are looking to provide sustainable and functional alternatives toward progressing human risk assessment of chemicals using animal-free models for next-generation risk assessment. My group and I are currently developing a battery of assays using advanced *in vitro* models to simulate the human kidney toward the characterization of nephrotoxic chemicals, including, but not limited to, pharmaceuticals, cosmetics, food and biocides.

What was your motivation for starting a Ph.D. program?
My motivation to begin a PhD can be traced as far back to when I began my higher education in studying for my BSc in Biomedical Sciences. This feeling only strengthened the further I advanced in my education, mostly from the times I spent doing internships at the University Medical Centers of both Maastricht and Utrecht in the Netherlands, and the Institute of Health and Biomedical Sciences in Brisbane,

Australia. I avidly enjoy the workspace and culture of research science and enjoy the freedom I have to pursue my personal goals in academia.

How do you see the future of your research topic (follow-up research / social impact)? What do you hope for?
I strongly believe in the future of our research. The use of animal-free alternatives have often been a key talking point in not only the sciences, but narratives surrounding many aspects of modern industrial practice. We still have a long way to go before we can look to fully replace animal models in toxicological research, but I am a firm believer in the work, my group, consortium and I are doing towards widening the scope and validity of animal-free alternatives moving forward. ➔

Does the project meet your expectations, why or why not?
Yes, it does. I have been enjoying my time here, I have fantastic colleagues and supervisors and the time I spent during my internships helped prepare me for this project. I have enjoyed the networking prospects the wide scope of my project provides, allowing me both the time and opportunity to learn from established professionals and develop my portfolio.

Do you consider research communication as an important aspect of your PhD and why so?
Yes, research communication has been, and will continue to be a vital part of my PhD. I am regularly involved in hosting meetings, writing reports, and providing updates with the ONTOX consortium on behalf of my group. This means there is regular communication between the various members of the consortium as well as other external collaborators. Such lines of communication can sometimes involve stakeholders and others not directly within the research filed so it is also of utmost importance that I am able to convey information efficiently depending on the audience.

Are you a member of a society and what do you expect from being a member?
I am currently a member of the European Society of *In Vitro* Toxicology (ESTIV). Being a part of this amazing community has given me access to several workshops and webinars. I recently had the pleasure of attending a week-long workshop at the Luxembourg Institute of Science and Technology where I was able to learn from an array of toxicologists from both industry and academia, network with my peers and even have a tour of their fantastic facilities.

What is the best advice that you have received as a PhD student or would like to give to another PhD student?
You must have a strong belief in yourself, your project, and your ability to succeed. PhD candidacies can be very difficult and its important to not lose focus of your goals, nor try and compare yourself to others.

What goals do you have regarding your career after finalization of your PhD? Would this be inside or outside academia, and why? Would you consider going abroad?
I am still undecided and I have not been giving it much thought, however I would like to continue to work in this field whether I continue on in academia or move to industry. I am currently focused on developing my skills and portfolio so that I am prepared for whatever comes after my PhD. I have already been abroad many times so would not be opposed to doing so again, but for now my future remains here in the Netherlands.

Please answer the question from the last toxafette PhD-candidate: Do you think a Ph.D. degree was necessary for you, and why?
I very much want to expand my knowledge and I know that obtaining my PhD can help me to establish myself in the field of toxicology. The opportunity to attain my PhD has already provided me with a whole host of networking opportunities and allowed me to travel the world, broadening my character. On a career level, a PhD opens many doors in both industry and academia and although I am still undecided, I would very much like to explore the possibility of a tenure track after I finish.

International Congress of Toxicology

Maastricht (The Netherlands), September 18-21, 2022

By Jeske van Boxel
Amsterdam Institute for Life and Environment, Faculty of Science, Vrije Universiteit Amsterdam, The Netherlands.

My presentation at the ICT 2022:
The use of plastics has increased considerably over the past half century, resulting in more plastic waste. Plastics can degrade to microplastics (MPs, <5 mm) and there is a concern that MPs may affect human health, but to date, not much research has been performed on this. Therefore, the effect on reproduction and developed were tested in *C. elegans* in this study. The intake of PS beads was determined with fluorescent polystyrene. Afterwards, during puberty, *C. elegans* were exposed to diverse PS-MPs to determine fertility. It was discovered, that PS-MPs can cause a delay in lawn clearance. Additionally, the parent and offspring were exposed to the same conditions, whereafter development, body length and behaviour was determined in the offspring. There was an acceleration of the development, suggesting that *C. elegans* go faster through the different life stages. Additionally, there is a dose dependent decrease in body length for the 200 nm PS MPs. For the 50 and 1000 nm, there was also a decrease in body length but was not dose dependent. The behaviour was not affected. Future studies may focus on the impact of MP exposure on lifespan and determine the levels of oxidative stress in *C. elegans*.

Three most interesting learning/insights from the conference:
The most interesting presentations were also about reproductive toxicology. This is my most interest since the AURORA project, where I am working on, is a project focused on the toxicological effects of MPs on placental function and embryonic development. I liked the session: 'Observing the unobservable: using human fetal tissues to improve generalisability and reproducibility of experimental models in developmental toxicity studies'. All presentations in this session were useful for me, especially the presentation of M. van Duursen named 'Challenges of using animal and *in vitro* models to understand human developmental toxicology'. This presentation was giving me some more information about the different toxicological models for testing developmental toxicity. Additionally, the presentation of L. Mamsen was also very interesting, since I work with cells which are male or female. In this study, they discovered that there is an increased levels of POPs in the placentas with male foetuses in comparison with female foetuses. This suggests that when I work with placental cells from a male foetus, it may give different results then placental cells from a female foetus.

In addition, there was another session named 'Advanced *in vitro* model integration into micro physiological system for the study of pharmacokinetics and risk assessment'. This session showed current developments of advanced *in vitro* models, such as human stem cells, organ on a chip. In my future research, I would like to use placenta on a chip model since it could provide cell-cell communication but also could show the toxicological effects in the microenvironment. Additionally, I learned that this model represent a good opportunity for applicability in risk assessments in different ways, e.g. metabolic activity.

In addition, I met a lot of people working in the same field as I do, which could be useful for the future. One women in particular, named Maartje Rietdijk, could help me with finding out some important markers for the inflammatory system. We discussed that we could work together in the future and maybe she can help me with some assays for the inflammatory system in the placenta. ➔

Scientific “take home message”:
There should be more research on the field of environment and exposure to several compounds. We are moving forward with that, but not fast enough.

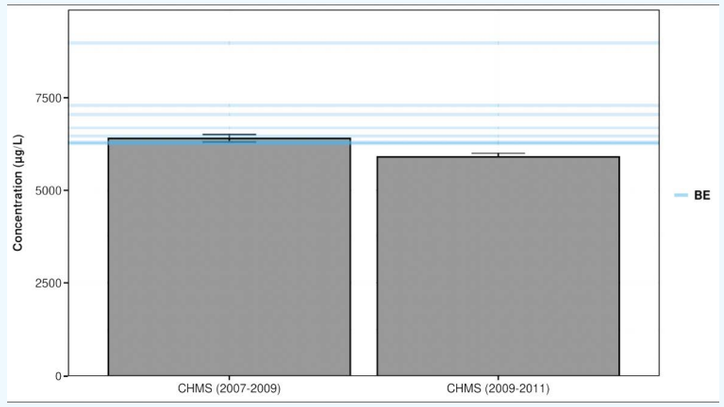
What did the conference organization and yourself do to make the conference a climate neutral event?
To be honest, I do not think that the conference strived to make the conference climate neutral. For myself, I came by train and (electrical) bus which does not affect the climate.

A new online tool that helps interpret human biomonitoring data

The International Society of Exposure Science (ISES) international human biomonitoring (i-HBM) working group has developed a new online tool that helps users interpret human biomonitoring data. This tool, known as the Human Biomonitoring Health-Based Guidance Value (HB2GV) dashboard, is available on the ISES website: https://intlexposurescience.org/i-hbm/

The purpose of the tool is to facilitate the search for human biomonitoring health-based guidance values. The dashboard contains a list of available guidance values for a variety of chemicals. Users can quickly search through the list of guidance values and download the information. The tool is also interactive and allows users to compare results from biomonitoring studies or programs, such as the Canadian Health Measures Survey (CHMS), to relevant guidance values. See the figure for an example of the comparison of results from the 2007-2009 and 2009-2011 CHMS with several biomonitoring equivalents (BEs) available for zinc measured in blood. More information about how to use the online tool can be found on the dashboard itself under the User Guide tab.

The i-HBM working group recently published an article in the International Journal of Hygiene and Environmental Health to announce the release of the HB2GV dashboard. The article also presents more information about health-based guidance values and discusses considerations when using guidance values to interpret human biomonitoring data. This article, entitled “Interpreting biomonitoring data: Introducing the international human biomonitoring (i-HBM) working group’s health-based guidance value (HB2GV) dashboard” is available online: https://doi.org/10.1016/j.ijheh.2022.114046



TERUG NAAR INHOUD

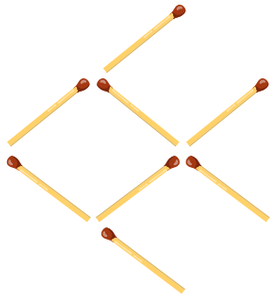
Christmas Puzzle

Dit jaar een puzzel met luciferhoutjes. Pak een luciferdoosje uit de la en probeer de oplossingen te vinden. Maak kans op een mooie prijs én eeuwige roem. Fotografeer je oplossing en stuur deze naar de redactie van de TCDD via redactie@toxicologie.nl onder vermelding van “uitslag kerstpuzzel 2022”.

This year a puzzle with matchsticks. Take a matchbox and try to find the solutions. Have a chance to win a great prize and eternal fame. Photograph your solution and send it to the editors of the TCDD via redactie@toxicologie.nl, stating “result Christmas puzzle 2022”.

1. Move two matchsticks so the glass is reformed without the coin inside.

2. Can you make the fish swim in the opposite direction by moving only three matchsticks?

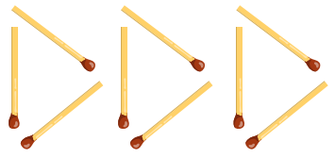


3. Move one matchstick to make a corrrect equation.

4. Change three matchsticks into six without breaking any of them.

5. Using just six matchsticks, make four equilateral triangles.

6. Move three matchsticks to make four equilateral triangles.



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