Dear Readers,

Welcome to the first edition of the Toxicology Group’s newsletter for 2020.

Obviously we are living in challenging times at the moment. Most events have been cancelled until at least July 2020. However I would like to flag up one of our events that will proceed: ICH Q3E (Extractables and Leachables) - setting the scene. This is now to run as a virtual event with quite an innovative premise (to my mind). Presentations will be shared in advance and the event itself will facilitate an “executive summary” by the presenter, followed by Q&A. It would be great if RSC Toxicology members could support this initiative and let’s see how it goes.

Another new meeting venture is the proposed Toxic Tort meeting in the autumn. This will be a meeting (rather than a clash!) of toxicologists and lawyers to discuss and share their differing perspectives in this important and developing area, as the recent publicity such as the film Dark Waters and the BBC Horizon programme about the Corby cases shows.

Last year was very busy with events and we have some meeting reports to keep you entertained during lockdown! There is also another winning poster to contemplate. Congratulations to Andrea Svarcova for her poster determining polychlorinated naphthalenes in human breast milk, which was presented at the 11th International Symposium on Biological Monitoring in Leuven, Belgium in August 2019.

We also continue to develop our Faces of Toxicology series; another video has recently “wrapped” and should be available soon and we hope to also share these through the RSC Education platform.

Enjoy the reading, be well, and stay safe.

Kate Jones
Chair, RSC Toxicology group
Committee members

**Chair:** Kate Jones (HSE)

**Treasurer:** John MacLachlan (retired)

**Secretary:** Chris Waine (bibra)

**Members:** Lindsay Bramwell (Newcastle University), Sarah Bull (WRc plc / TARA Consulting), David Hart (retired), Mark Hosford (International Platinum Group Metals Association), John Hoskins (Consultant), Anais Kahve (Broughton Nicotine Services Ltd), Trudi Knight (Birmingham University), George Kowalczyk (Consultant), Jo Larner (University of Hertfordshire), Mike Quint (Consultant), Martin Rose (Consultant), Paul Russell (Unilever), Ovnair Sepai (PHE), Andrew Smith (MRC-Leicester),

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Keep in Touch

MyRSC is the RSC’s social media platform. RSC Toxicology has a group on this site and we would encourage you all to sign up via the link below:

[http://my.rsc.org/groups/home/462](http://my.rsc.org/groups/home/462).

This is an easy way for us to share information about the group and to have discussions. Our web pages will continue to host forms and more static content. We’ve now got 280 people signed up to the MyRSC group – but as we have nearly 500 Toxicology group members, there’s still a way to go to get everyone on board!

In recognition that not everyone wants to use MyRSC, we have also established a [LinkedIn group](https://www.linkedin.com/groups/12014086) and a [Twitter account](https://@RSCToxGroup). Please do join in with the conversation!
Forthcoming meetings

Please take note of the following meetings and sign up early to avoid disappointment. Bursaries are available to any RSC Toxicology member for attendance at our meetings, subject to the usual conditions.

ICH Q3E (Extractables and Leachables): setting the scene

7 May 2020, 1pm – 4pm (BST)
This is still proceeding but now as a virtual event – please register!
In collaboration with the Joint Pharmaceutical Analysis Group, RSC Toxicology is organising this meeting, which will seek to provide an overview of the ICH process, the current situation for ICH Q3E and opportunities to influence the desired outcomes.

Plastics, From Cradle to Grave – and Resurrection II

<<This event has been postponed until June 2021>>
Further to the successful conference held last year, a follow up conference has been organised to expand on the key themes, looking at where we have come from, where we have got to and where we want to go.

This conference brings together academic and industrial speakers sectors with the aim of focussing on assessing challenges and opportunities for researchers, industry and government. There will be a thematic link between the current use of plastics, toxicology and standardisation, the complex issues with respect fit for purpose sampling and analysis, and the future of plastic usage.

Toxic Tort in the UK: Current Perspectives and Recent Cases

!Save the date!
1 October 2020, London, United Kingdom
A new joint meeting with UKELA.

Current Issues in Contaminated Land

!Save the date!
Wednesday 2 December 2020, London, United Kingdom
Ever-popular joint meeting with SoBRA. Following another successful, sell-out, meeting (see meeting reports in this issue), please mark the next one in your diary already!
The RSC Environmental Chemistry and the Toxicology Groups joined forces with the Environmental Physics Group from the Institute of Physics (IoP) to organise a one-day meeting on indoor air quality on 17th September 2019. 35 delegates convened in the IoP new flagship building in London to hear about and discuss the latest findings in indoor air chemistry and physics, and the challenges ahead.

The first speaker of the day was Ben Barratt from King’s College London, who presented a fascinating introduction on the links between indoor and outdoor air. Ben shared findings from various studies, including one comparing NO\textsubscript{2} measurements from background monitoring stations, sensors installed outside and insides homes, and portable devices for personal exposure. The results clearly indicated that the usual demarcation between outdoor and indoor air quality becomes increasingly blurry when personal exposure is taken into account, with the overall exposure consisting of a mixture between the two. Ben also presented the preliminary results from another study in which portable PM\textsubscript{2.5} monitors were attached to backpacks worn by school children in London to determine during which part of the day children were exposed to the most pollution. Initial results show clear spikes during their commute to and from school (outdoor), but also in the evening as a result of cooking (indoor). The highest concentrations of PM\textsubscript{2.5} were found on the London Underground and when someone was smoking or cooking indoors (~350 $\mu$g/m\textsuperscript{3}). In comparison, concentrations on a busy high street were much lower (~50 $\mu$g/m\textsuperscript{3}), yet these are the only emissions that current pollution curbing measures are tackling.

Janet Barlow from the University of Reading spoke next on the topic of natural ventilation processes in urban buildings. This is particularly timely in the context of buildings becoming increasingly more air-tight in an attempt to be more energy efficient, as typically 1/3 of heat is lost due to air leakage. Janet introduced the main drivers of indoor ventilation (pressure and heat) and the other physical factors that affect it, including room layouts, wind speed and direction, glazing and sunshine, thermal mass and human behaviour. In particular, Janet focused on an infiltration study carried out in an old office block on Marylebone Road, which used a number of sensors deployed in different locations (outdoors, indoors and in an internal courtyard) to characterise the rates of infiltration and its main drivers. Janet also discussed the REFRESH project investigating the interactions between the built environment and its occupants. In particular, the project highlighted the poor management of indoor environment conditions. Janet suggested that a clearly visible (e.g., a wall clock) traffic light system for a specific indoor pollutant could be used in shared indoor environments (e.g., offices) so that all occupants can be made aware of when to take remedial action (e.g., opening a window).

The first afternoon session was devoted to modelling and measurements of indoor chemistry with talks from Nicola Carslaw (University of York) and Coralie Schoemaeecker (University of Lille). Nicola introduced the main concepts of indoor air
chemistry, stressing how the chemical regimes of these environments can be very different from those found outdoors, in particular with respect to the type and abundance of species and to the physical conditions (light, humidity, etc.). As a result, while most of outdoor atmospheric chemistry is initiated by the photochemical formation and reactivity of the hydroxyl radical (OH), indoor air chemistry is instead kicked off by the reaction of ozone (O₃) with volatile organic compounds (VOCs). While outdoor air can affect indoor via infiltration, the main sources of indoor air pollution are cooking and cleaning activities. In particular, the VOCs released by most commercial cleaning products (e.g., limonene, linalool and α-pinene), once oxidised by ozone, can form a number of secondary and tertiary products, some of which are harmful to health. As many key indoors chemical species are challenging to measure, models such as the Indoor Detailed Chemical Model (INDCM) are often the best tools for providing insight into the complex chemistry of indoor environments. Nicola also discussed the importance of indoor photolysis, and in particular the use of UV lamps for extreme cleaning in hospitals to fight the spread of bacterial infections. Studies show that these lamps lead to high concentrations of OH radicals, and consequently of highly oxidised (and potentially harmful) reaction products, begging the question of whether, whilst addressing one health issue, we are creating another.

Coralie focused on the measurement aspects of indoor air chemistry, initially describing the various techniques used in field campaigns in indoor environments such as schools. Monitoring indoor VOCs by thermal desorption tubes revealed that up to 60% of VOCs were emitted by the occupants in a lecture room. Squalene in particular, a polyunsaturated hydrocarbon, is naturally shed from human skin and readily reacts with ozone to form semi-volatile products that can be respiratory and skin irritants. In addition, the increased surface-to-volume ratio found in indoor environments means that surfaces can significantly interact with the chemistry, as both sources and sinks airborne species. Field studies found that furniture, glued flooring and painted walls acted as sources of trace species, notably formaldehyde and other VOCs. Comparison of observed concentrations with models such as INDCM highlighted areas of uncertainty that are in need of further characterisation in real indoor environments, such as surface uptake and deposition and photolysis processes driven not just by transmitted external light, but also by some types of artificial lighting (e.g., uncovered fluorescent bulbs).

The third and final session of the day started with Benjamin Jones from the University of Nottingham, who focused on the relationship between building ventilation, indoor air quality and occupants’ health. Following a retrospective on indoor ventilation through the ages (e.g., how the ancient Egyptians built air shafts within the Great Pyramids), Ben focused on how to optimise ventilation rates for a large variety of building types. As it is difficult and time-consuming to measure the ventilation rate for every specific indoor environment (such as each classroom in a school), we are now moving away from a fixed recommended value (or range of values) for the ventilation rate (e.g., 7.5-10 L s⁻¹) towards a more dynamic approach in which a proxy variable (e.g., CO₂ concentration) is monitored and the ventilation rate adjusted accordingly so that the proxy does not exceed a particular threshold. The final part of Ben’s talk focused on a novel statistical approach aimed at selectively targeting particular indoor pollutants to maximise health and economic benefits of good indoor air quality. This method identified particulate matter, formaldehyde and acrolein as the main priorities to ameliorate indoor air.
The last talk of the day was given by Phil Symonds from University College London (UCL) who focused on radon gas in indoor environments. Radon is formed from the radioactive decay of uranium contained in a number of geological formations around the globe, and can seep into buildings from cracks in the foundations or flooring. Radon occurrence is higher in particular regions (e.g., Cornwall) depending on the local geology. Radon itself is radioactive, and exposure to it is the second leading cause of lung cancer world-wide after smoking. Phil showed the results of the analysis of a large dataset consisting of radon measurements made in 470,689 UK homes between 1980 and 2015. This study found that energy efficiency measures tend to increase the airtightness of properties and thus have an adverse effect on indoor radon levels. For instance, homes with double glazing installed had radon levels up to 67% higher than those without. This study highlighted how the push to improve the energy performance of the UK’s housing stock must not compromise on indoor air quality.

Appropriately, the meeting was hosted in the new IoP building, which was designed with sustainability in mind: it features ground source heat pipes, solar panels and a green roof, with installation including a huge screen with footage of the Moon’s surface and a cloud chamber.

Lindsay Bramwell (Newcastle University, lindsay.bramwell@newcastle.ac.uk) and Valerio Ferracci (Cranfield University, v.ferracci@cranfield.ac.uk) Prof Janet Barlow (University of Reading) illustrates the main drivers of heat and air flow in indoor environments.
Nicola Carslaw (University of York) introducing the chemical regimes of indoor air chemistry.

Meeting space in the IoP’s new flagship building.

Dr Phil Symonds (UCL) tackles the trade-off between energy efficiency and indoor air quality.
Happy 10th Birthday SoBRA! Some highlights from SoBRA’s 10th anniversary December Conference. Thanks to all SoBRA members for making this society a real success.

View programme & presentations
This one-day conference was organised by the RSC Energy, Sustainability and Environment Division, as befits a global issue, hosting speakers who provided valuable insights into the topic from both the UK water sector and also from national, international and global perspectives.

At a global scale, the UN Sustainable Development Goal 6 (SDG6) relating to clean water and sanitation includes a target of clean, accessible water for all by 2030. As of 2015, 30% of the world’s population does not have access to safe drinking water and 60% lack access to safe sanitation facilities. We have some way to go to reach our target, particularly considering that water scarcity affects 40% of the global population. By 2025, some 1.8 billion people are likely to experience absolute water scarcity and ⅜ of the world will live under water-stressed conditions.

England’s Environment Agency reported that the country is set to run short of water within 25 years. The population of the UK as a whole is expected to rise from 67 million to 75 million by 2050. By 2040, more than half of our summers are expected to be hotter than the 2003 heatwave, leading to more water shortages and potentially 50-80% less water in some rivers.

With these dynamics in mind, each of the speakers focused on the importance of developing solutions to these intractable problems through the acquisition and interpretation of accurate chemical data; these data may then facilitate rational decisions on critical issues such as:

- Water conservation
- Catchment management/planning
- Managing water leakage
- Managing water risks
- Resilience
- Decentralisation of supply and treatment
- Water reuse
- The value of water
- The market in water
- Public health education
- Hygiene
- Sanitation

The first speaker was Dr Martin Padley, a Director of United Utilities, who drew out four particularly important issues affecting his company:

- The colour of the water – where, in NW England, there has been a marked increase in raw water colour/dissolved organic carbon (DOC) variability over recent years.
- Extreme weather – with the frequency of such events demonstrably increasing over the last 25 years.
- Taste and odour – with customers tending to use these organoleptic parameters to self-judge the ‘safety’ of their water.
- The presence of geosmin (a naturally occurring organic compound with a distinct earthy flavour) and the use of granular activated carbon (GAC) to counteract it.

He went on to stress the need for effective process risk management and the importance of focusing on assets, processes and people to achieve this.

The next talk was by Neil Dewis, a Director of Yorkshire Water. He spoke about the history of water use and water treatment and considered how Our Green Future - the 25 Year Plan to Improve the Environment focuses on the polluter pays principle and thereby brings additional responsibilities for farmers in overseeing environmental aspects of land and catchment management. He developed this theme into a discussion of the concept of sustainable landscapes, involving stakeholder partnerships including water companies.
Dr John Carstensen, Head of Profession, Climate and Environment at the Department for International Development, then spoke about water issues relating to international development. He outlined the complementary approach that the two previous presenters had described to SDG objectives and went on to reinforce the importance of water as a resource and the detrimental impact that climate change was already having. He discussed the relationship between water scarcity and gross domestic product (GDP) alongside water security issues – including economic development and, particularly, urbanisation. He summed things up by stressing the critical importance of taking an interdisciplinary approach when seeking to resolve matters.

Dr Priyanka Jamwal from the Ashoka Trust for Research in Ecology and the Environment in Bangalore then spoke about some of the practical issues facing the quantification of water quality in India. The Indian water quality regulatory framework assesses quality and compliance using 1,245 monitoring stations. She described the rapid increase in the population of Bangalore over the last 20 years and discussed the benefits of passive sampling devices (some of which her NGO had developed, jointly with the University of Portsmouth) and also the topics of citizen science and affordable sensors to make monitoring site-specific rather than generic. She also mentioned the importance of an interdisciplinary approach and highlighted the important link between SDG6 and other SDGs, especially those relating to ecology and greenhouse gases.

Dr Rob Fuller a water sector adviser with WaterAid, the largest global NGO focusing on water, spoke optimistically about the achievability of SDG6. In his interesting talk highlighting the issue and consequences of unplanned urbanisation, he explained how planning in low income countries usually leaves a lot to be desired. He also discussed in some detail how remote sensing, chip-based analysis, citizen science and the increasing importance of ‘utility on a phone’ (using applications for payment and monitoring) will be playing an ever-expanding role in delivering SDG6.

The final talk of the morning was from Dr Graham Alabaster, Chief of Sanitation and Waste Management at UN Habitat. He explained the background to the development of indicators for the SDGs and the subsequent development of methodologies to capture both baseline and progress information. This itself is very much a work in progress, involving checking what methodologies and data are currently available and investigating discrepancies and mismatches between data sets that should be measuring similar things. He explained how helpful it was for professional bodies such as the RSC to engage and offer input into these tasks.

The afternoon session began with a talk by Dr Hannah Rigby from Imperial College, who described her work on the transfer of a number of organic contaminants to the food chain through agricultural land applications of wastes and the implications of this with respect to water sustainability issues.

Dr Tony Fletcher, an environmental epidemiologist from Public Health England, provided an interesting perspective on the formidable issue of perfluorinated compounds (PFCs) – especially perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA). His talk included some very interesting case studies on the problems surrounding the persistence of these chemicals in the environment and in humans.

Dr Caroline Gauchotte-Lindsay from University of Glasgow spoke on emerging contaminants in drinking water and wastewaters – including xenobiotics such as nanoparticles or microplastics, pharmaceuticals and personal care products. She considered analytical methods that are now being used to measure the concentrations of some of these moieties and provided a number of examples of published results together with their implications. She went on to describe how such considerations can help in better understanding the operation of water treatment plants and how this might factor in when designing upgrades and monitoring strategies.

The penultimate talk was given by Anastasia Kaschenko, CTO and co-founder of Majik Water. She explained how the age-old concept of dew harvesting had led their SME on a journey of discovery and innovation, investigating how such a seemingly simple technology might be applied and prototyped in low-income countries. She went on to describe how the company realised they had produced a technology without a valid business model, and she discussed how grappling with this disconnect had pivoted the company’s business planning to concentrate on drastically improving the efficiency of existing off-the-shelf materials and components. They now aim to reduce the cost of high-volume air to water units and to compress the lead time between technology development and its application.
The final speaker of the day was the recipient of the RSC ESED Sustainable Water Award for 2018, **Professor Dionysios Dionysiou** from the University of Cincinnati. His presentation discussed contaminants of emerging concern (CECs) and the detailed chemistry of advanced oxidation processes (AOPs). He examined various benefits and disbenefits associated with a number of aspects and types of AOP, explaining the importance of considering factors such as matrix, cost, energy, treatment conditions, transformation products, radical scavenging, toxicity and waste disposal when weighing up the options.

Professor Dionysiou was presented with the **RSC 2018 Sustainable Water Award** by Dr Camilla Alexander-White, Senior Policy Advisor Environment and Regulation.

The proceedings highlighted the critical value of good data and evidence-based decision-making for achieving a future of sustainable water. Each of the inspiring presentations illuminated and reinforced strategies and tactics employed by the chemical industries.

Slides for the day’s presentations can be found here.

**Resources:**

With thanks to ESED for this article, especially to Dr. Glynn Skerratt (secretary of the RSC Environmental Chemistry Group). Thanks also to Martin Rose for representing the RSC Toxicology group.
The 11th International Symposium on Biological Monitoring in Occupational and Environmental Health (ISBM) was successfully organized in Leuven, Belgium in August 2019 by ICOH’s Scientific Committee on Occupational Toxicology (SCOT), in collaboration with the SCs on Rural Health, Toxicology of Metals and Nanomaterial Workers’ Health.

RSC Toxicology group sponsored one of the poster prizes (over 60 were on display) and we were pleased to award Andrea Svarcova the prize for her poster on determining polychlorinated naphthalenes in human breast milk (reproduced overleaf).

**Faces of Toxicology**

For those of you who have not yet checked out these videos, a playlist can be found [here](#). This video series aims to showcase the variety of careers available in toxicology. The series begins with an animated overview of toxicology as a science followed by individual toxicologists talking about their work. The Toxicology Group Committee is working to add further videos, so if you are interested in being a “face” of toxicology, please [get in touch](#).

We are continuing to add new videos; another should be added shortly. We are also hopeful that the videos will soon appear on the RSC’s education platform [A Future in Chemistry](#).

**Chemistry Humour**

Did you hear the one about cobalt, radon, and yttrium?

*It was CoRnY.*

What should you do if no one laughs at your chemistry jokes?

*Keep telling them until you get a reaction.* (Or maybe not!)
**Determination of polychlorinated naphthalenes in human breast milk from mothers living in the Czech Republic**

**Andrea SVARCOVA, Ondrej PARIZEK and Jana PULKRABOVA**

**Introduction**
- Polychlorinated naphthalenes (PCNs) represent a sub-group of 75 congeners with physico-chemical properties similar to polychlorinated biphenyls (PCBs).
- PCNs are currently not produced, but they are unintentionally formed by high-temperature industrial processes, where chlorine is present. An example could be the waste burning or melting of non-ferrous metals (in the manufacture of cement, magnesium, copper or aluminum refining).
- PCNs are hepatotoxic and some of them exhibit dioxin-like toxicity. Nowadays, PCNs have caused an increasing scientific concern and were recently included as persistent organic pollutants (POPs) on the list of the Stockholm Convention.
- The occurrence of PCNs in the environment (air, sediment, soil, water and biota) and in human exposure to them, has caused a need to monitor these emerging compounds.

**Aims of the study**
- To optimize an instrumental method using gas chromatography coupled to tandem mass spectrometry (GC–MS/MS) for the identification/quantification of 11 PCNs.
- To test and validate the existing sample preparation procedure for the simultaneous determination of non-apolar compounds such as PCBs (n=18), OCs (n=13), BFRs (n=22) together with PCNs (n=11) in human breast milk.

**Samples characterization**
- Samples of breast milk (n = 20) were obtained from mothers living in two different cities of the Czech Republic: Karviná (n = 13, heavily air polluted) and Ceske Budejovice (n = 7, control locality).
- Approximately 30 mL of breast milk was collected from mothers on the third day after the birth of the baby directly in the maternity hospital. The age of mothers ranged from 19 to 46 years (mean: 31.5 years), they proved to be healthy and non-smokers.

**Experimental Procedure**

**Instrumental parameters**
- Agilent GC 7890A (USA)
- Agilent 7000B GC/MS Triple Quad (USA)
- Ionization EI
- Column: DB-5MS
- (30 m x 0.25 mm x 0.25 μm), (Agilent, USA)
- Injection mode: PTV
- Injection volume: 2 μl

**Optimization of GC-MS/MS method**

<table>
<thead>
<tr>
<th>Congener</th>
<th>LOQs (ng/ml)</th>
<th>Linear range (ng/ml)</th>
<th>Reliability value (R²)</th>
<th>Linear range (ng/ml)</th>
<th>Reliability value (R²)</th>
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</thead>
<tbody>
<tr>
<td>PCN 1/2</td>
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<td>0.9933</td>
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<td>0.9900</td>
<td>0.005</td>
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</tr>
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**Results**

**Table 1: Limits of quantification (LOQs), recoveries and repeatabilities (n=6) of analytical method, spiking level 500 pg/g lw (whole cow's milk)**

<table>
<thead>
<tr>
<th>Analyte</th>
<th>LOQs (pg/g lw)</th>
<th>Recoveries (%)</th>
<th>Repeatabilities (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCN 1/2</td>
<td>2</td>
<td>77</td>
<td>4</td>
</tr>
<tr>
<td>PCN 4</td>
<td>2</td>
<td>111</td>
<td>6</td>
</tr>
<tr>
<td>PCN 8</td>
<td>2</td>
<td>114</td>
<td>5</td>
</tr>
<tr>
<td>PCN 18</td>
<td>10</td>
<td>117</td>
<td>6</td>
</tr>
<tr>
<td>PCN 20</td>
<td>10</td>
<td>115</td>
<td>7</td>
</tr>
<tr>
<td>PCN 41</td>
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<tr>
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<tr>
<td>PCN 75</td>
<td>500</td>
<td>119</td>
<td>15</td>
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</table>

**Figure 1: Concentrations (μg/g lw) of the major congener PCN 20 in breast milk samples from Ceske Budejovice and Karviná**

<table>
<thead>
<tr>
<th>Concentrations of all detected PCNs (μg/g lw)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceske Budejovice</td>
</tr>
<tr>
<td>PCN 20</td>
</tr>
<tr>
<td>PCN 42</td>
</tr>
<tr>
<td>PCN 52</td>
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<tr>
<td>PCN 56</td>
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<tr>
<td>Mean</td>
</tr>
<tr>
<td>Median</td>
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<tr>
<td>Min</td>
</tr>
<tr>
<td>Max</td>
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<tr>
<td>1.125</td>
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<tr>
<td>603</td>
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</tbody>
</table>

**Conclusions**
- The validation of analytical procedure using GC–(MS/MS) was performed on cow's milk (n=5) at a concentration of 500 pg/g lw, the recoveries ranged from 77 % to 125 % with RSD <15 % and LOQs reaching 2 – 500 pg/g lw.
- PCN 20 congener as the most frequently detected compound was quantified at levels ranging from 151 to 1125 pg/g lw.
- In addition, congeners PCN 42 (3 samples; <125-380 pg/g lw), PCN 52 (3 samples; <125-676 pg/g lw), PCN 56 (6 samples; <125-693 pg/g lw) and PCN 66 (4 samples; <250-260 pg/g lw) were determined in breast milk samples at concentrations corresponding to the data from publish studies originated in Sweden and Ireland.2,3
- These data represent the initial results in the context of human biomonitoring conducted in the Czech Republic.

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