NIHR | Health Protection Research Unit in Environmental Exposures and Health at Imperial College London

# 2021/2022 International Scientific Advisory Board Report

Imperial College London

UK Health Security Agency

KING'S College LONDON

MRC Toxicology Unit

UNIVERSITY OF CAMBRIDGE

# Table of Contents

# 1. OVERVIEW

## Mission and vision

The mission of the HPRU in Environmental Exposures and Health (EEH) is to undertake the highest quality research on the health effects associated with exposure to a range of environmental pollutants, including those in the ambient and indoor settings and in water.

Our aims are 1) to improve the understanding of the distribution, determinants and pathways linking these exposures to health effects, 2) to provide scientific evidence that will impact directly on public health practice and policy and, 3) to train the next generation of research leaders in environment and health.

During its second year (2021/22) the EEH HPRU progressed its research to advance understanding of the causes and effects of key environmental issues affecting public health as evidenced below.

## Strategy and objectives

Air pollution, noise, illicit drugs and tobacco are major underlying causes of chronic diseases while emerging hazards such as microplastics, particles resulting from brake and tyre wear and e-cigarettes pose possible risks to human health. Combined these represent a considerable burden to the NHS and public purse with air pollution and tobacco being responsible for approximately 120,000 premature deaths/year in the UK. Exposures to many environmental hazards are established and ubiquitous and there is potential to reduce morbidity and mortality from disease, increase healthy life expectancy, reduce health inequalities with appropriate interventions and controls. By advancing understanding of these exposures and combining this with a knowledge of susceptibilities we can lessen their health impacts. Finally, there needs to be translation of this knowledge to application and policy. We undertake this with a dedicated knowledge translation lead.

Thus, our aims are to improve the understanding of the hazards, exposures and causal pathways linking these exposures to health effects, to provide scientific evidence that impacts directly on public health practice and policy. Further, there is a need to train the next generation of research leaders in toxicology, environment and health.

Addressing these objectives, the research programme is organised into four complementary themes focusing on furthering understanding of the risk of ambient and indoor air pollutants on health, by examining a range of adverse endpoints in specific population subgroups (e.g., adverse birth outcomes and cognitive function in school children) and in specific locations (indoor, homes and offices, transport micro-environments including the London Underground).

To achieve this, we utilise improved exposure assessment methods including data geocoding and linkage along with ‘omic’ technologies to produce an integrated approach to environmental health research and risk assessment. This approach, across our themes, allows us to focus activity on the established adverse outcome pathway framework that provides a basis in which to assess the weight of data and identify data gaps on the molecular pathway that links exposures to adverse outcomes at the cell, organ and population level. This framework allows the advancement of knowledge to better inform environment and health policy.

## Progress/achievements in the second year

### Progress with leadership, governance and management arrangements

Imperial College, UKHSA (formerly PHE), King's College and MRC Toxicology Unit at Cambridge have continued to develop excellent partnerships utilising their complementary skills. This is evidenced, in part, by our work responding to COVID-19 which has involved original research in ambient air and surface tracking of the SARS-CoV2 virus, the effects of air pollution and E-cigarettes on susceptibility to infection and outcomes of infection.

There have been no challenges with the leadership, governance and management arrangements this year. We have continued to hold regular Executive Group and Theme meetings online and these have worked very well with good attendance from team members.

Full details of the leadership, governance and management arrangements can be found in Annex 1.

### Implementation of the research strategy

Theme I focuses on population exposures from all sources. Although progress has been slowed down by the pandemic in a number of projects, we have made good progress with NatCen, where we selected a subset from the Health Survey for England (HSfE) and tested our questionnaire & sampling protocols. In addition, we have agreed UK relevant priority toxicants, developed analytical methods and SOPs utilising both UKHSA and Imperial laboratories. Our indoor air quality research in schools has been published (Varaden et al).

Theme II focuses on health effects of exposure and benefit of mitigation. Several publications related to the work on mental health have been published (Newbury et al; Bakolis et al; Peters et al) as have papers related to diesel exposures in professional drivers (Lim et al, 2021, 2022; Bos et al). Redirected pandemic related research examined the link between SARS-CoV2, air pollution and lower respiratory tract infections (Walton et al) while the WHO air quality guideline review was support by an examination of natural desert dust health impacts (Kelly & Fussell).

Theme III is focused on the mechanistic linkage between chemicals found in particulate air pollution (Fransen et al) with a particular focus on asthma (Chen et al) and the interaction of these chemicals with biochemical pathways that activate immune and inflammatory responses in the lung. This theme is an important linkage between the epidemiology and knowledge application.

Theme IV continues to be involved with the COVID response (Ward et al; Riley et al; Elliott et al) as well as addressing health challenges related to chemical exposures (Ball et al; Collins et al), industrial fires (Griffith et al) and microplastics (Nematollahi et al).

The HPRU is very focussed on knowledge translation and an excellent example of knowledge translation this year are our reports on pathways to achieve WHO PM2.5 goals in the UK (https://www.imperial.ac.uk/school-public-health/environmental-research-group/research/modelling/pathway-to-who/) and a health Impact assessment of current and past air pollution on asthma in London. (https://www.london.gov.uk/sites/default/files/hia_asthma_air_pollution_in_london.pdf

Finally, we were very pleased that the additional funding secured allocated to 2021/22 is **£5,210,164** a great return on the NIHR investment, with 8% in collaboration with Industry.

The impact of the ongoing pandemic during year 2 continued to have some level of impact on many of our laboratory-based projects either through restricted working practices, consumable shortages, or staff absences through sickness. Recruitment issues also continued in some of our experimental studies, such as our investigations into e-cigarettes, and biomonitoring. These issues were offset however with our investigations instigated in year 1 involving environmental sampling programmes for the virus in the London transport network and Imperial College campus buildings.

## Top achievements during Year 2

Considering the various challenges resulting from restrictions due to the pandemic, the HPRU has still managed to achieve a great deal including:

- We are particularly pleased with our ongoing research on air pollution impacts across the life course. In particular, our work on the effects of air pollution on mental health and dementia have major public health ramifications.

- Our collective efforts around COVID – Elliott's REACT programme and Kelly & Green's SARS-CoV-2 virus screening on London public transport system to help improve public confidence in travel. UKHSA work to help understand any interaction between e-cigarettes and SARS-CoV2 assisted in developing the evidence necessary to respond to this concern.

- Our appearance at New Scientist Live North in Manchester (March) and again in London (October) involved staff from all partners (UKHSA, ICL, MRC/UoC and KCL). This is listed as a major achievement because as the first in-person outreach activity in two years following COVID it took a lot of flexible and fast organisation and commitment. We specifically focused on emerging public health concerns around the links between air pollution and brain health, both cognitive development in children and dementia risk in the elderly, environmental microplastic and bioaerosol exposure. We also performed quizzes and polls to evaluate the public's understanding of environmental risks and to establish what they felt should be our research priorities going forward. In doing so we had direct interaction and gained valuable knowledge about concerns that will influence our project choices as we move forwards.

- We have expanded the HPRU work outside of the established remit. Both new projects are in Theme 4, (projects 7 and 8). One addresses chemicals regulatory work with a project to validate an in vitro test method for xenobiotic mediated cytochrome P450 induction while the second examines the requirements for Toxicological Training in the UK in particular, though its findings are applicable internationally.

# 2. RESEARCH THEMES

During its first year the EEH HPRU's research advanced understanding of the causes and effects of key environmental issues affecting public health. Progress has continued in the second year with more recruitment and the impact of delays caused by the pandemic has been reduced.

## Theme I: Assessment of Population Exposures

**Theme Leads:** Emma Marczylo (UKHSA) and Benjamin Barratt (ICL)

### Theme Overview

Both the Chief Medical Officer's 2017 annual report and the Toxic Chemicals in Everyday Life Inquiry Report by the Environmental Audit Committee (EAC) highlighted the need for robust research to quantify UK exposures to environmental hazards. This Theme combines direct and indirect methods of exposure assessment to improve our exposure knowledge. Human biomonitoring (HBM) and air sampling (both outdoor and indoor) will determine exposures to chemicals, metals, gases, nanoparticles, bioaerosols and e-cigarettes within sample populations. Modelling tools will be developed to predict UK population exposures. Data generated from this Theme will inform the epidemiological, mechanistic and responsive projects across themes 2, 3 and 4.

### Aims/Objectives

To advance the understanding of exposures to a range of known and emerging environmental toxicants and support interventions to improve public health by improving risk assessment and management.

- Identify and/or characterise exposures of concern within indoor and outdoor environments, including chemicals, gases, bioaerosols and toxicants released from consumer products.
- Undertake human biomonitoring studies to analyse environmental toxicants from a subset of the Health Survey for England cohort and markers of smoking/vaping within at risk groups including pregnant women and mental health patients.
- Model exposures from indoor environments and consumer products to support improved risk assessments and work within the other themes to provide a better understanding of health effects of environmental exposures.

### Progress against short, medium and long term objectives

Except for Project 1, all other projects have been delayed to some extent by Covid restrictions or recruitment (Project 6). Plans are in place to address these issues and if there are no further lockdowns we plan to deliver on Projects 1-5. In project 6 we have been unable to appoint a suitable PhD student and are now taking this work forward with staff time at UKHSA, however we anticipate that we will need to raise additional funding for completion.

## Theme I Project 1: Human Biomonitoring (HBM)

**Project Leads:** Ovnair Sepai, Lorraine Stewart (UKHSA), Leon Barron (ICL)
**Research Team:** Tim Marczylo, Atallah Elzein, Adam Laycock and Jinkang Zhang (UKHSA)

### Aims

To advance our understanding of the nature and level of chemical exposure of English citizens and the potential health risks thereby leading to better protection of population health. Collation of a baseline database of exposures to environmental toxicants will enhance risk assessment and assist in tracking trends in exposure levels and success of any public health interventions subsequently implemented.

### Progress

**Background**: Approximately a quarter of all deaths worldwide are attributable to environment exposures. Exposure to a mixture of chemicals is a factor of modern life. HBM is an important tool which enables the quantification these exposures from all routes (inhalation, dermal, ingestion) and sources (air, land, food water). This work will assess the exposure of the English population to some key chemicals and test the feasibility of integrating an HBM module into the Health Survey for England (HSfE).

**Methods**: A subset of 300 individuals, aged 18-49 years was selected from the participants in the HSfE (approximately 10,000) for this HBM study. Participants complete a questionnaire that included questions designed to collect elicit information concerning different sources of exposures to the substances of interest (see Figure 1). An additional online questionnaire was used to collect other relevant information for the HBM module. Collected blood and urine samples were sent to UKHSA and ICL laboratories for analysis. Where possible samples will be bio-banked for future research/ investigations.

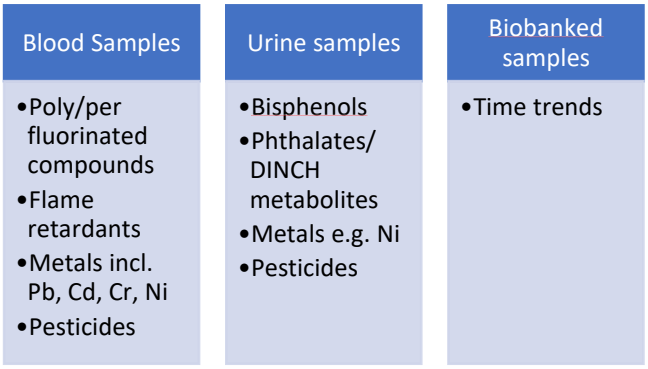



Figure 1: Preliminary list of substances to be analysed in blood and urine samples collected from participants.

**Results**: Samples collected during the trial run in September 2021 have been analysed for metals. 70% were found to have lead levels exceeding the intervention level for pregnant women and children of 10µg/dL.

**Conclusions**: Fieldwork commenced 3 months and on completion we will be able to determine the level of exposure of the general population and integrate these data with dietary sources and environmental contamination.

### Impact

- The main output will be the ability to evaluate the level of risk from exposure to environmental chemicals.
- Will provide the evidence to inform national chemical regulation and public health policy.
- The results will be compared to international data sets and be used to inform future surveys.

## Theme I Project 2: Biomarkers in smoking and vaping populations

**Project Leads:** Tim Marczylo (UKHSA), Debbie Robson (KCL)
**Research Team:** Ann McNiell, Eve Taylor (KCL), Adam Laycock (UKHSA)

### Aims

We are investigating two at risk populations from exposure to e-cigarette aerosols: We aim to assess exposure to toxicants from vaping, smoking, dual use, NRT use and non-use in 1) people using mental health services and 2) during pregnancy. We are assessing smoking and vaping prevalence and characteristics of people with mental health condition (MHC).

### Progress

**Background**: People with MHC have high rates of smoking and experience a substantially higher burden of tobacco-related diseases, than people without MHC. Smoking during pregnancy exposes the developing foetus to toxicants with adverse effects at critical stages of development.
E-cigarettes (vaping) help people quit smoking and expose people to far lower levels of toxicants. People with MHCs or who are pregnant are rarely included in vaping biomarker research. Therefore, as pregnant women and people with MHC may benefit from switching from smoking to vaping, we need to investigate the levels of tobacco related biomarkers in these populations who vape, smoke or do neither.

**Methods**: 1) Systematic review of tobacco-specific nitrosamine (TNSA) levels among people who vape, smoke or do neither.
2) Cross-sectional survey (n=27474) of smoking/vaping prevalence and characteristics among people with/without MHC.
3) Pilot study of tobacco-related biomarker levels among 19 people in a secure mental health setting, who vape, dual use, use NRT or do not use.
4) Six-month longitudinal study investigating exposure to toxicants from smoking and vaping in community mental health services (n=240).
5) Cross-sectional biomarker study in first-trimester pregnancy.

**Results**: 1) 22 studies identified, and 8 meta-analyses conducted. TSNA-exposure in vapers was significantly lower than smokers, but higher than non-users. 2) Smoking, vaping and dual use was higher in those with MHCs, especially multiple MHCs than those with no MHC history. Smoking but not vaping characteristics was associated with a history of MHCs. 3) Smoking and vaping behaviours analyses, urinary biomarker analyses is underway.

### Impact

Taylor et al (2022) Smoking and vaping prevalence and product use and mental health in Great Britain: A population survey" under review in BMC Medicine.

## Theme I Project 3: Acute CO exposure

**Project Leads:** Tim Marczylo (UKHSA), Ian Mudway (ICL)
**Research Team:** Jinkang Zhang, Tim Marczylo (UKHSA)

## Aims

Acute CO-poisoning is associated with lasting neurotoxicological effects. It is suspected that cases of CO under-reported. The aims of the EDCO study are to report proportion of patients attending Emergency Departments with symptoms typical of CO-exposure and giving positive responses to the COMA (Cohabitees, Outside, Monito, Alarm) mnemonic and to measure COHb levels and smoking status to inform interventions.

## Progress

**Background**: Low-level exposure to carbon monoxide (CO) is a significant health concern but difficult to diagnose due to non-specific symptoms. We aimed to establish the prevalence of low-level CO poisoning in patients presenting to the emergency department

**Methods**: A cross-sectional study of patients with symptoms of CO exposure was conducted in four EDs. We collected data on symptoms using the 'COMA' screening tool and measured carboxyhaemoglobin. An investigation of patients' homes was undertaken to identify sources of CO exposure.

**Results**: Based on ED assessment of 4175 participants, prevalence of suspected CO exposure was 0.62% (95% CI; 0.41% to 0.91%). CO testing in the home confirmed 1 case of CO presence and 21 probable cases. Levels of carboxyhaemoglobin within the normal clinical range were found in 19 probable cases and in the confirmed case.

**Conclusions**: This study provides evidence that ED patients with non-specific symptoms and no clear history of CO exposure are at risk from CO poisoning. Our findings suggest components of the COMA screening tool may be useful indicators of CO exposure over and above an elevated COHb. COHb levels were poor predictor of CO exposure.

We have now established a biobank of samples that will enable this project to investigate potential novel biomarkers of CO exposure using non-targeted mass spectrometry techniques.

## Impact

- First manuscript submitted for publication
- Clinicians should have a high index of suspicion for CO exposure so that this important diagnosis is not missed.
- A biobank of samples has been established for biomarker discovery work.

## Theme I Project 4: Assessing (nano-)particle exposures from consumer products including those using advanced materials

**Project Leads:** Matthew Wright (UKHSA) and Ian Mudway (ICL)
**Research Team:** Matthew Wright, Adam Laycock, Rachel Smith (UKHSA), Ian Mudway (ICL)

## Aims

The aim of this project is to measure the concentrations, chemical content, temporal and size distributions of aerosols produced during use of consumer products containing advanced materials, especially nanomaterials, to estimate indoor exposures and hence inform risk assessments. The goal is to improve currently ill-defined hazard profiles associated with potential inhalation exposure to these materials.

## Progress

**Background**: Little is known about associated inhalation exposures, important for assessing potential public health risks from 'nano-enabled' consumer products. So-called 'colloidal' spray products claiming to contain metal nanoparticles, have proliferated in online marketplaces in recent years. Here we assessed the characteristics and metal constituents of these products and the aerosols produced when sprayed and evaluated potential health risks associated with their use.

**Methods**: A survey of online marketplaces was undertaken to identify products and a representative sample (10 products) obtained. Products were sprayed (25 sprays in 2 minutes) inside a small chamber with samples of the 'neat' product, droplet and air samples collected for metal analysis via ICP-MS. Aerosol properties were monitored using Condensation Particle Counter (aerosol concentration) and Aerodynamic Particle Sizer (size distribution).

**Results**: As in similar previous studies a disparity between measurement and manufacturer claims of elemental content was observed, with most containing much less mass of metal than claimed. Mass size distributions suggested that almost all mass is found in 5 µm and larger aerosols, indicating that deposition would largely occur in extrathoracic and upper airways, although some products (4/10) did also produce particles in the sub-5 µm range.

| Product # | Element claimed | Conc$^{n}$ claimed (ppm) | Mass per spray (mg) | Measured element conc$^{n}$ in product (ng/mL) | Mass of element expected/spray (ng) | Measured vs stated conc$^{n}$ (%) | Peak number concentration (cm$^{-3}$) | Element quantifiable in air sample | Element detected in air sample |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Ag | 45 | 0.147 | 29935 | 4408 | 66.5% | 214 | Y | Y |
| 2 | Cu | 50 | 0.114 | 3706 | 422 | 7.4% | 49 | N | Y |
| 3 | Mg | 12 | 0.140 | 810 | 113 | 6.7% | 300 | Y | Y |
| 4 | Cu | 20 | 0.138 | 17988 | 2484 | 89.9% | 186 | N | Y |
| 5 | Ag | 40 | 0.119 | 28227 | 3350 | 70.6% | 91 | Y | Y |
| 6 | Cu | 50 | 0.106 | 6215 | 657 | 12.4% | 47 | N | Y |
| 7 | Pt | 10 | 0.107 | 0 | 0 | 0.0% | 16 | N | N |
| 8 | Ag | 15 | 0.132 | 222 | 29 | 1.5% | 323 | N | Y |
| | Zn | 20 | 0.132 | 272 | 36 | 1.4% | 0 | N | N |
| 9 | Zn | N/S | 0.092 | 363 | 33 | 3.6% | 192 | N | N |
| 10 | Ag | N/S | 0.076 | 2 | 0.1 | N/S | 410 | N | N |

N/S = Not stated on product literature

**Conclusions**: Aerosol concentrations were very low compared with other indoor sources e.g. cooking, and product market penetration appears low. Hence potential public exposure to metal nanoparticles from this product type under normal use is not expected to be significant – however some products indicate higher-risk uses and exposure via ingestion route appears more likely than via inhalation.

## Impact

**Poster presentation:** Aerosols produced from metal-containing 'colloidal' consumer spray products, Wright MD, Laycock A, Smith R. International Aerosol Conference 2022, Athens, Greece, 3-9th September 2022.

## Theme I Project 5: Bioaerosol quantitation and effects

**Project Leads:** Pippa Douglas, Emma Marczylo (UKHSA), Fred Piel (ICL)
**Research Team:** Emma-Jane Goode (UKHSA), Muhammad Saleem Khan, (ICL)

## Aims

1. Explore the health risk of living near permitted composting sites (PCSs) on disease severity in children and adults with cystic fibrosis (CF) across the UK.
2. Review the literature on cellular responses to fungal bioaerosols *in vitro*.
3. Identify collaborative opportunities through a cross-partner meeting across multiple HPRUs and wider networks.

## Progress

**Background**: Bioaerosols are ubiquitous in both outdoor and indoor air. Fungi are of particular interest as they are associated with asthma, allergies and complications in other respiratory diseases, including CF. Elevated concentrations of *Aspergillus fumigatus*, a pathogenic fungus prevalent in people with CF, are emitted from PCSs. To better understand the impact of bioaerosols on health, associations with vulnerable populations and underlying biological pathways linking exposure to outcome need to be identified. This is a field of research that overlaps multiple disciplines with the potential to make greater impact through collaboration.

**Methods**:

1. A semi-individual cross-sectional study was used to investigate the impact of living near a composting facility on lung function, pulmonary exacerbations and infections in CF sufferers.
2. A PRISMA based literature review was used to identify what drives allergic inflammatory responses to the known fungal allergens at the airway epithelial barrier.
3. Opportunities for future collaboration were identified through a cross-partner meeting between representatives from the four HPRUs.

**Results**:

1. Lung function was lower (ppFEV1 1.07% (95% CI: -2.29%, 0.16%)) and number of days/year of pulmonary exacerbations higher (1.02 (95% CI:1.01-1.04)) in adults with CF living <4 km from a PCS.
2. Despite study heterogeneity, key biological pathways contributing to the allergic response to fungal exposures and associated knowledge gaps were identified (Fig. 1).
3. Training, sample/data sharing, and stakeholder mapping were prioritised as collaborative opportunities.

**Conclusions**:

1. This work has indicated the need to better assess clinical relevance of these findings using more refined exposure assessment methods.
2. Pathways and knowledge gaps are key to informing further experimental work within Theme III.
3. Bioaerosol research represents a valuable opportunity for greater collaboration and impact.

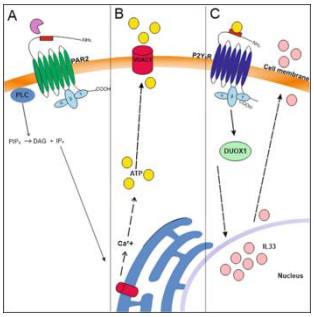



*Figure 1 - Potential PAR2 and IL33 pathways in epithelial cells. A: PAR2 activation by proteases, B: Ca2+ induced ATP release, C. Purinergic and DUOX1 dependent IL33 release*

## Impact

**Publications**:

- Saleem Khan, M., Douglas, P. Hansell, A.L., Simmonds, N.J., Piel F.B. Assessing the health risk of living near composting facilities on lung health, fungal and bacterial disease in cystic fibrosis: a UK CF Registry study.
- Submitted to Environmental Health.
- Emma-Jane Goode and Emma L Marczylo. What drives allergic inflammatory responses to the known fungal allergens at the epithelial barrier in the airways? To be submitted to Allergy.

**Collaborations**:

- Informs experimental work in Theme III/Project 7
- Stakeholder mapping with partners across 4 HPRUs and BioAirNet (one of the UKRI-funded Strategic Priorities Fund Clean Air Programme networks).

## Theme I Project 6: Indoor air pollution

**Project Leads:** Sani Dimitroulopoulou (UKHSA), Ben Barratt (ICL)
**Research Team:** Charlotte Landeg-Cox, Alice Middleton, Tim Marczylo, Kaja Milczewska, Christina Mitsakou (UKHSA)

## Aims

To develop a microenvironmental/exposure model to predict indoor concentrations of volatile and semi volatile organic compounds (VOCs and SVOCs) at home. The predicted concentrations will be used to assess cumulative risk from exposure to the most frequently occurring and health relevant VOCs and SVOCs in the home environment. The validation of the microenvironmental modelling tool will be achieved through collaboration with Imperial College.

## Progress

**Background**: Indoor exposure to chemicals contributed significantly to personal exposure in developed countries, where people spend up to 90% of their time in the indoor environment. Further data are required to identify the most abundant and health relevant VOCs and SVOCs at home, their concentrations and emission rates for the parameterisation of the model.
**Methods**: Systematic reviews were carried out, on VOCs/SVOCs concentrations measured in European residences, to look at their sources, and where possible, their emission rates, and to report the associated health effects from exposure to individual VOCs/SVOCs. The review followed the PRISMA methodology. A systematic search was conducted using the Global Health, Scopus and Environment Complete online databases. A search strategy was developed with key terms to explore the literature, restricted by publication language (English) and date (2000−2020).
**Results / Conclusions**:

Table 1
Individual Volatile Organic Compounds (VOCs) identified through measurements in residences and their calculated Weighted Average Geometric Mean (*WAGM*).

| VOC | *WAGM* (μg/m³) | VOC | WAGM (μg/m³) | VOC | *WAGM* (μg/m³) |
|---|---|---|---|---|---|
| Ethanol | 92.00 | Isobutane | 4.01 | 1-Methoxy-2-propanol/propylene glycol methyl ether (PGME) | 1.35 |
| Formaldehyde | 18.04 | 2-Ethylhexanol | 3.70 | 4-Ethyltoluene | 1.33 |
| Toluene | 15.90 | Dodecane/*n*-dodecane | 3.69 | 2-Butoxyethanol | 1.26 |
| Limonene [inc. *D*-limonene] | 13.65 | Hexane/*n*-hexane | 3.66 | 2-Carene | 1.10 |
| Hexanal/hexaldehyde/ hexanaldehyde | 13.30 | Heptane/*n*-heptane | 3.45 | Methyl-cyclopentane | 1.04 |
| *α*-pinene | 12.10 | Trimethylbenzene (including 1,2,4- Trimethylbenzene) | 3.22 | Isopropanol | 1.00 |
| Butane | 12.00 | Cyclohexane | 2.99 | 3-Ethyltoluene | 0.98 |
| Acetone | 11.40 | 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate (tpddib/TXIB) | 2.94 | 2-Ethyltoluene | 0.94 |
| Acetaldehyde | 10.14 | 2,2,4-Trimethyl-1,3-pentanediol monoisobutyrate (tpdmib/texanol) | 2.78 | Acrolein | 0.92 |
| 2-Methyl-1-propanol | 8.20 | Tetracholorethane | 2.68 | Styrene | 0.82 |
| 2-Methylbutane | 7.80 | Methyl-cyclohexane | 2.68 | Propylbenzene | 0.80 |
| 1-Butanol | 6.16 | Tetrachloroethylene/tetrachloroethene | 2.24 | Tetrachlorocarbon | 0.80 |
| Butylbenzene | 5.72 | Nonane | 2.21 | Trichloroethane | 0.73 |
| Decane/n-decane | 5.27 | Benzene | 1.99 | *p*-Isopropyltoluene/*p*-cymene | 0.56 |
| *m* + *p*-Xylene | 4.57 | Ethylbenzene | 1.84 | Trichloroethene/trichloroethylene | 0.53 |
| Undecane/n-undecane | 4.38 | Propanal/proprionaldehyde | 1.80 | Naphthalene | 0.50 |
| 3-Carene | 4.38 | Tridecane | 1.77 | Chlorobenzene | 0.42 |
| Pentanal | 4.34 | Pentane | 1.69 | Methylbenzoate | 0.33 |
| 2,2,4 Trimethylpentane | 4.33 | *o*-Xylene | 1.57 | 1,3,5- Trimethylbenzene | 0.33 |
| Octanal | 4.30 | *α*-Pinene | 1.56 | Pyridine | 0.12 |
| Ethyl acetate | 4.30 | Benzaldehyde | 1.55 | 1,3-Butadiene | 0.11 |
| *p*-Dichlorobenzene | 3.90 | Octane | 1.54 | 3-Ethenylpyridine/3-vinylpyridine | 0.06 |

*Table 1 - (from Halios et al., 2022) shows the most frequently occurring and health relevant VOCs in European residences.*

Sixty-five individual VOCs were identfied, 52 were emitted from building and construction materials (e.g. brick, wood products, adhesives, and materials for flooring installation etc.), 41 were emitted from consumer products (passive, electric and combustible air fresheners, hair sprays, deodorants) and 9 VOCs were emitted from space heating. This work will inform further research in other projects to understand the risk associated with these exposures.

## Impact


- Halios CH, Landeg-Cox, Lowther SD, Middleton A., Marczylo T, Dimitroulopoulou S. (2022). Chemicals in European Residences – Part I: a review of emissions, concentrations, and health effects of Volatile Organic Compounds (VOCs). Science of the Total Environment, 156201 https://doi.org/10.1016/j.scitotenv.2022.156201
- Landeg-Cox C, Middleton A, Halios CH, Marczylo T, Dimitroulopoulou S. Chemicals in European Residences – Part II: a review of emissions, concentrations, and health effects of Semi Volatile Organic Compounds (SVOCs). *In preparation*

## Theme II: Air pollution and health

**Theme Leads:** Heather Walton, Ian Mudway (ICL), Helen Crabbe (UKHSA)

### Theme Overview

Substantial evidence links air pollution to health impacts at concentrations commonly encountered in the UK. Data is robust for the impacts of fine particulate matter ($PM_{2.5}$) on cardiorespiratory diseases, but emerging evidence has demonstrated associations with adverse birth outcomes, sub-optimal developmental trajectories in children, the early aetiology of disease, impacts on mental health and dementia. If these observations can be shown to be robust and underpinned by causal pathways, they imply a substantial additional burden on population health, experienced across the life course. Addressing the evidence of the impact of air pollution on these emerging areas is the key aim of Theme II. We will do this by understanding the totality of air pollution exposures across the indoor to outdoor continuum in collaboration with Themes I and III.

### Aims/Objectives

Over the first two years of the HPRU the major ***short-term*** aims of Theme II are to deliver an updated meta-analysis on the effects of air pollutants on a range of birth outcomes and to extend work examining the links between long-term exposures to air pollution and dementia in support of COMEAP ongoing work in these areas. Through the ***medium-term*** we plan to extend the work on the neurological impacts of air pollution to a wider range of mental health endpoints and to improve exposure assessment, through the development of an integrated indoor exposure model, the development of a national model for ambient metals and an improved understanding in exposures in transport microenvironments. Over the ***longer-term***, we plan to extend work to look at the impact of cognition, across the life-course and to evaluate how changes in pollution exposures resulting from the introduction of Clean Air Zones, impact on a range of health and adverse physiological endpoints. We also plan throughout the lifetime of the HPRU to address the relative hazard of $PM_{2.5}$, primary combustion derived PM and $NO_2$, using both statistical and biomarker-based approaches.

### Progress against short, medium and long term objectives

All projects are running to timeline with several milestones completed on time or ongoing.

## Theme II Project 1: Air pollution and adverse birth outcomes

**Project Leads:** Rachel B Smith, Heather Walton (ICL), Karen Exley (UKHSA)
**Research Team:** Rachel B Smith, Heather Walton, Shawn Lee, Debbie Jarvis, Sean Beevers, Mireille Toledano, Bethan Davies (ICL), Karen Exley (UKHSA)

### Aims

The primary aim of this project is to produce updated meta-analyses for the expanding evidence base suggesting an association between air pollution and adverse birth outcomes, specifically term low birth weight (TLBW) and preterm birth (PTB). It aims to tackle some methodological shortcomings, such as population overlaps among primary studies used, and a lack of comprehensive quality assessment frameworks.

### Progress

**Background:** An increasing number of studies suggest an association between air pollution and adverse birth outcomes, such as low birth weight (LBW) and preterm birth (PTB). However, existing systematic reviews and meta-analyses (SR/MAs) are often of poor quality. This hinders the formation of robust concentration-response functions (CRFs) for incorporating consideration of the impact of air pollution reduction on adverse birth outcomes in policymaking.

**Methods:** The systematic reviews follow PRISMA 2020 guidelines. The protocols are registered on PROSPERO (TLBW: CRD42020206114 and PTB: CRD42022301743).

TLBW: Relevant studies were identified via EMBASE, MEDLINE, SCOPUS and Web of Science. We used NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, with bespoke modifications. Population overlap between studies identified and quantified, and considered 'intolerable' if >50%. Study selection for meta-analysis was undertaken according to various algorithms, prioritising study characteristics according to different hierarchies (continuous vs categorical effect estimates, population size, quality score). Random effects meta-analysis was used to calculate pooled effect estimates. Factors potentially explaining heterogeneity (e.g. geography, smoking adjustment, quality score) will be explored via sensitivity analyses. Methodology similar to TLBW, but literature searches will extend to major Chinese literature databases.

**Results:** TLBW: 2895 unique studies were retrieved. After screening, 100 eligible studies remained for data extraction/quality assessment. Figure 1 shows distribution of studies included in systematic review by pollutant and geography. Preliminary results indicate associations between $PM_{2.5}$ and $PM_{10}$ exposure during whole pregnancy and trimesters and elevated risk of TLBW, but were less consistent for

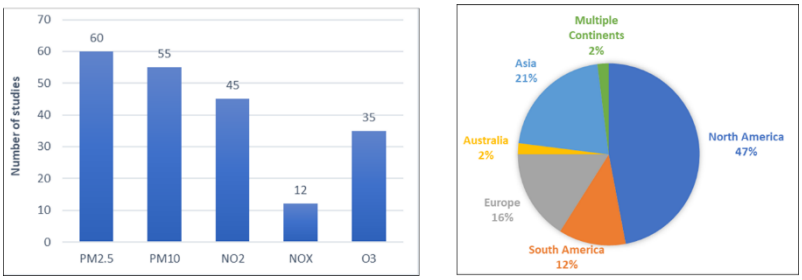



**Figure 1. Left: Number of studies included in the TLBW systematic review examining each air pollutant. Right: Geographic distribution of the 100 studies included in TLBW systematic review**

### Impact

The updated meta-analyses will facilitate the formation of robust concentration-response functions (CRFs) for policymaking. The CRFs will be incorporated into a pre-existing project that aims to ascertain the monetary benefit of air pollution reduction on various health outcomes. On the other hand, more advanced meta- analysis methodologies may be explored to produce more comprehensive findings.

## Theme II Project 2: Air pollution – impacts on the brain across the life course

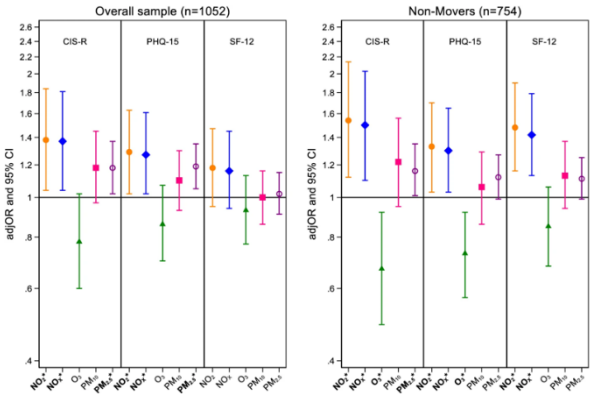
**Project Leads:** Ian Mudway (ICL), Valentina Guercio (UKHSA)
**Research Team:** Sean Beevers, Dave Green, Mireille Toledano, Klea Katsouyanni, Dylan Wood (ICL), Ioannis Bakolis (KCL), Tony Fletcher, (UKHSA)

### Aims

To increase understanding of the long-term impacts air pollution exposures on brain health across the life course, including early and late life cognition, mental health, and dementia risk and explore how changes in air pollution, driven by policy (London's Ultra Low Emission Zone), or unplanned natural events (COVID-19 pandemic lockdowns) impact on these neurological health endpoints.

### Progress

**Background**: Air pollution is a major cause of ill health and premature death globally, associated with significant economic costs. However, the health and societal costs of poor mental health related to poor air quality have not been costed into these evaluations due to limited evidence. Here we tested the hypothesis that long-term air pollution exposures are associated with poor mental health.




Adjusted odds ratios (adjOR) and their corresponding 95% intervals (CI) represent increase in risk for common mental disorders (CIS-R), physical symptoms (PHQ-15) and self-rated general health (SF-12) per IQR increase in air pollutant ($NO_2$, NOx, $O_3$, $PM_{10}$, $PM_{2.5}$) levels (μg/m³). All models are adjusted for age, sex, latent classes of SES, smoking status, ethnicity, frequency of drinking, physical activity and Lden.

**Methods**: A prospective longitudinal population-based mental health survey of 1,698 adults living in 1075 households in Southeast London, from 2008 to 2013. High-resolution quarterly average air pollution concentrations of $NO_2$, $O_3$, $PM_{10}$ and $PM_{2.5}$ linked to the home addresses of the study participants. Associations with mental health analysed using multilevel generalised linear models, after adjusting for large number of confounders, including the individuals' socioeconomic position and exposure to road-traffic noise.

**Results**: We found robust evidence for interquartile range increases in $PM_{2.5}$ and $NO_2$ to be associated with 18-39% increased odds of common mental disorders, 19-30% increased odds of poor physical symptoms and 33% of psychotic experiences only for $PM_{10}$. These longitudinal associations were more pronounced in the subset of non-movers for $NO_2$.

**Conclusions**: These findings suggest that traffic-related air pollution is adversely affecting mental health. Whilst causation cannot be proved, this work suggests substantial morbidity from mental disorders could be avoided with improved air quality.

### Impact

- **Contributions to Government Reports**: COMEAP Air pollution: cognitive decline and dementia report, 2022: https://www.gov.uk/government/publications/air-pollution-cognitive-decline-and-dementia; NERC Environmental Science and Mental Health Review, 2021: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://valuing-nature.net/sites/default/files/documents/VNP27-EnvSciMenHealthReview-A4-88pp%20reduced.pdf

- **Publications**: Br J Psychiatry. 2021;219(6):678-685. doi: 10.1192/bjp.2021.119; Neuroepidemiology. 2021;55(4):253-265. doi: 10.1159/00051539; Soc Psychiatry Psychiatr Epidemiol. 2021;56(11):2029-2039; Soc Psychiatry Psychiatr Epidemiol. 2021;56(9):1587-1599.

## Theme II Project 3: Indoor exposures and health

**Project Leads:** Ben Barratt (ICL), Helen Crabbe (UKHSA)
**Research Team:** Ben Barratt, Fred Piel, Adam Skillern (ICL). Giovanni Leonardi, Helen Crabbe, Rebecca Close, FETP Fellow (UKHSA).

### Aims

Overall to develop indoor air exposure models for studies of population health effects which include built environment characteristics, analysis of exposure measurement error, and measures of population movements (time activity patterns and population estimates). In this project we aim to 1) characterise indoor air quality and CO exposures 2) Propose a methodology for characterising exposures for an epidemiology study on the effects of indoor air quality on health 3) Examine health outcomes due to poor indoor air quality.

### Progress

**Background**: This project is dependent on outputs from other projects underway, notably Theme I Project 6, developing an exposure model for indoor air pollutants. Activities in the first two years focused the review of existing resources. Fieldwork and analysis will follow in Years 3-5.
**Methods**: For each aspect of the project 1) We scoped the resources available to the collaboration by reviewing datasets and projects that could contribute. Building on T1, P6 the exposure model can be applied to estimate indoor VOC and CO exposures given characteristics of homes. Utilizing ongoing funded projects we can characterise CO in homes by adding CO monitoring to WellHome, and analysing existing datasets (COPE study). 2) Wrote a protocol to define how we are going to use these measurements to estimate population level exposures. The protocol can outline the data collection methods and analysis plan for future epidemiology studies. 3) building on the previous HPRU, an extract of Hospital Episode Statistics data was analysed to identify trends and risk factors in intentional non fire CO related hospital admissions.
**Results**:
We were unable to recruit a PhD student for this project that has delayed progress.
1) A scoping report detailed the datasets and resources available to the collaboration. Several CO datasets are being aligned for the project. The Wellhome project has started to monitor indoor air quality in 100 homes in west London. CO will be added to the list of pollutants monitored. 2) A UKHSA FETP fellow will write a protocol detailing how these measurements can be used to develop an exposure model for epidemiology studies.
3) A manuscript on trends and risk factors for intentional CO hospital admissions has been submitted to a peer review journal. The figure shows the trends in hospital admissions over time for males and females.

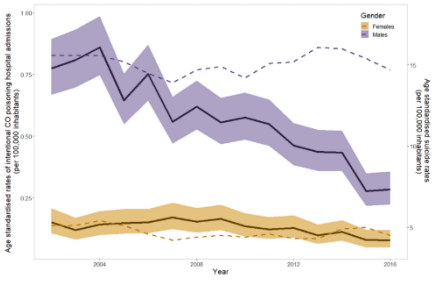



Figure 1. Age-standardised rates of intentional CO poisoning for males and females over time (2002-2016). Shades indicated 95% confidence intervals. Dashed lines present the age-standardised suicide rate, regardless of method, by gender in England (ONS, 2021). Population standardised based on the 2013 European Standard Population.

**Conclusions**:
While rates of intentional CO poisoning have decreased steadily in recent years, a lack of widespread in-home data makes a comparable assessment on unintentional CO poisoning rates challenging. An opportunity to add CO monitoring to an ongoing home environment study (WellHome) will enable progress to be made in this area.

### Impact

- A report on a scoping study to identify existing public-health and exposure datasets accessible to UKHSA and ICL for use in future epidemiological studies.
- Submission of a journal article on ‘Spatial and temporal trends and risk factors for intentional carbon monoxide poisoning hospitalizations in England between 2002 and 2016’, submitted to Journal of Affective Disorders.

## Theme II Project 4: Exposures in transport microenvironments and their impact on health

**Project Leads:** Dave Green (ICL), Emma Marczylo (UKHSA)

### Aims

To quantify exposures to primary particulate matter and co-pollutant gases in transport microenvironments and assess their impact on health and acute adverse biological responses. It will initiate work investigating the effects of air pollution on the London Underground in sensitive sub-populations, as well as expand on previous personal monitoring studies highlighting the high exposures to diesel fumes experienced by professional drivers.

### Progress

**Background**: Although people only spend a short period of time travelling every day, exposure in transport microenvironments can account for around 30% of their daily cumulative total exposure to some air pollutants. Quantifying exposure in transport microenvironments is therefore important in correctly establishing exposure; in particular for those travelling by car, bus, and London Underground whose exposure is poorly correlated with outdoor concentrations measured at their residential address.
**Methods**: Accurately measuring exposure in confined, spaces such as transport microenvironments, with no access to power, is challenging. The exposure of professional drivers in vehicles and London Underground workers has been achieved using personal measurement devices. Comparing the exposure to different gaseous and particulate air pollutants on overground and underground journeys has required a new mobile measurement system to be developed. This incorporates reference type instrumentation and filter samplers into a wheeled unit which can be easily moved around the transport network and travel alongside study participants.
**Results**: Taxi drivers experienced the highest BC exposures due to time spent working in congested traffic, while emergency services had the lowest. Peaks in exposure were observed while driving and were at times greater than 100 µg/m$^3$. Airtight cabin design and presence of an in-built filter in the electric taxis reduced the exposure to BC substantially compared to diesel taxis and provide important evidence for occupational health of professional drivers through exposure reduction measures in vehicle design. Preliminary results from the London Underground show high concentrations of $PM_{2.5}$, consistently in excess of 400 µg/m$^3$ in some locations on the Bakerloo Line during repeated journeys.

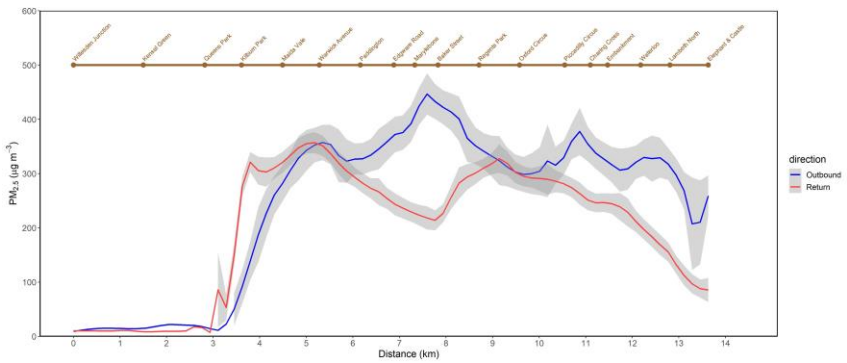



*Figure 2: Comparing Outbound and Return Journeys on the London Underground Bakerloo Line 2022*

**Conclusions**: Occupational and public exposure in transport microenvironments contributes significantly to daily cumulative total exposure. In car exposure can be reduced by improved vehicle design and use of in cab filtration.

### Impact

- IOSH final report: https://iosh.com/media/8902/the-driver-diesel-exposure-mitigation-study-full-report.pdf
- Publications: DOI: 10.1016/j.envint.2021.106532; DOI: 10.1016/j.envres.2021.110736; doi.org/10.3390/atmos11070749.

## Theme II Project 5: Disentangling effects of NO2 and PM2.5 in time-series analysis

**Project Leads**: Heather Walton (ICL), Karen Exley (UKHSA)
**Research Team:** Heather Walton, Klea Katsouyanni, Dimitris Evangelopoulos, Rachael Piper (ICL), Karen Exley, Helen Crabbe (UKHSA).

### Aims

The primary aim of this project is to aid in the separation of the short-term health effects of $NO_2$ and $PM_{2.5}$. More specifically, we will investigate whether disproportionate changes in the concentrations of the two pollutants can be used to strengthen inferences regarding the independence of their effects in time-series analysis.

### Progress

**Background**: Understanding the extent to which health effects associated with $NO_2$ are independent of those of $PM_{2.5}$ is important for policy. However, due to high correlations between the pollutants, disentangling their effects has proven difficult. In recent years, with the introduction of policies targeted at reducing traffic emissions (e.g., the mandatory installation of diesel particle filters), the ratio of $NO_2$ and $PM_{2.5}$ has been changing. It can be hypothesised that if the associations for $NO_2$ are an indicator for particulate matter, rather than a direct effect, the changing ratio should lead to a change in the time-series coefficient for $NO_2$, thus providing information regarding the independence of its effects.
**Methods**: (1) In collaboration with the RI-URBANS project, formulate a database of daily average $NO_2$ and $PM_{2.5}$ concentrations for different cities across the UK and Europe. (2) Perform time-trend analyses to investigate changes in the relative concentrations of $NO_2$ and $PM_{2.5}$. (3) Conduct an epidemiological time-series analysis to assess whether coefficients representing associations of the health effects of $NO_2$ and $PM_{2.5}$ have changed over time, and (4) evaluate the extent to which trends in the relative concentrations of the two pollutants play a role in modifying their estimated health risks.
**Results (Year 1 of PhD)**: A summary of the data collected thus far is provided in Table 1. In total $NO_2$ and $PM_{2.5}$ concentrations have been sourced for 21 cities, 11 of which are in the UK. Given that data collection is still in its infancy, further cities may also be considered.

**Table 1 Availability of daily average concentrations of $NO_2$ and $PM_{2.5}$ for different cities across the UK and Europe.**

| UK Cities | Data Availability | Wider EU Cities | Data Availability |
|---|---|---|---|
| London, UK | 1998-2022 | Barcelona, ES | 2013-2019 |
| Birmingham, UK | 2011-2022 | Madrid, ES | 2009-2019 |
| Leeds, UK | 2008-2022 | Budapest, HU | 2013-2019 |
| Glasgow, UK | 2013-2022 | Helsinki, FI | 2009-2019 |
| Sheffield, UK | 2013-2022 | Paris, FR | 2012-2019 |
| Manchester, UK | 2009-2022 | Zurich, CH | 2010-2019 |
| Edinburgh, UK | 2008-2022 | Athens, GR | 2009-2019 |
| Bristol, UK | 2008-2022 | Prague, CZ | 2009-2019 |
| Cardiff, UK | 2008-2022 | Stockholm, SE | 2010-2019 |
| Belfast, UK | 2008-2022 | Leipzig, DE | 2010-2019 |
| Newcastle, UK | 2008-2022 | | |

### Impact

As the aims of this project partially arose from recommendations made by the Committee on the Medical Effects of Air Pollutants (COMEAP) for further research to help establish independence of the health effects of $NO_2$ from those of $PM_{2.5}$, a foreseen output of the project would be to report back any findings from our analyses. In addition, the proposed work contributes more broadly towards the development of methodologies for disentangling the effects of highly correlated pollutants.

## Theme III: Biomarkers of exposure and effect

**Theme Leads:** Catherine Hawrylowicz (KCL), Martin Leonard (UKHSA)

### Theme overview

Research in this Theme deploys a 'whole systems' approach to study the mechanistic pathways linking ambient air pollution exposure to disease outcomes. It includes metabolic phenotyping technologies (metabolomics), a powerful tool which captures information on a range of toxicological and disease processes. As exhaust emission controls take effect, non-exhaust emissions from brakes and tyres are drawing increasing attention. Research on the health impacts of these emissions will new understanding requested by the Committee on the Medical Effects of Air Pollution (COMEAP). The link between air pollution and asthma continues to be the main focus of Theme III, especially understanding the mechanistic linkage between air pollution and asthma. Finally, our work on e-cigarettes and advanced materials is helping to fulfil UKHSA's requirement in this important area.

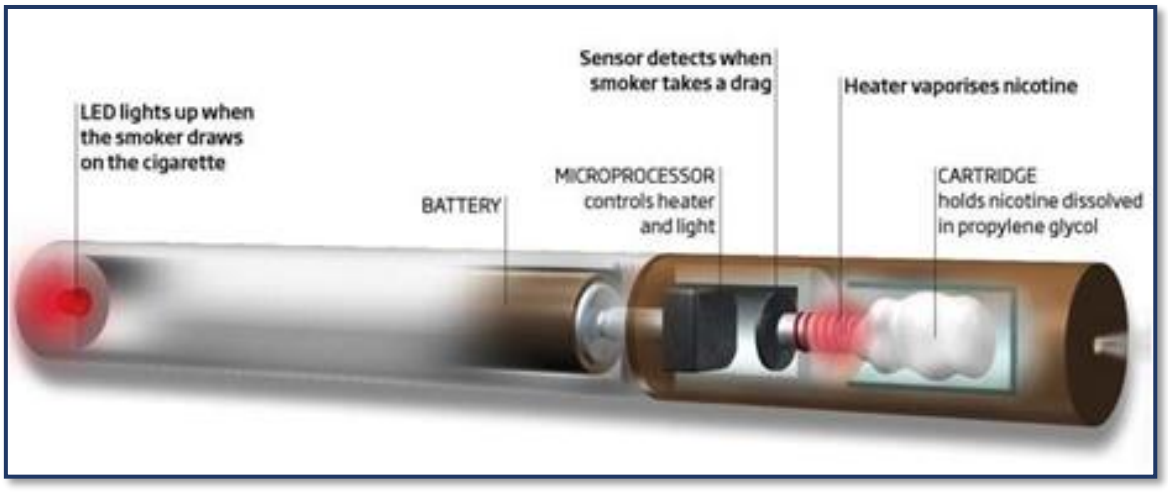
### Aims/Objectives

- Identify biomarkers following acute exposure to different air pollutants and define whether they discriminate between different sources.
- Examine non-exhaust PM emissions (brake, tyre and road wear) for toxicological impact in the lung and investigate the relative toxicities of exhaust PM and NO2.
- Investigate different air pollutant components for their influence on asthma and mechanisms of allergy?
- Determine the relative toxicities of e-cigarette components?

### Progress against short, medium and long term objectives

As this Theme is heavily dependent on laboratory activities several projects (3-6) were further delayed by COVID limited supplies of laboratory consumable items. Discussions have been had with all projects leads regarding the extent of the delays and these range from 6-12 months. Currently the project goals remain the same and we have plans in place to catch up time but this will be fully assessed again by end of year 3 and changes made if necessary.

*Project - In vitro high throughput toxicological assessment of electronic cigarettes flavours in human bronchial epithelial cells – Figure 1 Compositions of EC*



# Theme III Project 1: Understanding key molecular events following fibre and combustion particle pollutant exposure

**Project Leads:** Frank Kelly, Paul Elliott, Ian Mudway (ICL), Liza Selly, Anne Willis (UoC)
**Research Team:** Yiqun Han, Hanbin Zhang (ICL)

## Aims

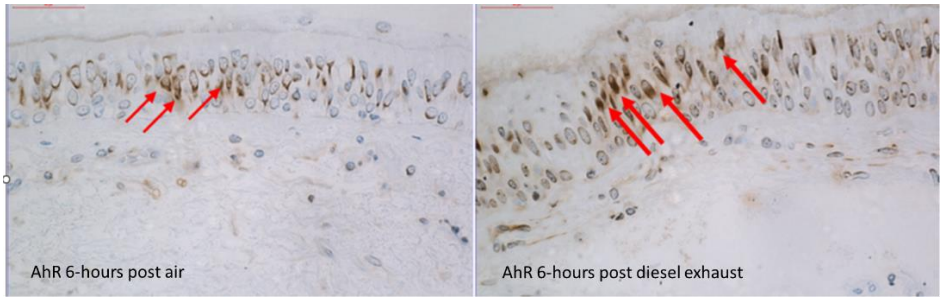
The aim is to further the understanding of the initial biochemical and physiological disturbances related to pollutant exposure that drive the causal adverse outcome pathways to disease and disease exacerbation necessary and strengthen the causal basis for the epidemiological findings of an association between air pollution and disease outcomes and interventions.

## Progress

**Background**: Diesel exhaust (DE) induces neutrophilia and lymphocytosis in experimentally exposed humans. These responses occur in parallel to nuclear migration of NF-κB and c-Jun, activation of mitogen activated protein kinases and increased production of inflammatory mediators. There remains uncertainty regarding the impact of DE on endogenous antioxidant and xenobiotic defences, mediated by Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) and the Aryl hydrocarbon Receptor (AhR) respectively, and the extent to which cellular antioxidant adaptations protect against DE.

**Methods**: Using immunohistochemistry we investigated the nuclear localization of Nrf2 and AhR in the epithelium of endobronchial mucosal biopsies from healthy subjects six-hours post DE ($PM_{10}$, 300 µg/$m^3$), as a marker of activation. Cytoplasmic expression of cytochrome P450s, family 1, subfamily A, polypeptide 1 (Cyp1A1) and subfamily B, Polypeptide 1 (Cyp1B1) were examined to confirm AhR activation; with the expression of aldo-keto reductases (AKR1A1, AKR1C1 and AKR1C3), epoxide hydrolase and NAD(P)H dehydrogenase, quinone 1 (NQO1) also quantified.

**Results**: DE exposure caused an influx of neutrophils to the bronchial airway surface ($p=0.01$), as well as increased bronchial submucosal neutrophil ($p<0.001$), lymphocyte ($p=0.007$) and mast cell ($p=0.002$) numbers. In addition, DE exposure enhanced the nuclear translocation of the AhR and increased the CYP1A1 expression in the bronchial epithelium ($p=0.001$ and $p=0.028$, respectively). Nuclear translocation of AhR was also increased in the submucosal leukocytes ($p<0.001$). In contrast, DE did not increase nuclear translocation of Nrf2 and was associated with decreased NAD(P)H: quinone-oxidoreductase-1 (NQO1) in bronchial epithelial cells ($p=0.02$), without affecting CYP1B1, aldo-keto reductases, or epoxide hydrolase protein expression.




**Conclusions**: These *in vivo* human data confirm earlier cell and animal-based observations of AhR and CYP1A1 induction by diesel exhaust. The induction of this phase I xenobiotic response occurred in the absence of the induction of antioxidant or phase II xenobiotic defences. Thus, DE associated PAHs induce their metabolism and acute inflammation without concomitant protective cellular adaptations.

## Impact

- Unosson J, et al. Acute cardiovascular effects of controlled exposure to dilute Petrodiesel and biodiesel exhaust in healthy volunteers: a crossover study. Part Fibre Toxicol. 2021;18(1):22.
- Selley L, et al. Alterations to the urinary metabolome following semi-controlled short exposures to ultrafine particles at a major airport. Int J Hyg Environ Health. 2021;237:113803.
- Purves J, et al. Air pollution induces Staphylococcus aureus USA300 respiratory tract colonization mediated by specific bacterial genetic responses involving the global virulence gene regulators Agr and Sae. Environ Microbiol. 2022;24(9):4449-4465

## Theme III Project 2: Health effects of non-combustion particles

**Project Leads:** Adam Boies, Liza Selley (UoC), Ian Mudway (ICL)
**Research Team:** David O'Loughlin, Molly Haugen Marion MacFarlane, Anne Willis UoC)

## Aims

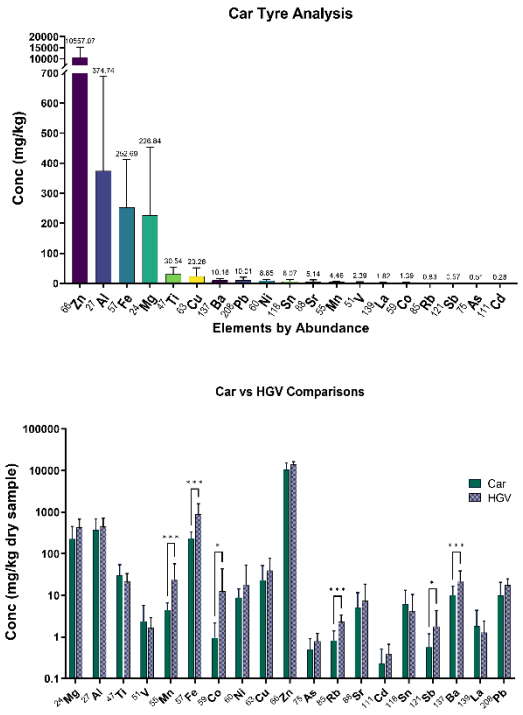
The aim of this project is to gain a simultaneous understanding of the composition, size, and morphology of non-exhaust PM, and an insight into their potential adverse effects. This will allow for a holistic human health risk assessment where we can understand which components (chemical or metal) are driving toxicity.

## Progress

**Background**:
Until now, research into the health effects of traffic PM has mainly focused on exhaust emissions. However, there are also non-exhaust particulate emissions from brake, tyre, and road wear.

Brake wear is the most prevalent constituent of roadside PM, accounting for around 55% by mass. Resuspended (abrasion) material represents 38%, and tyre wear makes up around 11%. Data forecasts that non-exhaust emissions are expected to rise to 9 kilotonnes by 2030, while exhaust emissions continue to fall.

**Methods**:
76 tyres, including samples of both car and HGV tyres, have been analysed by ICP-MS for 25 elements. The purpose of this study is to identify tracer elements, or a ratio of tracer elements which can be used to distinguish tyre rubber particulates from other sources.




**Top**: Car tyre rubber analysis sorted by abundance.
**Bottom**: Comparison between car and HGV tyre

**Results**:
Of the 25 elements examined ,19 were detected. Zinc was the most abundant, followed by aluminium, iron and magnesium (see figure above). Boron, Phosphorus, Chromium, Molybdenum, Tungsten, and Thallium were all below the detection limit, set at 3*(SD of 6 blanks). Manganese, Iron, Rubidium, and Barium were all significantly enriched in HGV tyres.

**Conclusions**: We have established a representative inorganic composition of tyre rubber that can inform air quality monitoring. This work is being written up as a manuscript. The next phase, assessing the potential health effects of non-exhaust PM, is due to commence in Q3 and Q4 2022, following the IARC Characteristics of Carcinogenicity.

## Impact

- Poster Presentation: Cambridge Particle Meeting, University of Cambridge, June 2022
- Presentation: London Metallomics Consortium, Young Investigator Symposium, London, September 2022
- Poster Presentation: UKHSA Annual Meeting, Leeds, October 2022

## Theme III Project 3: The role of AhR in asthma

**Project leads**: Catherine Hawrylowicz (KCL), Ian Mudway (ICL), Rachel Smith, Martin Leonard, Tim Gant (UKHSA).
**Research Team**: Dr Charlotte Cheadle (KCL), Drew Glencross (ICL), Zehra Ali-Khan (KCL)

### Aims

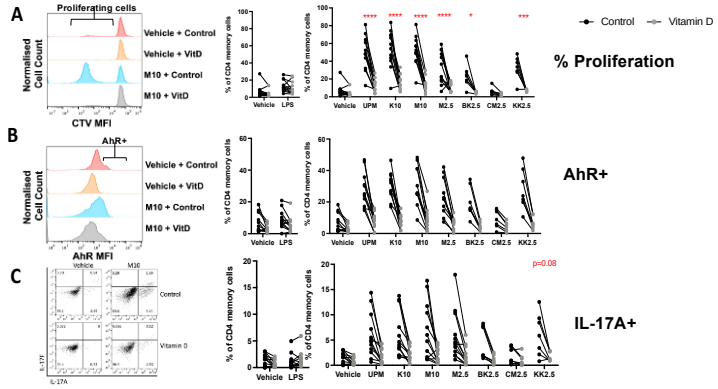
This project is evaluating a range of ambient PM samples for their effects on human cells to understand components that drive inappropriate inflammatory responses relevant to respiratory health. Our aims are to associate these with PM compositional data to identify relevant signalling pathways and explore potential mediators that may mitigate detrimental effects of PM.

### Progress

**Background:** Poor air quality triggers exacerbations in severe asthmatics, frequently characterised by inflammatory Th17 responses. Most studies have used standard reference PM samples that do not reflect the heterogeneity of contemporary ambient PM. We have compiled a range of real-world PM (London $PM_{10}$ & $PM_{2.5}$; and from three Thai cities $PM_{2.5}$) to assess their immune effects, gain insight into compositional differences, relevant signalling pathways and strategies to mitigate against detrimental PM effects.

**Methods:** Human cells (dendritic cells, T cells and neutrophils) were cultured with ambient PM and assessed for changes in cell phenotype and function by flow cytometry, gene expression by qPCR and secreted mediators by antibody capture assays.

**Pre-treatment of human dendritic cells with 1,25-dihydroxyvitamin D decreases PM-induced memory T cell proliferation, AhR expression & Th17 responses**




**Results:** Ambient PM matures healthy dendritic cells (DC), particularly PM fractions containing coarse particulates (>2.5 µm). PM pre-treated DCs enhanced memory CD4+ T cell proliferation and Th17 inflammation. Pre-treatment of DC with 1,25-dihydroxyvitamin D reversed PM-induced DC maturation and CD4+ T cell proliferative and pro-inflammatory cytokine responses. These data indicate that restoring vitamin D sufficiency may reduce PM-induced inflammatory responses. Mechanistic studies demonstrate that the AhR pathway is upregulated in both DC and T cells following PM-exposure, but that only T cell responses are significantly reduced by AhR-antagonism.

**Conclusions:** Vitamin D repletion may dampen PM-induced DC maturation and inflammatory T cell responses linked to exacerbations in severe asthma.

**Future studies:** These will investigate: (i) inflammatory endpoints in DCs and Tm from asthmatic individuals; (ii) continue investigating signalling pathways following PM-exposure and correlate ambient PM composition with biological responses; (iii) link to historical and an ongoing vitamin D repletion trial to determine whether repletion alters the inflammatory response to PM.

### Impact

- Glencross DA et al. Air pollution and its effects on the immune system. (2020). Free Radic Biol Med 151: 56-68 (highly cited)
- Glencross DA, Cheadle C, Hawrylowicz CM. (2022) Chapter 96 - Vitamin D and Adaptive Immunology in Health and Disease. In, Hewison, Feldman and Pike's Vitamin D, 5e Vol 2. (Accepted for publication)
- C Kewcharoenwong et al, Vitamin D3 regulates PM-driven primary human neutrophil inflammatory responses (under review)

## Theme III Project 4: E-cigarette toxicity and health effects from second-hand exposures

**Project Leads:** Tim Marczylo (UKHSA), Ann McNeill (KCL), Matthew Wright (UKHSA)
**Research Team:** Tim Marczylo, Matthew Wright, Felix Effah (UKHSA)

## Aims

To address established knowledge gaps around the safety of e-cigarette use, we aim to determine the adverse effects of flavoured e-liquids in human airway cells using both air-liquid interface models and high-throughput toxicity screening assays and to use chamber studies to evaluate the potential for second-hand exposure through analysis of aerosol for particles, nicotine, VOCs and flavouring compounds.

## Progress

**Background:** E-cigarettes help smokers switch from tobacco however there are concerns over their inherent toxicity and attractiveness to non- smokers. Though flavour chemicals used in e-liquids are generally considered safe for consumption, there is only limited data on inhalation of these chemicals. Adverse health effects from second-hand smoking are well established but few studies investigate the exposure to second-hand vape and the nature of exhaled vape.

**Methods**: A systematic review of the pulmonary effects of e-liquids was undertaken. We identified 54 nicotine-free flavoured e-liquids across 15 flavour categories. These were tested at three concentrations (0.25%, 0.5%, and 1% v/v) in human bronchial epithelial (HBEC-3KT) submerged cultures. Screening was performed using three *in vitro* endpoint assays comprising cell count, cell viability, and lactate dehydrogenase (LDH). Positive hits were further investigated for their effects on HBEC-3KT proliferation, mitochondrial health, and oxidative stress.

**Results**: A significant, dose-dependent decrease in cell count and increase in LDH release, were only observed with cinnamon, vanilla tobacco, and hazelnut e-liquids compared to PG/VG vehicle. A significant decrease in cell proliferation was observed for each of these three e-liquids. The strongest effects were observed with cinnamon. hazelnut and vanilla tobacco, but not cinnamon, as increased cytoplasmic ROS production compared to PG/VG controls. Only cinnamon decreased mitochondrial function.

**Conclusions**: Targeted restrictions of selected flavour chemicals may markedly reduce the potential toxicity of e-liquids. Future work will determine the effects of these three e-liquids in ALI.

Figure 4

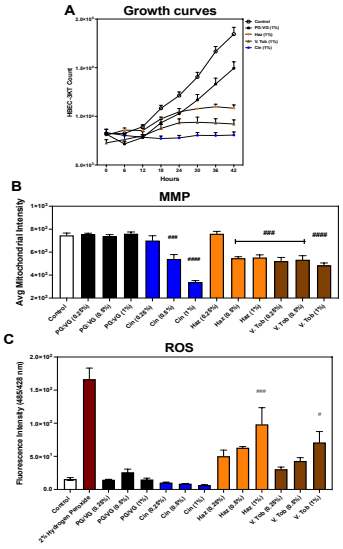



**Figure 1 | The dose-dependent effects of cinnamon, hazelnut and vanilla tobacco flavoured e-liquids on A) HBEC-3KT proliferation for 42h post-exposure, B) mitochondrial membrane potential (MMP) after 8h exposure, and C) reactive oxygen species production exposure after 3h exposure.** A one-way ANOVA with multiple comparisons, corrected using **Tukey** was used to determine statistical significance. Data are expressed as mean S.E.M (n=**6** per group). *$p$<0.05; **$p$<0.01; ***$p$<0.001; ****$p$<0.0001 vs Control; $^{\#}p$<0.05; $^{\#\#}p$<0.01; $^{\#\#\#}p$<0.001; $^{\#\#\#\#}p$<0.0001 vs PG/VG.

## Impact:

- Systematic review identified key flaws in published literature and is published.
- Lead e-liquids identified for ALI studies

# Theme III Project 5: Improved in vitro systems for evaluating and comparing inhalation toxicity of air pollutants including $NO_2$ and PM

**Project Leads:** Rachel Smith, Martin Leonard (UKHSA), Heather Walton (ICL)
**Research Team:** Chang Guo, Alison Buckley, Matthew Wright, Josh Bateman[i] (UKHSA)

## Aims

To develop systems for exposing respiratory relevant cell cultures to both gaseous and particulate air pollutants, to enable comparison of the biological effects and investigation of underlying molecular mechanisms of air pollutant components individually and in combination. To use such systems to explore the impact of pollutants difficult to disentangle via other approaches including epidemiological studies (e.g. $NO_2$ and PM).

## Progress

**Background**: It can be difficult to disentangle the effect of components of air pollution using solely epidemiological approaches but understanding can be important for air pollution policy making. Alternative approaches including *in vitro* studies can potentially be useful in this context.

**Methods**: A system to expose cell cultures to controlled concentrations of $NO_2$ has been developed (Figure 1) and characterised. Alveolar epithelial cells (NCI-H441) were exposed to 5 ppm $NO_2$ for 4 hours and in a following study to carbon black (CB) (3100 ng/cm$^2$), a surrogate for PM, using a Vitrocell™ Cloud system and $NO_2$ (5 ppm) either singly or in combination for 24 hours. Cell viability and expression of various markers were analysed.

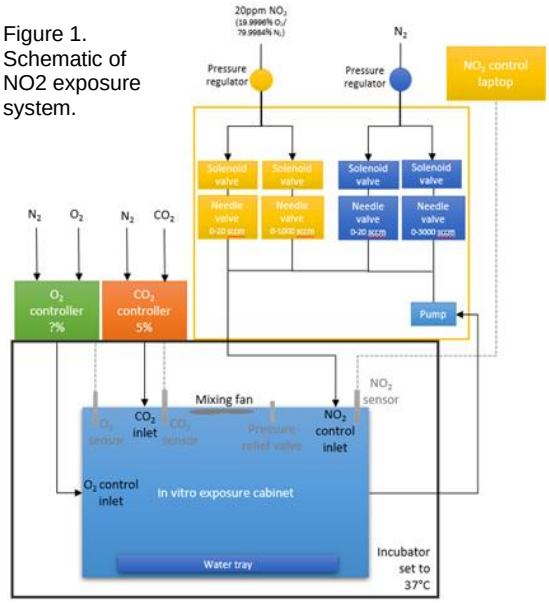



Figure 1. Schematic of NO2 exposure system.

**Results**: Characterisation of the performance of the exposure chamber indicated reliable control of $NO_2$ levels to time periods beyond 24 hours. Preliminary results indicate that 4 hr $NO_2$ exposure (5 ppm) did not change viability, membrane permeability, IL6/IL8 release or SOD1 expression in the H441 cells ($p<0.05$). Exposure to CB, $NO_2$ or CB±$NO_2$ for 24 hrs did not induce a cytotoxic response or alter barrier function of H441 cells but IL6 & IL8 were increased in response to exposure to CB, $NO_2$ and CB±$NO_2$.

**Conclusions**: An appropriate robust and sensitive system for exposing cell cultures to $NO_2$ has been developed. Pilot characterisation studies have been undertaken, exposing alveolar epithelial cells to $NO_2$ and CB. The next stage will be to further explore dose responses and use with more advanced co-cultures and more complete PM models.

## Impact

### Publications:

- Poster presented at ICT 2022: *Exposure models of nitrogen dioxide and particulate matter to assess mechanistic toxicology using advanced alveolar systems.* J.W.P. Bateman, A. Buckley, S. Robertson, M. Wright, S.H. Doak, R. Smith, M.J.D. Clift.
- Abstract submitted to 2022 UKHSA Annual UK Research Review Meeting on Outdoor and Indoor Air Pollution Research, 30th November 2022.

# Theme III Project 6: Use of improved in vitro systems to evaluate the mechanisms of toxicity and their relative significance for realistic inhalation exposures to advanced materials including nanomaterials

**Project Leads:** Rachel Smith, Martin Leonard (UKHSA), Stephanie Wright (ICL)
**Research Team:** Chang Guo, Alison Buckley, Adam Laycock (UKHSA)

## Aims

The aim of this work is to optimise the conditions needed for *in vitro* exposure of epithelial air liquid interface (ALI) cell cultures to inhalation relevant aerosols. Such work is essential to eliminate artifacts and to provide the most relevant mechanistic information on aerosol health hazards.

## Progress

**Background**: Airborne contaminants (e.g. PM2.5, nanoparticles (NPs), e-cigarettes, microplastics etc) have raised concerns over inadvertent exposure and their potential hazardous effects on human health through the inhalation route. To model the airway epithelium *in vitro* it is essential to use ALI systems to recapitulate organotypic function and to allow for realistic exposures to aerosol material. Aerosol exposure systems need careful optimization to ensure robust toxicity assessments.

**Methods**: An aerosol-exposure air-liquid-interface (AE-ALI) system combining aerosol generation system and Cultex$^{TM}$ exposure chamber was established. The effect of system parameters on NP aerosol deposition patterns was explored using nano-sized $CeO_2$ aerosols and ICP-MS combining laser ablation. Detailed characterization of the system, including assessing the effects of electrostatic precipitator voltage, aerosol flow rate, size of Transwell inserts, and exposure duration on cytotoxicity (LDH), was carried out using human lung alveolar cells (A549) and primary small airway epithelial cells (SAECs). SAECs were further used to explore for any further adverse effects such as oxidative stress, inflammatory responses, and DNA damage etc.

**Results**: NP deposition patterns vary significantly with system parameters, but appropriate choice of operating parameters produced broadly uniform deposition. Analysis of biological endpoints indicated that exposure duration (air only) had a significant impact on cell cultures (e.g. increased cytotoxicity and expression of selected genes including CXCL1, HMOX1, SPP1). System parameters, including exposure duration, had a significant effect on cell cultures, the extent of which varied with culture type.
The AE-ALI system has, and will, be used for *in vitro* exposure studies on more advanced materials including $CeO_2$NPs.

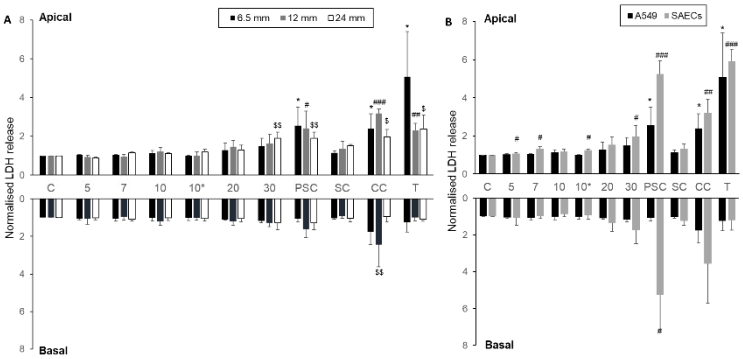



Figure (A) Cytotoxicity of A549 cells on Transwell inserts with different sizes (6.5 mm, 12 mm and 24 mm). (B) Cytotoxicity analysis of A549 cells and SAECs on 6.5 mm Transwell inserts. Three individual exposure experiments (three biological repeats per exposure) were performed for each size of Transwell insert or each cell type. Cells were exposed to air-only aerosols for 5, 7, 10, 10* (5 min exposure followed by another 5 min exposure, with 30 min interval recovery), 20 and 30 min. C, incubator control; PSC, positive system control; SC, system control; CC, chemical control (20% DMSO in cell culture medium for 1 hour); T, total cell lysis.

**Conclusions**: Detailed characterisation of AE-ALI systems is important to facilitate hazard identification of airborne contaminants in human relevant cell culture models and this system allows for this to occur.

## Impact

- A manuscript describing the optimisation and characterization of this AE-ALI system is under preparation.
- A second manuscript is also planned examining biological effects in response to $CeO_2$NP aerosols as part of a larger study.

## Theme III Project 7: Fungal bioaerosol exposure and air pollutant effects

**Project Leads:** Emma Marczylo (UKHSA), Kasia Hawrylowicz (KCL), Ian Mudway (ICL), Martin Leonard (UKHSA)
**Research Team:** Emma-Jane Goode, Abigail Dalzell (UKHSA)

### Aims

The overall aim is to understand and assess the health impacts from different fungal species and/or air pollutants implicated in allergic airway disease, beginning with: (a) establishing physiologically relevant *in vitro* airway model(s); (b) Assessing the mechanistic differences between individual fungi/fungal components driving the allergic response identified as priorities from Theme I/Project 5.

### Progress

**Background:**
Fungi are of particular interest in Allergic airway disease (AAD) as they are present in both outdoor and indoor air and are associated with asthma, allergies and other respiratory diseases. Our literature review as part of Theme I/Project 5 identified key pathways contributing to the allergic responses to fungal allergens. However, due to the heterogeneity of models and methods used, it is not clear whether there are common and/or specific pathways induced by different fungi/fungal components.

**Methods:**
Air-liquid interface (ALI) cultures (up to 28 days) were used to induce differentiation of nasal, bronchial and small airways epithelia cells into a columnar stratified epithelium with cilia and goblet cells. Cultures were harvested at 0, 7, 14, 21 and 28 days, and the expression of molecular markers of basal, ciliated and mucus producing cells were assessed with reverse-transcription quantitative PCR (RT-qPCR).

**Results:**
Different cell lines produce subtly different differentiated models, with some downregulation of basal (undifferentiated) cell markers and upregulation of markers of ciliated and mucus producing cells from day 7 (Fig. 1). No ciliated cells were seen in the differentiated cell lines, mucus was produced in some.

**Conclusions:**
The ALI differentiation of primary cell lines, and genes of interest (including known fungal receptors and genes identified in our review of the pathways driving fungal allergy) will also be measured to ensure that the most appropriate model(s) are selected to better understand which fungi/fungal components drive allergy and how.

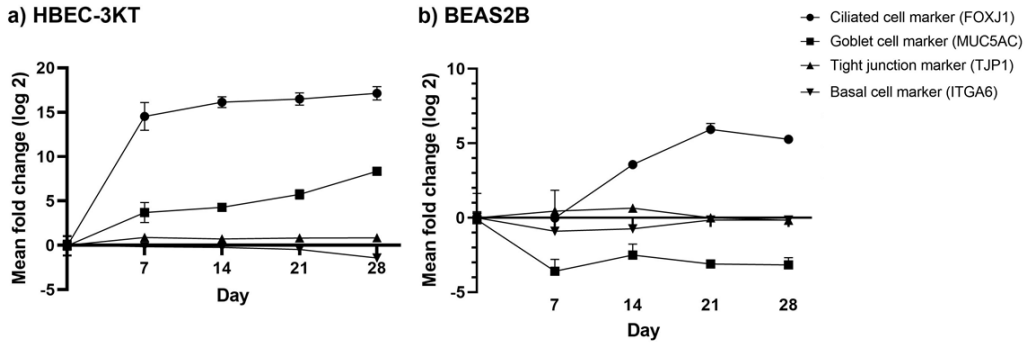



**Fig 1:** Different cell lines show varying expressions of differentiation markers a) HBEC-3KT or b) BEAS2B at air-liquid interface (ALI) for up to 28 days.

### Impact

The findings from this project will help to: (a) Establish fully characterised ALI airway model(s) with documented strengths and limitations to inform selection of the most appropriate model(s) for further experimentation (b) Improve understanding of the mechanistic pathways that drive fungal allergy, addressing the knowledge gaps identified in our literature review(c) Ultimately, inform improved advice to those suffering from fungal allergies and associated health care professionals to help them better manage their condition or prepare for sudden increases in demands for treatment.

## Theme IV: Emerging Environmental Issues and Preparedness

**Theme Leads:** Tim Marczylo (UKHSA), Stephanie Wright (ICL)

### Theme overview

Theme IV has a diverse portfolio of projects under the umbrella of emerging hazards and preparedness and aims to address current issues of public concern. Across the theme projects there is an initial focus on information gathering and the writing of reviews to identify key knowledge gaps that will drive the latter stages of this theme. This theme also includes a 20% responsive research capacity which may be utilised to respond quickly to any novel emerging issues. We have replaced a planned body of work on fracking because of the withdrawal of Government support for fracking within the UK and a new project on the health impacts of perfluorinated compounds has been included as a response to concerns raised by Defra and the Environment Agency.

### Aims and Objectives

The objectives of this theme include gaining a better understanding of:

1. The human health impacts from exposures to perfluorinated chemicals.
2. Develop methods to assess emissions from waste fires and biomass-fuelled power stations.
3. Toxicity of microplastics in *in vitro* respiratory and intestinal models.
4. The effects of environmental exposures on fertility.
5. Using quantification of emerging environmental hazards with an initial focus on fentanyl as a mechanism for emergency preparedness.

### Progress against short, medium and long term

Projects 1, 2 and 4 have been delayed due to recruitment. Other projects have short-term delays excepting Project 6 where we have failed to recruit a PhD student. Discussions are ongoing about replacing this project.

***Figure – Recent funding award received for project looking at plastic burning in Indonesia will contribute to Theme IV research.***

## Theme IV Project 1: Human health impacts from exposures to perfluorinated chemicals

**Project Leads:** Fred Piel (ICL), Ovnair Sepai and Robie Kamanyire (UKHSA)
**Research Team:** Sarah Dack, Selina Dagless (UKHSA), William Francis (ICL)

### Aims

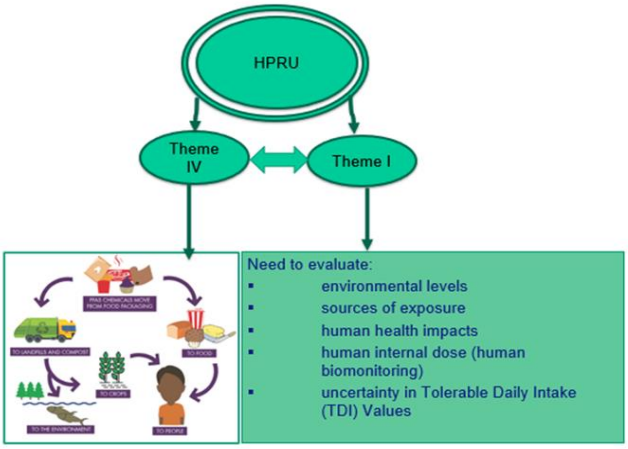
Perfluoroalkyls and polyfluoroalkyls (PFAS) are a large class of anthropogenic chemicals that repel water and oils and have been used in a wide range of surface coatings from cooking utensils, food packaging to clothing, furniture and carpets. PFAS are persistent in the environment and are bioaccumulative. There is limited toxicology data for most PFAS and therefore our aim in this project is to assess the main chemicals of concern and their potential health impacts/toxicity.

### Progress

**Background**: There are over 4,000 PFAS compounds with wide ranging consumer and industrial applications. The unique chemical and physical properties of PFAS have led to their widespread use in industrial, commercial and consumer products. The ubiquitous environmental distribution of PFAS, their environmental persistence and bioaccumulative properties present potential hazards to human health. PFAS have been found in a wide pool of biota such as fish, otters and humans, with growing concerns about their impact(s) on health.

**Methods**: The project will review current national and international evidence to identify the main UK PFAS chemicals of concern. Having identified these, we will assess and review the toxicity of these chemicals to identify those of highest relevance/concern to human health and conduct an epidemiological study, based on measurement data, to monitor risks to human health.

**Progress:** Progress on this project has been limited, in light of challenges in recruiting a PhD and research associate. A PhD has now been recruited starting in October 2022.




Preparatory work has been initiated through meetings with stakeholders such as the Environment Agency to share data on sources and environmental measurements. Literature searches and initial screening are underway.

### Impact

- Identify the main UK PFAS chemicals of concern and submit a manuscript for publication on the PFAS of concern relevant to the UK.

- Review pathways of toxicity of these chemicals to identify those of highest relevance and concern to human health and guide public health policies and regulations.

## Theme IV Project 2: Microplastic toxicity in human in vitro models

**Project Leads:** Stephanie Wright, Frank Kelly (ICL), Tim Gant, Tim Marczylo, Rachel Smith, Matthew Wright (UKHSA), Marion MacFarlane (UoC).

**Research Team:** Eric Auyang (ICL), Lorna Jones, Matthew Wright, Sameirah Macchiarulo (UKHSA), Jenny Katsouli (ICL/UKHSA), Jorge Bernadino de la Serna (ICL).

### Aims

To increase understanding of the potential adverse effects of microplastic exposure on human health.

1. Conduct structured reviews on the effects of microplastic's in the GI and respiratory systems.
2. Fabricate microplastic particle and fibre test materials.
3. Investigate effects of microplastic test materials in cell systems.
4. Understand how the alveolar protein corona affects the translocation of microplastic particles across epithelial and endothelial membranes.

### Progress

**Background:** Plastic materials release micro- and nanoscopic particles, termed 'microplastic' (and 'nanoplastic'). These particles contaminate the food chain and the air, resulting in human oral and inhalation exposure. This project investigates both microplastic particle and fibre exposures and hazards in the alimentary (canal (AC)) and respiratory systems, and the role of the lung microenvironment protein corona on microplastic particle translocation across cell membranes.

**Methods:** Laboratory methods have included cryomilling, antisolvent crystallization and electrospinning for test material fabrication, and cell culture systems (mono-, triple-culture and organ-on-chip) and assays for hazard characterisation, with advanced microscopy to understand particle membrane translocation.

**Results:** Reviews have not found evidence of a risk to human health but indicate a potential for hazard at some doses, mainly in *in vitro* systems. Microplastic particles have been fabricated via cryo-milling and fibres have been fabricated via precipitation and electrospinning methods. Materials have been characterised, revealing the potential for metal (Al) contamination following contact with Al foil. Initial cell exposures indicate hazard potential for PET microplastics at higher concentrations in the AC.

**Conclusions**: There are negative effects on cell (Caco-2) proliferation at high doses. These exposure levels are higher than currently understood human exposure levels indicating a low risk for cytotoxicity based on current understanding. However, the complexity of materials and lack of understanding of both hazard and exposure indicates a need to better understand risk relative to exposure & physicochemical properties.

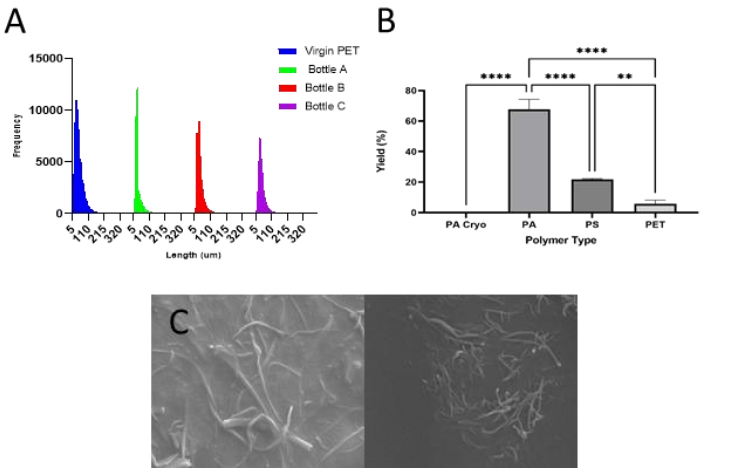



*Figure 1. A) Size distributions of cryomilled polyethylene terephthalate (PET) microplastics from four sources; B) yield of polyamide (PA), polystyrene (PS), and PET microplastics (<5 µm) from antisolvent crystallization and cryomilled (PA Cryo). Plots are mean ± SD, n=3. *p <0.05; C) SEM images of PA and PS fibres.*

### Impact

There is a high level of public interest in microplastics and UKHSA has dealt with several queries public and parliamentary in respect of the effect of microplastic particles on human health. We have reported the work of the HPRU in answering some of these queries. SW co-authored a recently published WHO report on microplastics and human health. Literature reviews are about to be submitted for publication and microplastic fabrication papers are being prepared.

## Theme IV Project 3: Drugs of misuse

**Project Leads:** Derryn Grant (ICL), Tim Gant, Tim Marczylo (UKHSA), Leon Barron (ICL)

## Aims

This project aims to develop a fast, quantitative analytical method for opioids and their metabolites in wastewater to estimate community consumption. It starts with the monitoring of heroin across 10 sites in England. This method will be developed with the intentions of scaling it to monitor opioid use across England.

## Progress

**Background**: In the UK, drug-related deaths have been increasing reaching a record high in 2021 with two-thirds of said deaths being related to misuse. Since the 1990s, half of all drug-related poisoning involved opiates. Opioids have also been suspected of being weaponised. For example, an aerosolised fentanyl may have been used in a hostage situation in Russia in 2002.

**Methods**: Daily samples taken from wastewater treatment plants (WWTPs) across England are defrosted in the cold-room overnight before analysis. A 15 mL portion of said samples are then prepared using solid-phase extraction (SPE), filtered and re-constituted into 150 µL samples for LC-MS/MS analysis. In addition to this, an analytical method has been developed using SPE with LC coupled to full-scan high resolution mass spectrometry (LC-HRMS) to identify other opioids in wastewater from a spectral library of approximately 1,200 compounds.

**Results**: During this year, samples have been analysed to target the heroin metabolite, 6-monoacetyl morphine (6-MAM). Across nine sites from England, 6-MAM has been quantified in the range 0-100 ng/L in wastewater. Additional sites are currently being added to the programme to expand the geographical and population coverage. Concentrations were statistically different between sites where large geographical distance existed. However, there was no-statistically significant differences in 6-MAM concentrations across the sites and across days of the week. This aligns with knowledge that heroin is not used recreationally, as is already known. Following LC-HRMS analysis, it was possible to identify other opioids in wastewater, including more potent fentanyl substances using accurate mass, retention time and isotopic similarity score (Fig. 1).

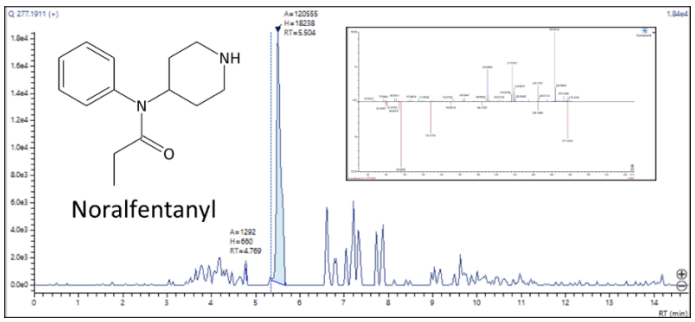



*Figure 1. Detection of noralfentanyl in a 24-h composite wastewater sample from the UK, 2022*

**Conclusions**:
Our current measurements reflect known the way it is known that heroin is misused in that it is not a recreational drug and so there is no statistically significant difference across the amount of 6-MAM in samples across days of the week. Data has also shown to be significantly statistically different across sites which are a large distance apart.

## Impact

- Won best poster prize at Institut Mondor de Recherche Miomédicale Summer School 6th – 8th July 2022.
- Won best poster prize at the MRC Centre and HPRUs Joint Annual Training Day 22nd September 2022.

## Theme IV Project 4: Health impact of living near a biomass-fuelled electricity generating installation

**Project Leads:** Fred Piel, Bethan Davies, Dave Green, Paul Elliott (ICL), Tim Marczylo (UKHSA)
**Research Team:** Brandon Parkes (ICL)

### Aims

The aim of this project is to identify any associations between adverse health effects in the local population and emissions from existing biomass-fuelled electricity generating installations by. emission with be quantified from UK installations and adverse health effects to be investigated including mortality, chronic diseases (allergy, asthma, heart disease, COPD) and respiratory hospital admissions.

### Progress

**Background**: The UK is shifting electricity generation towards "renewables" including biomass. DEFRA advise burning biomass "could have adverse air quality impacts", particularly PM and $NO_2$ associated health outcomes, including exacerbations of asthma and COPD. Beyond combustion of biomass, there is concern over the health effects of the production and transportation of feedstock.

**Methods**: The literature of health impacts on local populations was reviewed. Large combustion plants (LCPs, >50MWth) and medium combustion plants (MCPs) used for biomass-fuelled electricity generation in England were identified through the Environment Agency (EA). LCPs are subject to annual air quality assessments and reports. Quantifying emissions and exposure might be possible through previous dispersion modelling data. Otherwise, ground-based exposures to pollutants will be modelled, before investigating health impacts using small-area studies methodology. Confounders considered include deprivation and other sources of pollution including domestic biomass combustion.

**Results**: Evidence from the literature review conducted in 2021was limited. Data on LCPs provided by the EA and local population identified at postcode level (Table 1). Different feedstocks are employed globally, but wood pellets predominate in UK.

**Conclusions**: Insufficient published data is available to draw conclusions about health effects in UK. The Drax Power Station is responsible for over 80% of biomass combustion in England. Modelling exposures to air pollutants is not feasible without access to model input data from UK Environment Agencies.

### Impact

**Table 1**. Summary of biomass-fuelled electricity generating installations, LCPs in England with normally resident population of postcodes with centroids within 5km of centroid of postcode where LCPs are located.

| Operator | Site Location | Postcode | Biomass Combustion (TJ) | Population within 5km (2011 census) |
|---|---|---|---|---|
| Drax Power Limited | Drax Power Station | YO8 8PH | 124,706.8 | 10,255 |
| EPR Ely Limited | EPR Ely | CB6 2QE | 3,085.0 | 10,003 |
| Iggesund Paperboard (Workington) Limited | Biomass CHP | CA14 1JX | 4,656.0 | 28,576 |
| GREP1 Limited | Biomass Power Plant | NG34 9GH | 2,984.6 | 23,300 |
| BWSC Generation Services Limited | Brigg Renewable Energy Plant | DN20 9LT | 3,510.9 | 17,617 |
| Lynemouth Power Limited | Lynemouth Power Station | NE63 9NW | 2,280.5 | 36,819 |
| BWSC Generation Services Limited | Kent Renewable Energy CHP Plant | CT13 9ND | 2,304.8 | 10,687 |
| BWSC Generation Services Limited | Snetterton Renewable Energy Plant | NR16 2JZ | 3,827.4 | 4,629 |
| Cramlington Wood Energy Partnership Limited | Cramlington Biomass Plant | NE23 3JA | 2,295.3 | 47,185 |

## Theme IV Project 5: Understanding public exposures to toxicants from waste fires

**Project Leads:** Alec Dobney, Tim Marczylo, Tim Gant (UKHSA), Frank Kelly (ICL)
**Research Team:** Laura Mitchem, Alessia Freddo (UKHSA)

### Aims

There is little knowledge on emissions from waste fires, making the health impact predictions, subsequent risk assessment advice, and associated health messaging challenging. The objective of this study is to produce a literature review which can provide evidence on toxicant emissions during waste fires to improve public health management.

### Progress

**Background**:

There is considerable uncertainty in relation to the public exposure to products of combustion from waste fires due to the variety of materials burned and associated conditions e.g. oxygen content and fire-fighting strategies, and the challenging environmental sampling. Published air quality assessment studies were gathered to provide a better understanding of toxicant emissions to assist with the public health management.

**Methods**:

A Source-Pathway-Receptor (SPR) model was applied to the context of toxicants from waste fires, whereby the current state of knowledge was systematically compiled and important knowledge gaps were identified. A comprehensive search strategy used a combination of associated Subject Headings terms and free text terms, implementing the search in Medline and EMBASE.

**Results**:

Our search identified 5629 records. Of these, some were discarded based on title and abstracts. Sixty-four records were subsequently included in the full-text evaluation. From those, 8 relevant studies were selected, which included fire incidents in general waste landfills and tyre landfills, that took places across Europe and America, in both rural and urban settings. The period of air monitoring varied between several days to several months and included the analysis of particulate matter ($PM_{2.5}$ and $PM_{10}$); benzene; dioxins and furans; PCDDs/Fs; PBDDs/Fs; PBDEs; PAHs; $CO_2$; CO; $O_3$; $SO_2$; $NO_3$, and metals.

**Conclusions**:

The data gathered has enabled a comparison with the current prediction of toxic emissions during waste fires and provided the basis for future considerations on the establishment of monitoring and analytical methods required to fill further gaps for the public health management.

### Impact

Manuscript in preparation

## Theme IV Project 6: Air pollution and infertility

**Project Leads:** Mireille Toledano, Rachel B. Smith, Sean Beevers, Paul Elliott (ICL), Valentina Guercio, Giovanni Leonardi (UKHSA)

### Aims

The incidence of male and female infertility has increased in recent years. Advanced maternal age is known to be the leading factor responsible but other factors that affect both men and women including air pollution, may contribute. Epidemiological evidence suggests linking exposure to ambient air pollution with fertility disorders in men (i.e. reduced sperm quality) and women (e.g. reduced fecundity demonstrated by time to pregnancy, TTP) is still inconsistent with many study limitations. We will evaluate the association between exposure to ambient air pollution and reduced fecundity by using UK COSMOS, an ongoing study that provides information on many potential confounding variables.

### Progress

Project not started due to delays recruiting PhD student.

## Theme IV Project 7: Validation: Test chemical augmentation of a new non-animal test method for assessing metabolism based on CYP450 enzyme induction

**Project Leads:** Miriam Jacobs (UKHSA)
**Research Team:** Emma Quartermain, Tim Gant, Tim Marczylo, Barbara Kubickova (UKHSA)

### Aims

To validate an OECD test method for xenobiotic mediated cytochrome P450 induction in vitro. The specific aims are:1) Contribute to the HepaRGTM CYP induction validation test method augmentation report, to the OECD Test Guideline Programme, for Test Guideline (TG) adoption, 2) set-up the HepaRGTM CYP enzyme induction test method with the established pharmaceutical reference chemicals (Bernasconi et al 2019) and, 3) test a set of proficiency chemicals that address a broader chemical applicability domain (Jacobs et al 2022), to augment the reference chemicals (Bernasconi et al 2019).

### Progress

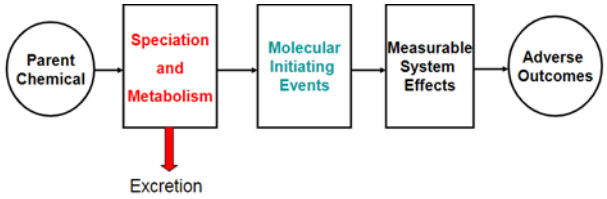
**Background**:
This work is a new initiative in the HPRU to develop our capacity to support the OECD test methods programme for chemical hazard identification. This work will validate a method to detect cytochrome P450 enzyme (CYP) induction by chemicals. CYP induction can significantly alter in vivo exposure to CYP substrates/metabolites, therefore human relevant CYP data is valuable in chemical toxicity safety assessment. A draft OECD TG for an in vitro CYP HepaRG™ test method that detects overall enzymatic activity induction of 3 human CYP isoforms (1A2, 2B6, and 3A4) has been developed and validated for a set of pharmaceutical proficiency chemicals. To support TG adoption, the OECD member countries requested additional work to demonstrate the ability of this assay to detect increased CYP enzyme activity mediated by industrial, pesticide and food additive chemicals, together with an indication on regulatory uses.

**Methods**:
Preparatory laboratory work is being conducted, along with collation of required materials. The SOP will be followed, whereby cryopreserved immortalized human HepaRG™ cells are exposed to different concentrations of the test chemicals to induce CYPs. The cells are then incubated with CYP marker substrates and substrate turnover is determined by quantification through LC-MS. Protein content is determined using a BCA protein assay.

**Results and Conclusions**:
Results generated in two other laboratories will be validated in this study. No results or conclusions at present. Work is about to commence.

**Acknowledgement:**
We gratefully acknowledge co-funding from Defra for this study.

Figure 1. Role of metabolism in changing an administered chemical form, resulting in a chemical that can initiate an adverse outcome pathway, or resulting in inactive metabolites that are excreted.




### Impact

This work will support the considerations requested for acceptance and adoption of a new OECD TG.

## Theme IV Project 8: Mapping toxicological training in the UK and identifying future need

**Project Leads:** Kerry Broom, Tim Gant (UKHSA)
**Research Team:** Sarah Judge (BTS), Kerry Broom, Tim Gant (UKHSA)

### Aims

The Education and Skills Gap Project examined the provision of education and training required for UK regulatory toxicology roles.

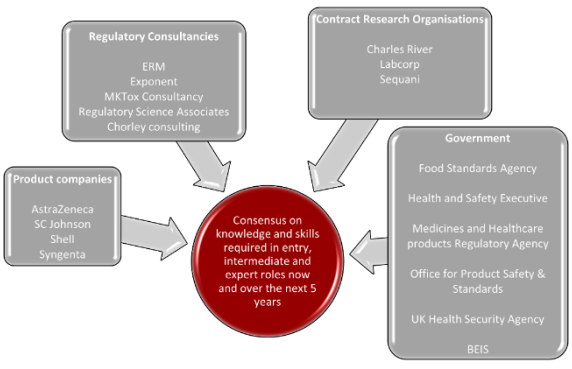
- Aim 1. Determine the knowledge and skills required for regulatory toxicology roles
- Aim 2. Evaluate the current provision of education and training
- Aim 3. Facilitating the provision of education and training to fill the knowledge and skills gaps identified.

### Progress

**Background**: Toxicology is an applied science that draws on a knowledge of pharmacology, chemistry, physiology and molecular biology. Toxicology evaluates hazard and exposure from xenobiotics whether they are therapeutic, chemicals, natural substances or environmental contaminants and seeks to minimise risk for human health.

**Methods**: Phase one ran from January - July 22, where representatives were recruited from 17 employers of people in regulatory toxicology roles across sectors. Sectors included product companies, Regulatory consultancies, Contract research organisations and government. Representatives were asked to list knowledge and skills important for working in regulatory toxicology. A spreadsheet with categories for guidance was provided. The representatives were then asked to score the knowledge and skills on their importance and level of qualification required. Phase two is the production of a report and is underway.

**Results**: The figure shows the 17 representatives across the regulatory toxicology sector.




751 knowledge/skills items were identified from the representatives. The knowledge/skills categories include core theoretical knowledge, core experimental techniques, hazard identification/characterisation, and risk assessment. This was consolidated to 189 after removal of duplicates. Data is being analysed for the skills/knowledge expected at entry (undergraduate), intermediate (5yrs experience), and expert level (>10 years experience).

**Conclusions**: After report production, the next steps are to collaborate with course leaders and academics at UK universities to provide the knowledge/skills required, to promote careers. These are necessary for all levels, but the expert level also requires consistency for Continuing Professional Development courses.

Funding from the British Toxicological Society supported this work.

### Impact

- Poster presentation, British Toxicology Society Annual Congress, April 2022
- British Toxicology Society oral presentation, Committee on Toxicity meeting 20th June 2022

# 3. ACADEMIC CAREER DEVELOPMENT PROGRAMME

## Mission

Our mission is to address the gaps in training available in quantitative data sciences and informatics for the risk assessment of environmental exposures and health impacts. To do this we have established a multidisciplinary academic career development programme (ACDP), combining scientific expertise in fundamental toxicological, epidemiological, and environmental research to train the next generation of research leaders in these fields.

## Recruitment and appointments

Throughout 2022, our recruitment procedure, based on identifying excellent PhD candidates and early-career researchers (ECRs) through consistent and inclusive processes encouraging diversity and equality, has enabled us to continue to appoint outstanding students and we now have 13 PhD students and 8 ECRs in total in the HPRU-EEH.

## Training activities

We have updated our induction activities: an online induction session and a buddy scheme for informal help and support for new starters. Additionally, as pandemic restrictions have eased, we were able to hold a 'Meet Your Buddy' in-person lunch and our default for induction sessions and other activities (below) have been and will be in-person, unless circumstances change, with option to join online for those unable to travel. We have maintained the ACDP portal in Microsoft Teams, providing a single point of access to a collection of remote training resources and information on news, events, and career opportunities. We are actively promoting participation in NIHR Academy activities. We also facilitate our students and ECRs in shadowing senior members of our HPRU in national committees (e.g., COT, COMEAP, COMARE).

Our journal clubs and seminars series, led by ECRs, are ongoing, giving regular opportunities for our PhD students and ECRs to discuss new studies in their field/present their research/ provide exposure to diverse topics. We are continuing to build capacity in quantitative methods through a series of workshops, led by ECRs, combining theory and practical sessions. This year's workshop, on time series analysis, was highly successful in terms of attendance (30 and 70 attendees for theory and practical sessions, respectively) and feedback received.

Our annual training event, held September 2022, was in-person. HPRU PhD students and ECRs gained experience in presenting their research projects as posters, flash oral presentations, or plenary oral presentations to a live audience, with time for questions and discussion. They had the opportunity to network within and beyond their HPRU Theme and Project, and the keynote (Dame Dr Jenny Harries) gave them an insight into the scientific process in government and policy. A talk from the head of the college's Equality, Diversity and Inclusion Centre (EDIC) built further awareness of the importance of EDI in their future research and career. Members of all the other HPRUs were invited to attend and for one of their students to present a poster. Furthermore, our PhD students are able to present on the UKHSA PhD student day which brings together all PhD students who are part of or affiliated with UKHSA including all of those within the HPRUs.

The major update to our training programme, building on the ISAB feedback from last year, is the launch of a more formalised version of the ACDP, starting in October 2022. This will include a schedule of monthly core activities released at the beginning of each academic year; to set expectations in terms of involvement and engagement, and a more systematic approach to feedback and evaluation. This will further improve the structure of our programme and ensure students are equipped with a rounded understanding of environment and health research, and a range of professional skills required for their career progression. The ACDP will include multi-disciplinary core modules, on topics such as risk assessment, toxicity, biostatistics and data science, translation to policy, and career progression. We believe that this will also help increase engagement and involvement of PhD students and ECRs in our ACDP activities and the sense of cohort.

### Impact

PhD students and ECRs are involved into 16 of the 26 ongoing projects of the HPRU EEH, in close partnership with UKHSA. They have contributed to 20+ PCIEP events and to over 25 publications. They take initiatives to create podcasts (The Envirohealth Podcast) and a sustainability initiative, which reach far beyond the HPRU.

### Future strategy

Over the coming year, we will assess the benefits of the formalised activities outlined above, through feedback and evaluations. The ACDP is increasingly founded on co-design with our students and ECRs being represented on the ACDP Committee; choosing the theme of the workshops; co-organising the journal club and seminar series; and designing surveys. We believe the inclusion of students and ECRs in many aspects of the ACDP and beyond is important to their ACD and ensures EDI. We will continue to work with the EDIC to further integrate strategic EDI objectives into our training programme. We will continue stimulating ACD interactions with other HPRUs and activities of the NIHR academy. Finally, we will continue building capacity in general quantitative methods, including statistics, big data and coding through dedicated workshops and other ACD activities.

## 4. PUBLIC AND COMMUNITY INVOLVEMENT, ENGAGEMENT AND PARTICIPATION

Our aim is to engage with and involve the public in a scientific dialogue on environmental health to ensure that the impact of our research extends beyond academic and policy realms and is responsive to the concerns of the public. To this end, our PCIEP Strategy has continued to be informed by the NIHR INVOLVE National Standards for Public Involvement in Research. Over the last year we have demonstrated an ongoing commitment to engaging the public with our research across all themes aiming to embed the UK Standards for Public Involvement. The following highlights how we have been implementing our strategy.

### Governance Structures

Our aim is to ensure that the public voice is clearly present in our research management, leadership, and decision-making processes. Our Joint PCIEP Committee continues to meet once every two months to ensure that PCIEP is firmly embedded in the Unit at a strategic level.

We continue to hold meetings with our Public and Community Oversight Group (PCOG) jointly with the HPRU-CRTH and the MRC-CEH. The PCOG appointed a non-professional Chairperson who represents this group in meetings with the leadership team, bringing the public perspective to the highest governance structure of these units. Various members of our PCOG have been invited to participate in stakeholder groups and liaison committees for various projects associated with our Unit. This to ensure that the public voice is clearly present in our governance structures at all levels.

We will continue to use the UK standards for Public Involvement as a quality benchmark to assess the strengths and weaknesses of our involvement, engagement and participation activities and identify improvements.

### Support and Learning

We recognise the importance of providing regular opportunities for researchers to engage and involve members of the public in their research at various stages of the research cycle. To facilitate this, we have conducted regular meetings with our Public and Community Advisory Group (PCOG), our researchers and members of the leadership team. During these meetings, our researchers have had the opportunity to ask our PCOG for advice on various aspects of their research e.g., research plans, protocols, and materials under development.

In December 2021 we announced the first round of our new funding scheme “PCIEP Seed Fund”, a new initiative targeted at early career researchers and PhD students, with the aim of encouraging and enabling

early career researchers to develop and deliver new and innovative involvement, engagement and participation initiatives. Applicants had the opportunity to submit proposals for a maximum amount of £1000 for public involvement, engagement and participation with a broad audience. We received six applications of which three were successful. Our second round for funding will be announced in early December 2022.

We have recently launched our "PCIEP monthly newsletter", with the aim of keeping our researchers informed on PCIEP training opportunities, activities and events where they can actively engage in PCEIP initiatives, and of updates on policies and guidance related to best PCIEP practice.

### Inclusive Opportunities

We have continued to expand the diversity and inclusion in our PCIEP activities by using various networks and online platforms to engage with hard-to-reach groups (e.g., the VOICE Digital Platform and The Young Persons' Advisory Network (YPAN). Some of our projects have also adopted community-based approaches to research, actively involving the local community, residents and local ambassadors from various ethnic backgrounds and Socio-Economic status in the designing, implementation, and dissemination of our research protocols.

We are currently in the process of reviewing our PCOG membership with a focus on improving diversity (Objective 4). We will seek to identify relevant lay members of the public, stakeholders, and gatekeeper organisations to ensure broad representation both within the PCOG and in PCIEP workshops, involvement, and engagement activities. As part of this process, we have held discussions with our PCOG members centred around how can we implement the UK Standards for Public Involvement in Research within our Units/Centre with a focus on inclusive opportunities.

### Communications

We have continued to engage with the public in a scientific dialogue related to the issues around environment and health (Objective 7- PCIEP Strategy). We have been doing this through participation in various large public engagement events showcasing our research as a whole, at local and regional level including the Oxford Science and Ideas Festival (October 2021 and 2022), the Great Exhibition Road Festival (June 2022), the New Scientist Live North in Manchester (March 2022) and New Scientist Live London (October 2022). Our researchers have also participated in various local community festivals (e.g., local science festivals) and have continued delivering numerous talks and engagement activities to primary and secondary school children. In addition to public engagement events, our researchers have also been disseminating their research findings through media interviews, blogs posts and public facing reports.

We have also continued to develop our Unit's website, which serves as a central repository for information about research activities, events, publications, and opportunities for the public to engage with and participate in our research. We use our Twitter account (@HPRU_EEH) to disseminate our outreach activities, promote our PCIEP opportunities and establish a social media presence.

### Capturing and Reporting on Impact

We have continued to capture the impact that our activities have on our lay partners and researchers using post event feedback forms. The feedback gathered from the evaluation forms has provided the opportunity for reflection and learning to drive improvement in our future work (Objective 8- PCIEP Strategy).

Our researchers have been actively using our public engagement reporting tool for reporting, reflecting and learning (Objective 1- PCIEP Strategy). This tool has allowed us to keep a record of all PCIEP activities undertaken by each of our Themes, and to identify which of our themes may need more support to actively contribute to the attainment of our PCIEP strategy objectives.

## HPRUs Stand at New Scientist Live, Manchester – March 2022



## HPRUs Stand at Great Exhibition Road Festival, London – June 2022



## HPRUs Stand at New Scientist Live, London – October 2022


# 5. KNOWLEDGE MOBILISATION

Knowledge mobilisation (KM) brings together communities, scientists, public health practitioners, decision makers and other stakeholders with an interest in one or more topics, to catalyse change. KM maximizes the impact of health protection research to facilitate effective practice and policy change and improved services for patients and the public.

### Capacity building and Training

The KM Manager (KMM) is shared with the HPRU-CRTH as well as the Environmental Change HPRU at the London School of Hygiene and Tropical Medicine, allowing efficient knowledge transfer and exchange. The KMM participates in the pan-HPRU KM network to enable shared learning across the HPRUs. Through the network, the KMM developed a training survey to identify priority areas for KM training across all the HPRUs, co-organised a cross HPRU webinar on 'Parliament for researchers' in June 2022, and is co-facilitating a KM workshop at the 2022 UKHSA Conference in October.

KM presentations are given at the Theme meetings, and the KMM participates in both the Joint Academic Career Development (JACD) Committee and Joint Public and Community Involvement and Engagement and Participation (PCIEP) Committee. A session in the distinguished lecture series on KM and policy translation aims to embed KM in the Joint Academic Career Development programme. Imperial researchers provided a training day to members of the Guy's and St Thomas' Hospital and are now developing a CPD training programme on air pollution and health impacts.

The KMM has been involved with UKHSA internally led knowledge management work, using the HPRUs as Proof of Concept to examine knowledge captured by the HPRUs and to identify knowledge management solutions.

A joint PCIEP and KM Update email has been established to be circulated on approximately monthly basis. The aim of this update email is to share knowledge mobilisation opportunities, to be involved with government consultations or link into other related network events, or training opportunities.

UKHSA has become a Public Sector Research Establishment (PSRE) which contributes to the cross-government Life Sciences Vision. UKHSA is also part of the National Laboratory Alliance which aims to increase organisational effectiveness through knowledge sharing and co-developing capability. As UKHSA enters its second year as an organisation, PSRE links will grow, especially now as UKHSA is eligible for UKRI funding. A Theme II project has received NERC funding and NERC funding will be used to examine environment exposure and child health outcomes.

### Engagement with external stakeholders

The KMM has continued to build relationships and connections with stakeholders across formal/informal and multidisciplinary networks, including those across government (e.g., Civil Service Environment Network). Stakeholder mapping will continue to be conducted throughout the HPRU's lifetime. By identifying end-users and other stakeholders at the project and theme level, the HPRU-EEH can map and reach out to facilitate knowledge transfer and identify areas for new work where there are evidence gaps. A joint bioaerosols meeting and stakeholder mapping exercise between the EEH HPRUs in Leicester and Imperial, linking in BioAirNet has been successful and two abstracts have been submitted for presentation at the 2022 UKHSA Air Quality and Public Health Stakeholder Seminar in December.

The KMM and other researchers have participated in the STFC Air Quality Network meetings. These have been focussed on training and collaboration building. In particular, HPRU researchers are connected into the BioAirNet, Breathing City and TAPAS networks, and HPRU staff provided input into a Defra consultation on the Draft National Air Pollution Control Programme (NAPCP).

Working with the Institution of Environmental Sciences, the work of four HPRUs (CRTH, Environmental Change and Health and the two Environmental Exposures and Health Units) were highlighted in a webinar in February 2022. The MRC Toxicology Unit offered a small number of places to HPRU PhD students on their Integrated Toxicology Partnership Summer School, and four HPRU members gave presentations at the Royal Society of Chemistry Toxicology Award Seminar.

## Research into Impact

A Theory of Change model has been drafted which outlines how the HPRU projects lead to results that lead to impacts (Annexe 1).

The KMM regularly attends the Environmental Public Health Practice Board at the UKHSA to ensure dissemination of results to the regional and local Public Health Practice teams. There has been continued representation of HPRU staff on the expert Committee on the Medical Effects of Air Pollution (COMEAP), and on the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). These committees are sponsored and attended by Department of Health & Social Care, Department of Environment and Rural Affairs, Environment Agency etc. Representation allows information flow about current work programmes into the HPRU. The KMM also regularly attends to identify emerging topics.

Presentations from HPRU staff have been given in various settings including at the Westminster Commission for Road Air Quality (Group provides evidence to the All-Party Parliamentary Group on Air Pollution).

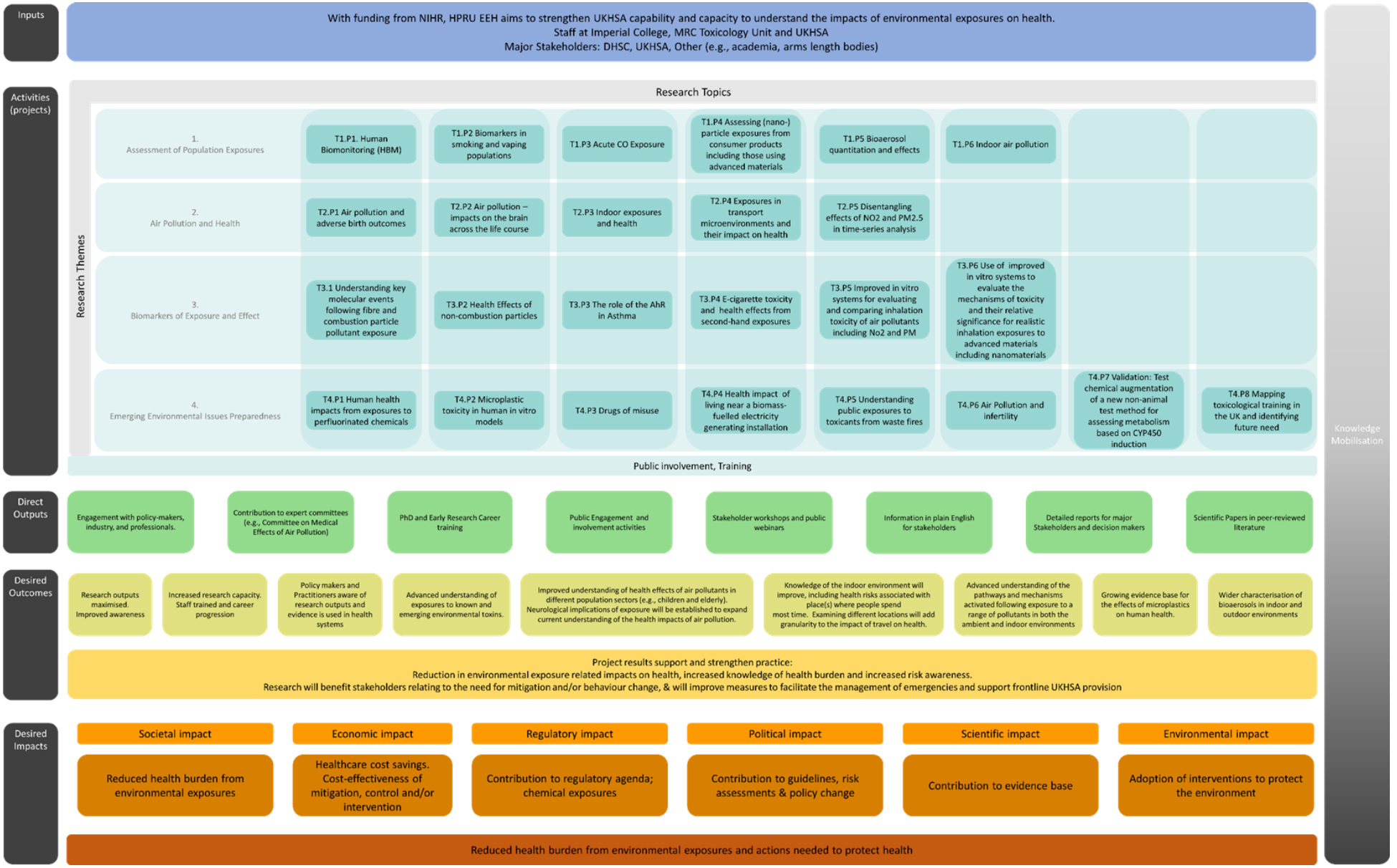
**HPRU research has led to reports on:**

Pathways to achieve WHO PM2.5 goals in the UK https://www.imperial.ac.uk/school-public-health/environmental-research-group/research/modelling/pathway-to-who

a health Impact assessment of current and past air pollution on asthma in London https://www.london.gov.uk/sites/default/files/hia_asthma_air_pollution_in_london.pdf.

An update to the Nicotine vaping in England evidence update was provided by Kings College researchers in the HPRU which falls under Theme 1, project 2.
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1107701/Nicotine-vaping-in-England-2022-report.pdf.

The research carried out in Theme II on Professional drivers and also transport microenvironments involving Transport for London is helping to generate evidence for the workforce. The work carried out under Theme IV examining the skills gap in toxicology training will feed into government but will also allow assessment of academic courses. This is a collaborative piece of work with academia and British Toxicology Society.




NIHR | Health Protection Research Unit in Environmental Exposures and Health at Imperial College London

# 6. COLLABORATION WITH OTHER HPRUs

From commencement of the HPRU-EEH we established a close partnership with the HPRU-CRTH. We set up common governance and management structures and established a joint Executive Group. The Academic Career Development and PCIEP Committees are jointly led and include representatives from all the partners of both HPRUs. The two external advisory groups, the PCOG and the ISAB, also provide recommendations on the work of both HPRUs.

The joint Academic and Career Development and PCIEP programmes are delivered in a fully integrated way across both HPRUs in order to maximise the use of the available resources and provide a broad range of opportunities for our students, ECRs and more senior researchers. It is our objective to extend the collaboration in these areas to other related HPRUs.

We work closely with the development award HPRU-EEH held at the University of Leicester. We have some common interests and are looking to leverage maximum public benefit from the projects in both HPRUs.

The Knowledge Mobilisation Lead continues to actively participate in the Pan-HPRU Knowledge Mobilisation Network. This network has regular meetings where best practice is discussed and experiences shared. The Knowledge Mobilisation Manager works across this HPRU, the HPRU-CRTH and the HPRU in Environmental Change and Health facilitating efficient knowledge management, transfer and exchange

The PCIEP Manager continues to participate as a member of the Cross-HPRU Behavioural Science Network and shares our work and experience in this area.

Together with the other HPRUs hosted at Imperial College (HPRU in Respiratory Infections, HPRU in Healthcare Associated Infections and Antimicrobial Resistance, HPRU in Modelling and Health Economics and HPRU-CRTH) we planned joint public engagement and outreach events for the Imperial Great Exhibition Road Festival held in June 2022 and continue to collaborate with these HPRUs as we prepare our application for the 2023 Festival.

We invited all HPRUs to take part in our 2022 Academic Career Development Programme's Annual Training Day event held in September 2022 and we were pleased that we had representation from the HPRUs in Modelling and Health Economics and in Healthcare Associated Infections and Antimicrobial Resistance, with a student from the HPRU in Modelling and Health Economics winning a prize for his poster presentation.

**Academic Career Development Programme - Annual Training Day Event – September 2022**

# ANNEXES

## Table of Contents

# ANNEX 1: GOVERNANCE AND MANAGEMENT

## HPRU Environmental Exposures and Health Director and UKHSA Lead

**Professor Frank J Kelly PhD, FRSB, FRSC, FKC, FMedSci – HPRU Director**

Professor Frank Kelly holds the inaugural Humphrey Battcock Chair in Community Health and Policy, within the School of Public Health in a new global centre of air pollution research. He previously served as Chair of Environmental Health at King's College London. He is the Director of the Environmental Research Group, Director of the NIHR Health Protection Research Unit in Environmental Exposures and Health and Deputy Director of the MRC Centre for Environment & Health.

The substantial research activity, over which he presides, spans all aspects of air pollution research from toxicology through to science policy. The experimental research examines the toxicity of airborne particulate matter, diesel and biodiesel exhaust emissions, wood smoke and identifies of biomarkers of exposure. A new area of investigation is ambient microplastics, where work is focusing on their identification, detection and potential health effects. He has led studies on the urban airshed within London, including the impact of the introduction of London's Congestion Charging Zone and the Ultra Low Emission Zone. During his leadership at King's, the London Air Quality Network developed into a first class dissemination and education resource for London residents.

Professor Kelly has published over 400 peer-reviewed papers as well as many conference papers and books (as author or editor) on the toxicology and health effects of ozone, nitrogen dioxide and particulate pollution. He provides policy support to the World Health Organisation on air pollution issues and is a member of the Health Effects Institute (HEI) Review Committee. He is past Chairman of COMEAP, the UK's Department of Health's Expert Committee on the Medical Effects of Air Pollutants, past President of the European Society for Free Radical Research and past Chairman of the British Association for Lung Research.

**Professor Tim Gant – UKHSA Lead**

Professor Tim Gant is the Head of Toxicology Department in the Centre for Radiation, Chemicals and Environmental Hazards, UK Health Security Agency (UKHSA). Professor Gant trained in Toxicology and Pharmacology at the School of Pharmacy, University College London. He undertook his PhD in Pharmacology also at the School of Pharmacy. He is a European Registered Toxicologist, Fellow of the British Society of Toxicology and a Member of the American Society of Toxicology.

He has undertaken postdoctoral periods with the National Cancer Institute, Bethesda USA (1988 to 1993) and Medical Research Council UK (1993 to 2002). He was appointed Tenure (2002) and group leader (2002 to 2011) with the Medical Research Council before moving to work with the Health Protection Agency (2011) to pursue interests in the translation of science to intervention and policy, research in government and the prevention of disease (Public Health). The Health Protection Agency (2011) subsequentially transitioned to Public Health England (PHE) (2013) and transitioned again in October 2021 to the UK Health Security Agency (UKHSA). He is Head of the Department of Toxicology at UKHSA which has a remit spanning risk assessment, public health, chemicals regulation and toxicological research including causation pathways.

He is a Visiting Professor at Imperial College London. He chairs the Postgraduate training sub-committee for UKHSA which oversees leadership for the training of about 90 UKHSA PhD students at any one time and is a co-lead for the Affiliated Research Centre of UKHSA which is incorporated within the Open University of the UK. He is Co-Editor Toxicology Letters for the journal of the European Society of Toxicology.

For the Health and Environment Sciences Institute, Washington DC he has served as ordinary member, vice Chair, Chair (3 years) and past Chair (1 year) of the emerging Issues Committee (EIC) and in the Chair's role been co-opted onto many of the committees of HESI. He is part of the Ototoxicology committee of HESI and still serves on the EIC. He serves on the scientific advisory board of ECETOC and for six years chaired the scientific sub-committee of the British Toxicological Society and is currently closely involved with three areas of ECETOC work in next generation risk assessment, in vitro to in vivo extrapolation, application of new approach methodologies (NAMs) in regulatory hazard assessment, and application of quantitative Adverse Outcome Pathways in regulatory toxicology.

## HPRU Leadership Structure

The Joint Executive Group is the senior management, strategy and decision-making forum of the HPRUs in Environmental Exposures and Health and in Chemical and Radiation Threats and Hazards. It comprises the Unit Directors, UK HSA Leads and the HPRU Managers. The Executive Group is responsible for identifying research priorities for the HPRU work programme and ensuring they relate to UK HSA research and policy needs.

The Executive Group is supported by the partner Leads from Kings' College London and the MRC Toxicology Unit at the University of Cambridge, Knowledge Mobilisation Lead, Public and Community Oversight Group Chair, as well as the Theme Leads, Training Programme Directors, Knowledge Mobilisation Manager and PCIEP Coordinator.

The Executive Group is also supported by advisory groups and representatives from across the Unit's research areas and core areas of activity, ensuring direct representation of these core areas in the highest governance structure of the Units (see Figure 1 below).

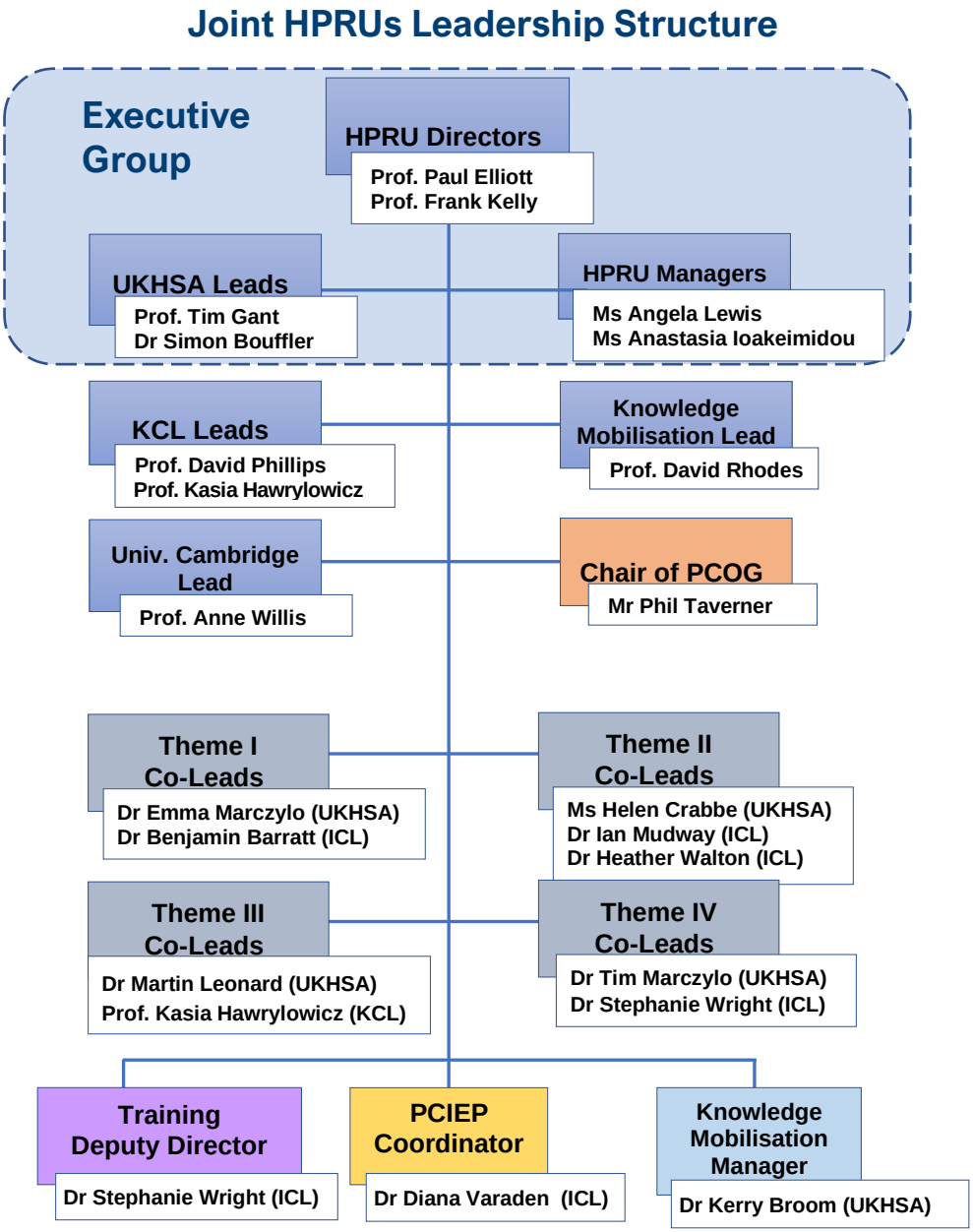



**Fig.1 NIHR HPRU in Environmental Exposures and Health Leadership Structure**

## International Scientific Advisory Board

The joint International Scientific Advisory Board (ISAB) is an independent group of senior international experts in research on environment and health which acts as a scientific advisory committee, providing feedback and recommendations to the HPRU's Director and UKHSA Lead on the strategic direction and priorities of the HPRU's research and training programmes.

The Chair, membership and terms of reference of the ISAB are agreed between the Directors and UKHSA Leads of the HPRU in Environmental Exposures and Health, HPRU in Chemical and Radiation Threats and Hazards and the Directors of the MRC Centre for Environment and Health.

*ISAB Membership*

### *Chair*

**Professor Jonathan Samet MD, MS**
Dean and Prof, Colorado School of Public Health, USA

*Key areas of expertise:* epidemiology of inhaled pollutants; environmental toxicology; novel methods for *environmental* risk assessment; public health protection with a focus on tobacco control, air pollution, and chronic disease prevention; public health policy.
Short bio of Prof Samet

*Members*

### *With specific focus on the remit of NIHR HPRU in Chemical and Radiation Threats and Hazards*

**Dr Mark P Little**
Senior Investigator, Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, USA

*Key areas of expertise:* radiation epidemiology - ionizing radiation and cancer/ cardiovascular risk; *radiation* biology; modelling of radio-biological processes.
Short bio of Dr Little

**Dr Mark R Sambrook**
CBR Division, Defence Science and Technology Laboratory, Salisbury, UK

*Key areas of expertise:* chemistry; detection and decomposition of high-toxicity chemicals/chemical warfare agents.

### *With specific focus on the remit NIHR HPRU in Environmental Exposures and Health*

**Professor Ana Navas-Acien**
Professor of Environmental Health Sciences, Director, Columbia University Superfund Research Program, Columbia Mailman School of Public Health, USA

*Key areas of expertise:* environmental epidemiology; interaction of environmental exposures with genetic and epigenetic variants.
Short bio of Prof Navas-Acien

**Professor Ellen Fritsche**
Professor of Environmental Toxicology, University of Dusseldorf, Germany

*Key areas of expertise:* environmental toxicology, neurotoxicology and developmental neurotoxicity.
Short bio of Prof Fritsche

### *With specific focus on the remit of the MRC Centre for Environment and Health*

**Professor Daniel Greenbaum**
President, Health Effects Institute, Boston, USA

*Key areas of expertise:* health effects of air pollution; environmental toxicology; development of air quality *management* policies and guidelines in the US and internationally.
Short bio of Prof Greenbaum

**Professor Chris Holmes**
Chair in Biostatistics, Department of Statistics, University of Oxford

*Key areas of expertise:* application of computational statistics and statistical machine learning to health research; genomics; metabolomics.
Short bio of Prof Holmes

***With specific focus on the remit of the NIHR / NHS***

**Professor Stephen Holgate**
MRC Clinical Professor of Immunopharmacology at the University of Southampton, UK.

*Key areas of expertise:* immunology and allergy; respiratory disease and health burden of air pollution.
Short bio of Prof Holgate

*ISAB Terms of Reference*

The role of the ISAB is to provide independent advice to the Executive Group of the NIHR HPRU in Chemical and Radiation Threats and Hazards and NIHR HPRU in Environmental Exposures and Health, and of the MRC Centre for Environment and Health on the strategic direction and implementation of the research programmes of these units.

**Scope and responsibilities:**

Assess the scope, content and quality of the research, training and public engagement activities within the context of the Centre and HPRUs' mission and strategic aims;

Advise on development of the scientific strategy underpinning the research and training programme, within the context of national/international developments in research on environment and health;

Advise on the alignment and impact of HPRUs and Centre's outputs in relation to the research and public health priorities of the funding agencies;

Advise on the appropriate deployment of resources and development of research and training capacity;

Review the level and range of scientific, educational and public engagement outputs of the HPRUs and Centre in relation to the stated milestones and deliverables;

Promote relevant contacts with government departments, agencies and other academic groups, nationally and internationally.

# ANNEX 2: ACADEMIC CAREER DEVELOPMENT SUPPLMENTARY INFORMATION

## Joint Academic Career Development Committee

The Joint Academic Career Development (JACD) Committee consists of representatives from each of the partners in the two HPRUs and the MRC Centre, and of the students and early career researchers. Its role is to guide and support the development of a robust multidisciplinary programme for training the next generation of environmental health scientists affiliated with these units.

*Joint Academic Career Development Committee Membership*

- JACD Programme Director - *Dr Frédéric Piel* (ICL)
- JACD Programme Deputy Director - *Dr Stephanie Wright* (ICL)
- HPRU-EEH representative - *Dr Matthew Wright* (UKHSA)
- HPRU-CRTH representative - *Dr Liz Ainsbury* (UKHSA)
- MRC Tox Unit representative – Dr *Kirsti Hornigold* (University of Cambridge)
- Researchers' Society representative - *Ms Melanie Egli* (ICL)
- HPRU-EEH Manager and ERG Associate Director – *Ms Angela Lewis* (ICL)
- HPRU-CRTH & MRC Centre Manager – *Ms Anastasia Ioakeimidou* (ICL)
- MRC Centre Research Coordinator - *Ms Eno Umoh* (ICL)

*Joint Academic Career Development Committee Terms of Reference*

The JACD shall conduct its business according to the following terms of reference:

- To support the development of a robust multidisciplinary training programme for the next generation of environmental health scientists affiliated with the HPRUs and MRC Centre.
- To discuss training strategy, training portfolio and early career research experience.
- To receive updates on the Training Programme and monitor progress.
- To regularly engage with affiliated students, early-career researchers, fellows and supervisors.

The Committee shall normally meet every two months either in person or by videoconference.

Minutes of the Committee meetings shall be taken in turn by one of the Committee members.

Members of the Committee unable to attend a meeting may nominate a replacement providing that the Chair is notified at least a week in advance of the meeting.

The Committee may from time to time propose adjustments to its membership.

A member of the Committee shall immediately cease its functions if, by notice in writing to the Committee Chair s/he resigns their membership.

# ANNEX 3: PUBLIC AND COMMUNITY INVOLVEMENT, ENGAGEMENT AND PARTICIPATION (PCIEP) SUPPLEMENTARY INFORMATION

## Joint Public and Community Involvement, Engagement and Participation Committee

The Joint PCIEP Committee consists of representatives from each of the partners in the HPRUs and the MRC Centre, led by the PCIEP Coordinators in the two HPRUs. It is responsible for coordinating and supporting the activities of the Public and Community Oversight Group (PCOG), and for the implementation of the PCIEP strategy and activities, co-developed with the PCOG.

### *Joint PCIEP Committee Membership*

- PCIEP Coordinator, HPRU-EEH – *Dr Diana Varaden* (ICL)
- PCIEP Coordinator, HPRU-CRTH - *Ms Antoinette Amuzu* (ICL)
- MRC Centre PCIEP Lead – *Dr Ian Mudway* (ICL)
- HPRU-EEH representative - *Dr Philippa Douglas* (UKHSA)
- HPRU-CRTH representative - *Dr Liz Ainsbury* (UKHSA)
- MRC Tox Unit representative - *Dr Liza Selley* (University of Cambridge)
- MRC Centre & HPRU-CRTH representative - *Dr Bethan Davies* (ICL)
- HPRU-EEH Manager and ERG Associate Director – *Ms Angela Lewis* (ICL)
- HPRU-CRTH & MRC Centre Manager – *Ms Anastasia Ioakeimidou* (ICL)

### *Joint PCIEP Strategy*

Please see the Joint PCIEP Strategy Document.

## Public and Community Oversight Group

The new Public and Community Oversight Group (PCOG) has been set up with the aim of advising the HPRUs in Environmental Exposures and Health, in Chemical and Radiation Threats and Hazards and MRC Centre for Environment and Health, ensuring that the public and community voice impacts the research strategies, projects and functions of these units and that our research is accountable, transparent and relevant to the public. The new PCOG benefits from the skills, expertise and experience of over 35 members, including members of the general public, industries, local government, community and patient groups, academics and third sector organisations.

### *PCOG Membership*

*Chair - Mr Phillip Taverner*

Phil Taverner has a long career in health and social care management and public engagement. He chaired the National Institute for Clinical Excellence (NICE) Committee on Provision of Support for Adult Carers (2017-2020) and is currently a member of a NICE Quality Standards committee, a public member of the Cochrane Airways Priority Setting Group, and a lay reviewer for the British Medical Journal. Previously, he was Assistant Director of an NIHR unit in Southampton (2008-2015), responsible for managing the local Public Health Research programme, and Assistant Director of the National Society for the Prevention of Cruelty to Children in South-East England (2000-2008). He holds a BSc in Sociology with Social Work from the University of Bath.

*PCOG Members*

| | |
|---|---|
| – Catherine Sutton | Airborne Allergy Action |
| – Leigh George | Allergy UK |
| – Zak Bond | Asthma UK/ British Lung Foundation |
| – Margaret Jackson | Big Locals |
| – Stuart Upton | BRE Group |
| – Professor Andre Ng | British Cardiovascular Society |
| – Roger Barrowcliff | Clean Air Thinking |
| – Stewart Martin | COMARE |
| – Adam Spencer | Communities.gov.uk |

| | |
|---|---|
| – Rebeca Cosgriff | Cystic Fibrosis Trust |
| – Chris Large | Global Action Plan |
| – Anna Tarkington | Guy's and St Thomas' Charity |
| – Jemima Hartshorn | Mums for lungs |
| – Carol Goodchild | UKHSA Peoples Panel |
| – John Phipps | UKHSA Peoples Panel |
| – Robert Goundry | UKHSA Peoples Panel |
| – Peter Gosling | UKHSA Peoples Panel |
| – Colette Kelly | UKHSA Peoples Panel |
| – Ian Wright* | UKHSA Peoples Panel |
| – Geoff Driver | UKHSA Peoples Panel |
| – Mike Nielsen | UKHSA Peoples Panel |
| – Lee White | UKHSA Peoples Panel |
| – Sahiqa Kauser | UKHSA Peoples Panel |
| – Andrew Wood | UKHSA Peoples Panel |
| – Roger Gibb | UKHSA Peoples Panel |
| – Eve Smyth | UKHSA Peoples Panel |
| – Salim Vohra | Public Health by Design |
| – Pete Bryant | Society for Radiological Protection |
| – Philip Plant | Society of Radiographers |
| – Andy Cope | Sustrans.org.uk |
| – Grainne McGill | University of Strathclyde |
| – Adam Thomas | University of the West of England (Bristol) |
| – Ruth Morse | University of the West of England (Bristol) |
| – Isabella Myers | Independent consultant |

*PCOG Terms of Reference*

Please see the PCOG Terms of Reference.

## ANNEX 4: KNOWLEDGE MOBILISATION SUPPLEMENTARY INFORMATION

Knowledge mobilisation brings together different communities to share knowledge to catalyse change. It is a two-way process which enables advances in health protection research to create benefits for patients and the public by supporting research informed decision-making by policy makers, public health practitioners, the public, and other stakeholders.

Our Knowledge Mobilisation Strategy outlines our approach to promoting the use of the knowledge generated by the HPRU:

- internally, by developing expertise and establishing a culture within the partner organisations that actively seeks to apply the research evidence on chemical and radiation hazards for decision making on public health protection;
- externally, by increasing the understanding of the value of research among those who can use research findings to address the rapidly emerging policy agenda on chemical and radiation risk management.

HPRU-EEH Knowledge Mobilisation Strategy

## ANNEX 5. HPRU PUBLICATIONS

Below is a list of HPRU EEH related publications by HPRU-EEH members from 01 April 2021 to 31 March 2022.


1. Alli, A. S., Clark, S. N., Hughes, A., Nimo, J., Bedford-Moses, J., Baah, S., .Arku, R. E. (2021). Spatial-temporal patterns of ambient fine particulate matter (PM2.5) and black carbon (BC) pollution in accra. Environmental Research Letters, 16(7) https://doi.org/10.1088/1748-9326/ac074a

2. Bakolis, I., Hammoud, R., Stewart, R., Beevers, S., Dajnak, D., MacCrimmon, S., Mudway, I. S. (2021). Mental health consequences of urban air pollution: Prospective population-based longitudinal survey. Social Psychiatry and Psychiatric Epidemiology, 56(9), 1587-1599. https://doi.org/10.1007/s00127-020-01966-x

3. Ball N, Bars R, Botham PA, Cuciureanu A, Cronin MTD, Doe JE, Dudzina T, Gant TW, Leist M, van Ravenzwaay B.A framework for chemical safety assessment incorporating new approach methodologies within REACH. Arch Toxicol 96, 743–766 (2022) https://doi.org/10.1007/s00204-021-03215-9

4. Ball, N., Bars, R., Botham, P. A., Cuciureanu, A., Cronin, M. T. D., Doe, J. E., .van Ravenzwaay, B. (2022). A framework for chemical safety assessment incorporating new approach methodologies within REACH. Archives of Toxicology, 96(3), 743-766. https://doi.org/10.1007/s00204-021-03215-9

5. Bos, B., Lim, S., Hedges, M., Molden, N., Boyle, S., Mudway, D. I., & Barratt, D. B. (2021). Taxi drivers' exposure to black carbon and nitrogen dioxide in electric and diesel vehicles: A case study in london. Environmental Research, 195 https://doi.org/10.1016/j.envres.2021.110736

6. Chen, Y-H, Cheadle, C. E., Rice, V. L., Pfeffer, P.E, Dimeloe, S., Gupta, A, Bush, A, Gooptu B, Hawrylowicz, C H. The Induction of Alpha-1 Antitrypsin by Vitamin D in Human T Cells Is TGF-β Dependent: A Proposed Anti-inflammatory Role in Airway Disease. Frontier in Nutrition, 2021 Aug 12;8:667203 https://pubmed.ncbi.nlm.nih.gov/34458299/

7. Davies, B., Parkes, B. L., Bennett, J., Fecht, D., Blangiardo, M., Ezzati, M., & Elliott, P. (2021). Community factors and excess mortality in first wave of the COVID-19 pandemic in england. Nature Communications, 12(1) https://doi.org/10.1038/s41467-021-23935-x

8. Elliott, J., Whitaker, M., Bodinier, B., Eales, O., Riley, S., Ward, H., . . . Elliott, P. (2021). Predictive symptoms for COVID-19 in the community: REACT-1 study of over 1 million people. PLoS Medicine, 18(9) https://doi.org/10.1371/journal.pmed.1003777

9. Enlo-Scott, Z., Bäckström, E., Mudway, I., & Forbes, B. (2021). Drug metabolism in the lungs: Opportunities for optimising inhaled medicines. Expert Opinion on Drug Metabolism and Toxicology, 17(5), 611-625. doi:10.1080/17425255.2021.1908262

10. Evangelopoulos, D., Chatzidiakou, L., Walton, H., Katsouyanni, K., Kelly, F. J., Quint, J. K., . . . Barratt, B. (2021). Personal exposure to air pollution and respiratory health of COPD patients in london. European Respiratory Journal, 58(1) https://doi.org/10.1183/13993003.03432-2020

11. Evangelopoulos, D., Katsouyanni, K., Schwartz, J., & Walton, H. (2021). Quantifying the short-term effects of air pollution on health in the presence of exposure measurement error: A simulation study of multi-pollutant model results. Environmental Health: A Global Access Science Source, 20(1) https://doi.org/10.1186/s12940-021-00757-4

12. Evangelopoulos, D., Dajnak, D., Wood, D., Fecht, D., & Walton, H. (2022). Health impact assessment of current and past air pollution on asthma in London.

https://www.imperial.ac.uk/media/imperial-college/medicine/sph/environmental-research-group/Health-Impact-Assessment-of-current-and-past-Air-Pollution-on-asthma-in-London.pdf

13. Fecht, D., Chadeau-Hyam, M, Owen, R., Gregson, J., Halliday, B. P., Lota, A. S.,.etc. (2022). Exposure to elevated nitrogen dioxide concentrations and cardiac remodeling in patients with dilated cardiomyopathy. Journal of Cardiac Failure, 28(6), 924-934. https://doi.org/10.1016/j.cardfail.2021.11.023

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15. Fransen, L. F. H., & Leonard, M. O. (2021). CD34+ derived macrophage and dendritic cells display differential responses to paraquat. Toxicology in Vitro, 75 https://doi.org/10.1016/j.tiv.2021.105198

16. Fransen, L. F. H., & Leonard, M. O. (2021). Small airway susceptibility to chemical and particle injury. Respiration, https://doi.org/10.1159/000519344

17. Fussell, J. C., & Kelly, F. J. (2021). Mechanisms underlying the health effects of desert sand dust. Environment International, 157 https://doi.org/10.1016/j.envint.2021.106790

18. Gouin T, Ellis-Hutchings R, Thornton Hampton LM, Lemieux CL, Wright SL. Screening and prioritization of nano- and microplastic particle toxicity studies for evaluating human health risks – development and application of a toxicity study assessment tool. Microplastics and Nanoplastics. 2022. 2(2). https://doi.org/10.1186%2Fs43591-021-00023-x

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23. James, T.; Collins, S.; Marczylo, T. Identification of Novel Simulants for Toxic Industrial Chemicals and Chemical Warfare Agents for Human Decontamination Studies: A Systematic Review and Categorisation of Physicochemical Characteristics. Int. J. Environ. Res. https://doi.org/10.3390/ijerph18168681

24. James T., Izon-Cooper L, Samuel Collins, Haydn Cole & Tim Marczylo. The wash-in effect and its significance for mass casualty decontamination, Journal of Toxicology and Environmental Health, (2022) Part B, 25:3, 113-134.

25. Karamanos, A., Mudway, I., Kelly, F., Beevers, S. D., Dajnak, D., Elia, C., . . . Harding, S. (2021). Air pollution and trajectories of adolescent conduct problems: The roles of ethnicity and racism; evidence from the DASH longitudinal study. Social Psychiatry and Psychiatric Epidemiology, 56(11), 2029-2039. https://doi.org/10.1007/s00127-021-02097-7

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38. Rashid, T., Bennett, J. E., Paciorek, C. J., Doyle, Y., Pearson-Stuttard, J., Flaxman, S., . . . Ezzati, M. (2021). Life expectancy and risk of death in 6791 communities in england from 2002 to 2019: High-resolution spatiotemporal analysis of civil registration data. The Lancet Public Health, 6(11), e805-e816. https://doi.org/10.1016/S2468-2667(21)00205-X

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45. Takemura, K., Satoru, Y., Downey, L., Evangelopoulos, D., et al. (2022). Impact of Body Mass Index on Survival Outcomes in Patients with Metastatic Renal Cell Carcinoma in the Immuno-oncology Era: A Systematic Review and Meta-analysis. European Urology Open Science Volume 39, May 2022, Pages 62-71. https://doi.org/10.1016/j.euros.2022.03.002

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50. Varaden, D., Leidland, E., Lim, S., & Barratt, B. (2021). “I am an air quality scientist”– using citizen science to characterise school children's exposure to air pollution. Environmental Research, 201 https://doi.org/10.1016/j.envres.2021.111536

51. Verheijen, M. C., Meier, M. J., Asensio, J. O., Gant, T. W., Tong, W., Yauk, C. L., & Caiment, F. (2022). R-ODAF: Omics data analysis framework for regulatory application. Regulatory Toxicology and Pharmacology, 131 https://doi.org/10.1016/j.yrtph.2022.105143

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53. Wang, J., Alli, A. S., Clark, S., Hughes, A., Ezzati, M., Beddows, A., . . . Arku, R. E. (2022). Nitrogen oxides (NO and NO2) pollution in the accra metropolis: Spatiotemporal patterns and the role of meteorology. Science of the Total Environment, 803 https://doi.org/10.1016/j.scitotenv.2021.149931

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## ANNEX 6: EXTERNAL FUNDING SECURED

**Below is a list of externally funded projects held by EEH HPRU PIs that are contributing to the workplan of the HPRU (01 April 2021 – 31 March 2022)**

| Project Title | Funder | Project Start Date | Project End Date | HPRU PI | HPRU Theme | Total Budget Awarded | Pro-rata in second year |
|---|---|---|---|---|---|---|---|
| GSTT Fellowship | GSTT | 0110/2021 | 30/09/2022 | Varaden | TI:P1 | £89,150 | £44,575 |
| Toxicological assessment of electronic cigarette flavours and flavour-derived e-liquid constituents | Other non commercial | 01/01/2020 | 31/12/2023 | T. Marczylo | TI:P2 | £105,000 | £35,000 |
| Integrated Observation System for Clean Ai | NERC | 01/03/2021 | 30/09/2025 | Green | TI:/P3 | £78,870 | £22,534 |
| RI-URBANS | EU-H2020 | 01/10/2021 | 30/09/2025 | Green | TI/P3 | £92,000 | £23,000 |
| BioAir net | Other non commercial | 01/12/2020 | 01/12/2023 | Douglas/Marczylo | TI:P5 | £507,471 | £169,156 |
| Communicating air pollution as a health risk - Towards a participatory approach | ESRC | 01/10/2020 | 30/09/2021 | Varaden | TI:P6 | £117,000 | £58,500 |
| Breathe London II | GLA | 14/12/2020 | 13/12/2023 | Barratt | TI:P6 | £786,000 | £262,000 |
| Public Health Impact of UK's Clean Air Zones | MRC | 01/10/2020 | 30/09/2025 | Elliott | TII:P1 | £1,599,873 | £159,987 |
| Public Health Impact of UK's Clean Air Zones | MRC | 01/01/2021 | 31/12/2025 | Beevers | TII:P1 | £613,000 | £122,000 |

| Project Title | Funder | Project Start Date | Project End Date | HPRU PI | HPRU Theme | Total Budget Awarded | Pro-rata in second year |
|---|---|---|---|---|---|---|---|
| Relating Environment-use Scenarios in Pregnancy/Infanthood and Resulting airborne material Exposures to child health outcomes (RESPIRE) | UKRI/NERC | 01/11/2021 | 31/03/2025 | Gant | TII:P1 | £3.7M | £29,292 |
| MOBILE Air - Mother and Baby Interventions to Lower Exposure to Air Pollution (pilot phase) | GSTT | 01/10/2021 | 30/09/2023 | Barratt | TII:P1 | £292,205 | £146,102 |
| Urban Health Observatory | GSTT | 13/09/2021 | 12/03/2022 | Kelly | TII:P1 | £94,000 | £94,000 |
| Children's Health in London and Luton (CHILL): Impact of London's Ultra Low Emission Zone on Brain Development in School Children | Barts Charity | 01/04/2020 | 31/12/2023 | Mudway | TII:P2 | £188,394 | £60,548 |
| Air Pollution and COVID19/other infections | GLA/TfL | 08/03/2021 | 07/06/2021 | Walton | TII:P2 | £29,989 | £19,989 |
| (ESA) Satellite Air Quality Modelling | 4Ei | 01/07/2020 | 31/12/2021 | Beevers | TII:P2 | £354,710 | £354,710 |
| A statistical framework for the apportionment of particulate contaminants and their health effect determination | MRC | 01/09/2021 | 31/08/2024 | Green | TII:P2 | £71,404 | £23,801 |
| Hazard Identification Platform to Define the Health Impacts associated with Indoor and Outdoor Air Pollutant Exposures, through the | UKRI/NERC | 01/08/2021 | 31/07/2025 | Mudway | TII:P2 | £510,000 | £85,000 |

| Project Title | Funder | Project Start Date | Project End Date | HPRU PI | HPRU Theme | Total Budget Awarded | Pro-rata in second year |
|---|---|---|---|---|---|---|---|
| Application of Mechanistic Toxicity (HIPTOX) | | | | | | | |
| West London Healthy Home and Environment Study (WellHome) | NERC | 01/08/2021 | 31/07/2025 | Kelly | TII:P3 | £2.8M | £466,666 |
| Participatory Research | Research England | 01/01/2022 | 31/07/2022 | Barratt | TII:P3 | £60,000 | £51,428 |
| Exposure to particulate matter on the the London Underground in healthy subjects and patients with chronic respiratory disease | MRC | 01/10/2020 | 30/09/2023 | Kelly | TII:P4 | £1.04M | £328,448 |
| MRC Centre for Environment and Health | MRC | 01/04/2020 | 31/05/2025 | Kelly | TII:P4 | £623,000 | £124,600 |
| Dust sampling research study to understand the health impacts on London Underground workers | TfL | 15/02/2021 | 14/08/2024 | Green | TII:P4 | £200,000 | £57,142 |
| Liverpool School Children Exposure Study | Defra | 01/09/2021 | 31/12/2022 | Barratt | TII:P4 | £68,000 | £51,000 |
| Investigating the consequences of measurement error of gradually more sophisticated long-term personal exposure models in assessing health effects: The London Study | HEI | 01/07/2020 | 30/06/2023 | Katsouyanni | TII:P5 | £582,000 | £194,000 |

| Project Title | Funder | Project Start Date | Project End Date | HPRU PI | HPRU Theme | Total Budget Awarded | Pro-rata in second year |
|---|---|---|---|---|---|---|---|
| Fellowship Multi-Dimensional assessment of the Impact of Measurement Error on the health effect estimates of long-term exposure to air pollution (M-DIME) | MRC | 10/12/2021 | 09/12/2023 | Evangelopoulos | TII:P5 | £216,625 | £45,130 |
| Pathways to Clean Air | Clean Air Fund | 01/06/2021 | 02/03/2022 | Beevers | TII:P5 | £300,000 | £300,000 |
| Asthma admissions in London | GLA | 22/03/2021 | 22/09/2021 | Walton | TII:P5 | £29,241 | £25,064 |
| Using Metabolomics to investigate metabolic signatures and associated pathways links to short-term exposure to air pollution | MRC | 01/07/2020 | 31/03/2023 | Kelly | TIII:P1 | £615,557 | £223,838 |
| AeroTox : Measurements for mitigating adverse health effects from atmospheric particulate pollution | EU-H2020 Euramet | 01/07/2020 | 30/11/2022 | Mudway | TIII:P1 | £149,442 | £60,000 |
| Disentangling the toxicological potential of NO2 and PM in complex mixtures | UKHSA | 01/04/2020 | 31/12/2023 | Smith | TIII:P5 | £133,000 | £38,000 |
| Nanoharmony - PhD Studentship | EU | 01/10/2020 | 30/09/2023 | Smith | TIII:P6 | £100,000 | £35,000 |
| Understanding UK airborne microplastic polluton: sources, pathways and fate | NERC | 01/10/2020 | 30/09/2023 | Wright | TIV:P2 | £591,000 | £197,000 |
| Contribution of microplastics to oral chemical exposure | UK HSA | 01/01/2020 | 31/12/2023 | Gant/Wright | TIV:P2 | £105,000 | £35,000 |

| Project Title | Funder | Project Start Date | Project End Date | HPRU PI | HPRU Theme | Total Budget Awarded | Pro-rata in second year |
|---|---|---|---|---|---|---|---|
| Microplastic exposure and human health | Common Seas | 01/03/2021 | 28/02/2023 | Wright | TIV:P2 | £241,376 | £120,688 |
| UK Microplastics Material Repository | MRC | 01/06/2021 | 30/09/2021 | Wright | TIV:P2 | £100,000 | £100,000 |
| The RAMS (Respiratory Assessment of Manual Sorters) study. An occupational assessment of airborne dust to manual sorters in plastic material recycling facilities. | AXA | 01/09/2021 | 31/08/2023 | Levermore | TIV:P2 | £101,000 | £44,888 |
| Wastewater Analysis for Narcotics Detection | Dstl | 19/02/2021 | 31/03/2023 | Barron | TIV:P4 | £1,800,000 | £550,000 |
| The air quality health and economic costs and benefits of a zero carbon UK | NIHR | 01/07/2020 | 30/06/2023 | Beevers | TIV:P4 | £908,994 | £302,997 |
| Maximising the impact, reach and scalability of the Breathe London Community Air Quality Network | Bloomberg | 01/08/2021 | 31/07/2025 | Barratt | TIV:P4 | £664,886 | £107,481 |
| UK-China Collaboration to Optimise net zero Policy options for Air Quality and health (COP-AQ) | NERC | 15/11/2021 | 31/03/2022 | Kelly | TIV:P4 | £41,000 | £41,000 |
| | | | | | **TOTAL** | **£20,558,191** | **£5,210,164** |